2018 ESC / EACTS Guidelines on myocardial revascularisation

The Task Force on Myocardial Revascularisation of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

In collaboration with the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

Word count:
Body of text (without tables and Figures) – 25.325

References for print version

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Abbreviations and acronyms

ABC	age, biomarkers, clinical history
ABSORB II	A Bioresorbable Everolimus-Eluting Scaffold Versus a Metallic Everolimus-Eluting Stent II
AIDA	Amsterdam Investigator-Initiated Absorb Strategy All-Comers
ACCOAST	Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention or as Pretreatment at the Time of Diagnosis in Patients with Non-ST Elevation Myocardial Infarction
ACS	acute coronary syndrome
ACUITY	Acute Catheterization and Urgent Intervention Triage strategy
ADAPT-DES	Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents
ADP	adenosine diphosphate
AF	atrial fibrillation
AKI	acute kidney injury
ALPHEUS trial	Assessment of Loading With the $P2Y_{12}$ Inhibitor Ticagrelor or Clopidogrel to Halt Ischemic Events in Patients Undergoing Elective Coronary Stenting
AMI	acute myocardial infarction
ANTARCTIC	Platelet function monitoring to adjust antiplatelet therapy in elderly patients stented for an acute coronary syndrome
ARCTIC	Assessment by a Double Randomization of a Conventional Antiplatelet Strategy versus a Monitoring-guided Strategy for Drug-Eluting Stent Implantation and of Treatment Interruption versus Continuation One Year after Stenting
ART	Arterial Revascularisation Trial
AS	aortic stenosis
ASA	acetylsalicylic acid
ASE	American Society of Echocardigraphy
ATLANTIC	Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST-Elevation Myocardial Infarction to Open the Coronary Artery
ATLAS-ACS 2–TIMI 51	Anti-Xa Therapy to Lower cardiovascular events in Addition to Standard therapy in subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction 51
ATOLL	Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischaemic and bleeding events at short- and Long-term follow-up
AVR	aortic valve replacement
AWESOME	Angina With Extremely Serious Operative Mortality Evaluation
BARC	Bleeding Academic Research Consortium
BARI-2D	Bypass Angioplasty Revascularisation Investigation 2 Diabetes
BES	biolimus-eluting stent
BEST	Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease
b.i.d.	bis in die (twice daily)

BIMA	bilateral internal mammary artery
BMS	bare-metal stent
BRAVE	Bavarian Reperfusion Alternatives Evaluation
BRS	bioresorbable scaffolds
BVS	bioresorbable vascular scaffold
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CARDia	Coronary Artery Revascularisation in Diabetes
CAS	carotid artery stenting
CCS	Canadian Cardiovascular Society
CEA	carotid endarterectomy
CHA_2DS_2-VASc	Cardiac failure, Hypertension, Age ≥75 [Doubled], Diabetes, Stroke [Doubled] – Vascular disease, Age 65–74 and Sex category [Female])
CHAMPION	Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition
CHF	congestive heart failure
CI	confidence interval
CIN	contrast-induced nephropathy
CK-MB	creatine kinase-MB fraction
CKD	chronic kidney disease
CMR	cardiac magnetic resonance
COMPASS trial	Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease
COURAGE	Clinical Outcomes Utilizing Revascularisation and Aggressive Drug Evaluation
CPG	ESC Committee for Practice Guidelines
CT	computed tomography
cTn	cardiac troponin
CTO	chronic total occlusion
CTSN	Cardiothoracic Surgical Trial Network
CULPRIT-SHOCK	Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock
CURE	Clopidogrel in Unstable Angina to Prevent Recurrent Events
CURRENT-OASIS 7	Clopidogrel and Aspirin Optimal Dose Usage to Reduce Recurrent Events−Seventh Organization to Assess Strategies in Ischemic Syndromes 7
CVA	cerebrovascular accident
CvLPRIT	The Complete Versus Lesion-Only Primary PCI Trial
CYP2C19	cytochrome P2C19
DANAMI3-DEFER	The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment Elevation Myocardial Infarction: DEFERred stent implantation in connection with primary PCI
DANAMI3-PRIMULTI	The Third DANish Study of Optimal Acute Treatment of Patients with ST-segment

	Elevation Myocardial Infarction: PRImary PCI in MULTIvessel Disease
DAPT	dual antiplatelet therapy
DCB	drug-coated balloon
DEFINE-FLAIR	Define Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation DES drug-eluting stent
DES	drug-eluting stents
DK	double kiss
DUS	duplex ultrasound
EACTS	European Association for Cardio-Thoracic Surgery
EAPCI	European Association for Percutaneous Cardiovascular Interventions
EBC TWO	European Bifurcation Coronary TWO
ECG	electrocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EES	everolimus-eluting stent
EF	ejection fraction
EMS	emergency medical service
EROA	effective orifice area
ESC	European Society of Cardiology
ESRD	end-stage renal disease
EuroSCORE	European System for Cardiac Operative Risk Evaluation
EUROMAX	European Ambulance Acute Coronary Syndrome Angiography
EXCEL	Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularisation
FAME-2	Fractional Flow Reserve versus Angiography for Multivessel Evaluation 2
FDG-PET	fluorodeoxyglucose positron emission tomography
FFR	fractional flow reserve
FITT-STEMI	Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction
FMC	First medical contact
FREEDOM	Future Revascularisation Evaluation in Patients with Diabetes Mellitus
GFR	glomerular filtration rate
GLOBAL LEADERS	Long-term ticagrelor monotherapy versus standard dual antiplatelet therapy followed by aspirin monotherapy in patients undergoing biolimus-eluting stent implantation
GP IIb/IIIa	glycoprotein IIb/IIIa
GRACE	Global Registry of Acute Coronary Events
GRAVITAS	Gauging Responsiveness with A VerifyNow assay-Impact on Thrombosis And Safety
HAS-BLED	Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol
HEAT-PPCI	How Effective are Antithrombotic Therapies in primary PCI
HF	heart failure
HFrEF	heart hailure with reduced ejection fraction

HORIZONS	Harmonizing Outcomes with Revascularisation and Stents in Acute Myocardial Infarction
HPR	high platelet reactivity
HR	hazard ratio
i.v.	intravenous
IABP	intra-aortic balloon pump
ICD	implantable cardioverter defibrillator
iFR	instantaneous wave-free ratio
IMA	internal mammary artery
INR	international normalized ratio
IRA	infarct-related artery
IRIS-MAIN	Interventional Research Incorporation Society-Left MAIN Revascularisation
IRR	incident rate ratio
ISAR-CABG	Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts
ISAR-REACT	Intracoronary Stenting and Antithrombotic Regimen Rapid Early Action for Coronary Treatment
ISCHEMIA	International Study of Comparative Health Effectiveness With Medical and Invasive Approaches
IVUS	intravascular ultrasound imaging
LAA	left atrial appendage
LAD	left anterior descending
LBBB	left bundle branch block
LEAD	lower extremity artery disease
LGE-CMR	late-gadolinium-enhancement cardiac magnetic resonance imaging
LIMA	left internal mammary artery
LM/LMS	left main/left main stem
LMWH	low-molecular-weight heparin
LPR	low platelet reactivity
LV	left ventricle/left ventricular
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
MACCE	major adverse cardiac and cerebrovascular events
MACE	major adverse cardiac events
MADIT II	Multicenter Automatic Defibrillator Implantation Trial II
MATRIX	Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX
MCS	mechanical circulatory support
MI	myocardial infarction
MINOCA	myocardial infarction with non-obstructive coronary arteries

MLA	minimal luminal area
MR	mitral regurgitation
MSCT	multi-slice computed tomography
MT	medical therapy
MVD	multivessel coronary artery disease
MVO	microvascular obstruction
NAC	N-acetylcysteine
NCDR	National Cardiovascular Database Registry
NNT	number needed to treat
NOAC	non-vitamin K antagonist oral anticoagulant
NOBLE	Nordic-Baltic-British Left Main Revascularisation Study
NSTE-ACS	non-ST-segment elevation acute coronary syndrome
NSTEMI	non-ST-segment elevation myocardial infarction
NVAF	non-valvular atrial fibrillation
NYHA	New York Heart Association
OAC	oral anticoagulation
OASIS-5	Optimal Antiplatelet Strategy for Interventions-5
OCT	optical coherence tomography
ONCAB	on-pump CABG
OPCAB	off-pump CABG
OR	odds ratio
ORBITA	Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina
PARR-2	PET and Recovery following Revascularisation
p.o.	per os (orally)
PCI	percutaneous coronary intervention
PES	paclitaxel-eluting stent
PET	positron emission tomography
PF	platelet function
PIONEER	Prevention of bleeding in patients with AF undergoing PCI
PLATO	Study of Platelet Inhibition and Patient Outcomes
pLVAD	percutaneous left ventricular assist devices
PPI	proton pump inhibitor
PRAGUE-18	Comparison of Prasugrel and Ticagrelor in the Treatment of Acute Myocardial Infarction
PRAMI	Preventive Angioplasty in Acute Myocardial Infarction
PRECISE-DAPT	PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy
PRECOMBAT	Premier of Randomised Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease
PROCAT	Parisian Region Out of Hospital Cardiac Arrest

q.d.	quaque die (once daily)
RBBB	Right bundle branch block
RCT	randomised controlled trial
RE-DUAL trial	Randomised Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patients with Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention
REPLACE 2	The Randomised Evaluation in PCI Linking Angiomax to Reduced Clinical Events 2
RIVAL	Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes
RR	relative risk
RRR	relative risk reduction
SASSICAIA	Comparison of Loading Strategies With Antiplatelet Drugs in Patients Undergoing Elective Coronary Intervention
SAVR	surgical aortic valve replacement
s.c.	subcutaneous
SCAD	stable coronary artery disease
SCD-HEFT	Sudden Cardiac Death in Heart Failure Trial
SES	sirolimus-eluting stent
SHOCK	Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock
SMART-DATE	Smart Angioplasty Research Team-safety of 6-month duration of Dual Antiplatelet Therapy after percutaneous coronary intervention in patients with acute coronary syndromes
SITA	single internal thoracic artery
SPECT	single photon emission computed tomography
SR	sinus rhythm
STEEPLE	Safety and Efficacy of Intravenous Enoxaparin in Elective Percutaneous Coronary Intervention Randomised Evaluation
STEMI	ST-segment elevation myocardial infarction
STICH	Surgical Treatment for Ischemic Heart Failure
STS	Society of Thoracic Surgeons
SVG	saphenous vein graft
SVR	surgical ventricular reconstruction
SWEDEHEART	Swedish Web-system for Enhancement and Development of Evidence-ased care in Heart disease Evaluated According to Recommended Therapies
SYNTAX	Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery
TAP	T and protrusion
TAVI	transcatheter aortic valve implantation
TIA	transient ischaemic attack
TIMACS	Timing of Intervention in Acute Coronary Syndromes Trial

TIMI	Thrombolysis in Myocardial Infarction
TOTAL	Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI
TRIGGER-PCI	Testing platelet Reactivity In patients underGoing elective stent placement on clopidogrel to Guide alternative thErapy with pRasugrel
TRITON TIMI-38	TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction
TROPICAL-ACS	Testing responsiveness to platelet inhibition on chronic antiplatelet treatment for acute coronary syndromes
TVR	target vessel revascularisation
TWILIGHT trial	Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention
UFH	unfractionated heparin
ULN	upper limit of normal
VA	veno-arterial
VACARDS	Veterans Affairs Coronary Artery Revascularisation in Diabetes Study
VALIDATE	Bivalirudin versus Heparin in ST-Segment and Non–ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy
VKA	vitamin K antagonist

1. Preamble

Clinical practice guidelines summarize and evaluate all available evidence at the time of the writing process on a particular issue with the aim of assisting physicians in selecting the best management strategies for an individual patient with a given condition, taking into account the impact on outcome as well as the risk–benefit ratio of particular diagnostic or therapeutic means. Clinical practice guidelines are no substitutes for textbooks, but complement them, and cover the European Society of Cardiology (ESC) Core Curriculum topics. As such they should help physicians to make decisions in their daily practice. However, final decisions should be individualised by responsible physicians and the patient.

A great number of clinical practice guidelines have been issued in recent years both by the ESC as well as by other societies and organizations. Because of the impact on clinical practice, quality criteria for the development of guidelines have been established in order to make all decisions transparent to the user. The recommendations for formulating and issuing ESC and joint society guidelines can be found on the ESC website (**http://www.escardio.org/guidelines-surveys/esc-guidelines/about/Pages/rules-writing.aspx**). These Guidelines represent the official position of the ESC and the European Association for Cardio-Thoracic Surgery (EACTS) on this given topic and will be

regularly updated.

Members of this Task Force were selected by the ESC and EACTS to represent professionals involved with the medical care of patients with this pathology. Selected experts in the field undertook a comprehensive review of the published evidence for diagnosis, management (including treatment) and/or prevention of a given condition according to the ESC Committee for Practice Guidelines (CPG) and EACTS policy. A critical evaluation of diagnostic and therapeutic procedures was performed including assessment of the risk–benefit ratio. Estimates of expected health outcomes for larger populations were included, where data exist. The level of evidence and the strength of recommendation of particular treatment options were weighed and graded according to predefined scales, as outlined in **Tables 1 and 2**.

The experts of the writing and reviewing panels completed declarations of interest forms on what might be perceived as real or potential sources of conflicts of interest. These forms were compiled into one file and can be found on the ESC and EACTS websites (http://www.escardio.org/guidelines and http://www.eacts.org). Any changes in declarations of interest that arise during the writing period must be notified to the ESC and EACTS and updated. The Task Force received its entire financial support from the ESC and EACTS without any involvement from the healthcare industry.

The CPG-ESC and EACTS supervised and coordinated the preparation of these new Guidelines produced by the joint Task Force. These entities are also responsible for the endorsement process of these Guidelines. The ESC/EACTS Guidelines underwent extensive review by a wide panel of relevant external experts. After appropriate revisions it was approved by all the experts involved in the Task Force. The finalized document was approved by the ESC CPG and EACTS for joint publication in the *European Heart Journal* and the *European Journal of Cardio-Thoracic Surgery*.

The task of developing clinical practice guidelines covers not only the integration of the most recent research, but also the creation of educational tools and implementation programmes for the recommendations. To implement the guidelines, condensed pocket guidelines, summary slides, booklets with essential messages, and an electronic version for digital applications (smartphones, etc.) are produced. These versions are abridged and,

thus, if needed, one should always refer to the full text version, which is freely available on the ESC and EACTS websites. The National Societies of the ESC are encouraged to endorse, translate, and implement the ESC Guidelines. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.

Surveys and registries are needed to verify that real-life daily practice is in keeping with what is recommended in the guidelines, thus completing the loop between clinical research, writing of guidelines, and implementing them in clinical practice.

The guidelines do not, however, override the individual responsibility of health care professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

Table 1 Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

Table 2 Levels of evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

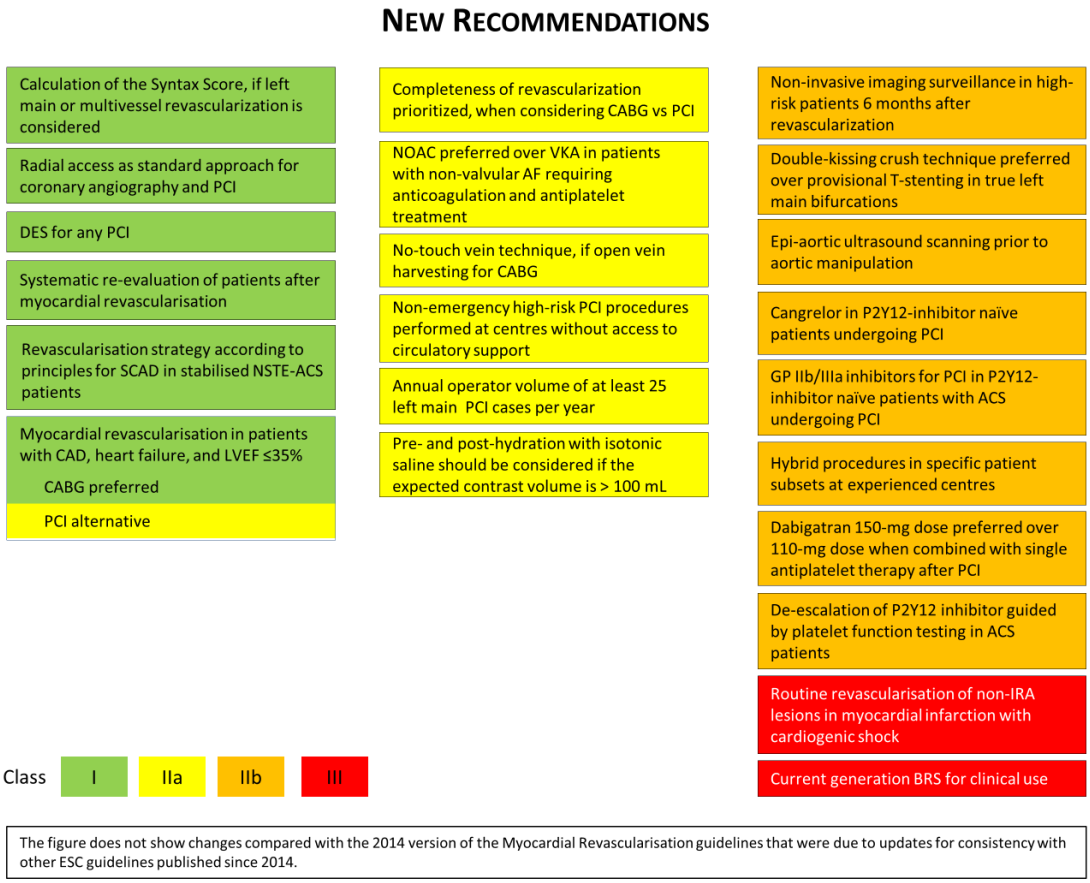
2. Introduction

With this guideline, it is now the third time that ESC and EACTS have brought together cardiologists and cardiac surgeons in a joint task force to review the ever-increasing body of evidence with the mission to draft balanced, patient-centred, practice guidelines on myocardial revascularisation. A summary of the key changes in comparison with the previous guideline is provided in **Figure 1** and **Figure 2.**

There is considerable overlap of the current document with other guidelines, specifically with those on “Stable Coronary Artery Disease”, “Non-ST-Elevation Myocardial Infarction”, “ST-Elevation Myocardial Infarction”, “Heart Failure” and the “Focused Update on Dual Antiplatelet Therapy”. Unless supported by new evidence, we followed the recommendations of these guidelines where pertinent to our guideline and refer to the respective chapters in the previous documents for detailed discussion. We reserve more in-depth discussion for the topics that are specific to issues pertaining to myocardial revascularisation that are not covered in other guidelines. To keep the current document concise and reader-friendly, we also moved some of the detailed descriptions of study results to the web addenda. Moreover, details of references that were published prior to 2015 are listed in the web appendix.

What is new in the 2018 version?

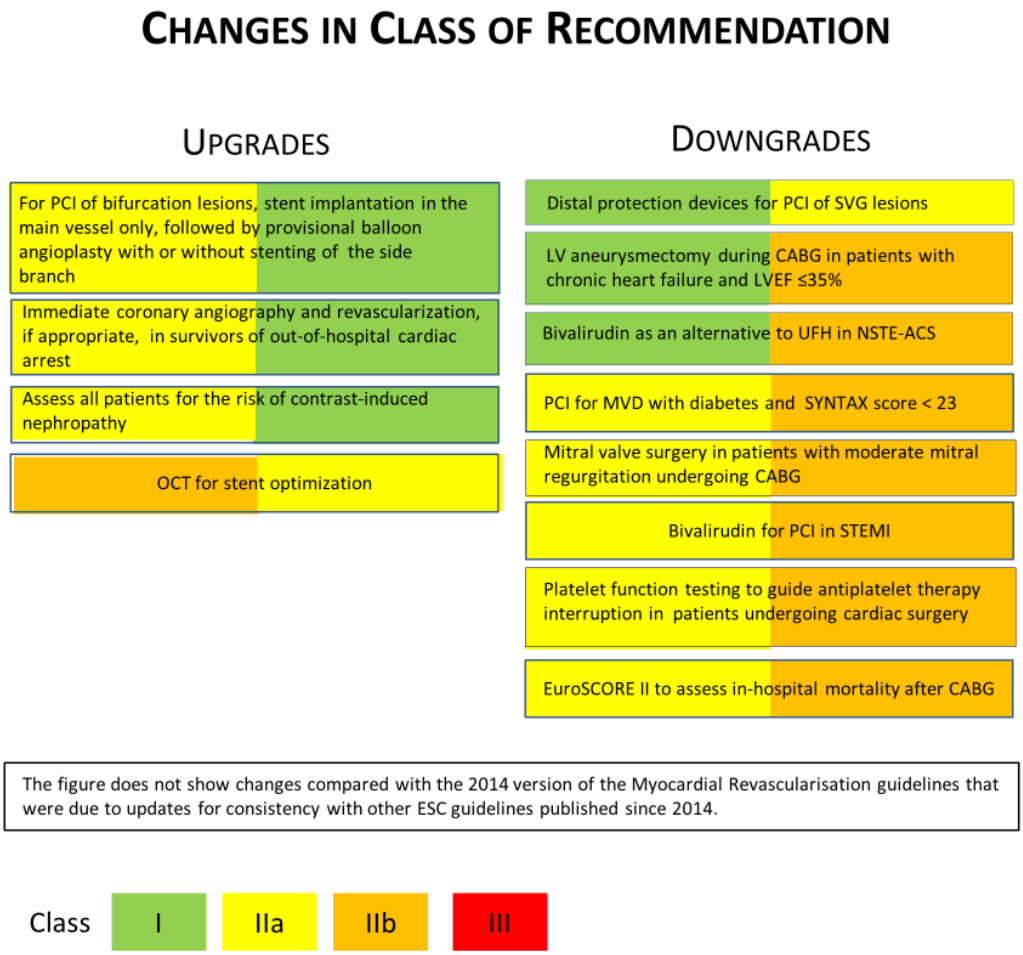
Figure 1



The figure does not show changes compared with the 2014 version of the Myocardial Revascularisation guidelines that were due to updates for consistency with other ESC guidelines published since 2014.

ACS = acute coronary syndromes; AF = atrial fibrillation; BRS = bioresorbable scaffolds; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CT = computed tomography; DAPT = dual antiplatelet therapy; DES = drug-eluting stents; GP = glycoprotein; IRA = infarct-related artery; LVEF = left ventricular ejection fraction; NOAC = non-vitamin K oral anticoagulants; NSTE = non-ST-elevation; PCI = percutaneous coronary interventions; SCAD = stable coronary artery disease; STEMI = ST-elevation myocardial infarction; VKA = vitamin K antagonists.

Figure 2



ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; LVEF = left ventricular ventricular ejection fraction; MVD = multivessel disease; NSTE = non-ST-elevation; OCT = optical coherence tomography; PCI = percutaneous coronary interventions; STEMI = ST-elevation myocardial infarction, SVG = saphenous vein grafts; UFH = unfractionated heparin

3. Diagnostic tools to guide myocardial revascularisation

The use of diagnostic imaging and functional testing modalities to detect patients with coronary artery disease (CAD) is discussed in detail in clinical practice guidelines for patients with stable coronary artery disease.[1] Further diagnostic assessment of patients with obstructive CAD is critical in order to identify patients and select specific lesions likely to benefit from myocardial revascularisation in additional to optimal medical therapy.

3.1 Non-invasive diagnostic tools

3.1.1 Assessment of myocardial ischaemia

Non-invasive diagnostic assessment of patients with CAD being considered for myocardial revascularisation comprises assessment of ischaemia and evaluation of viability in patients with regional wall motion abnormalities or reduced ejection fraction.

Functional testing to assess ischaemia is critical to the assessment of stable patients with CAD. Documentation of ischaemia using functional testing before elective invasive procedures for CAD is the preferred approach. It may also have a role in the assessment of some patients presenting with acute coronary syndrome. Because of the low sensitivity of exercise electrocardiogram (ECG) testing in the assessment of patients with symptoms of angina, non-invasive imaging is recommended as the first line test..[1] Detection of a large area of myocardial ischaemia by functional imaging is associated with impaired prognosis of patients and identifies patients who should undergo revascularisation (see **chapter 5** of this document).

In patients undergoing coronary computed tomography (CT), both CT-derived fractional flow reserve (CT-FFR) and CT perfusion represent possible approaches to evaluate lesion-specific ischemia. Although the evidence for both is limited at present, there is considerably more data from clinical investigations of CT-FFR. A number of trials have shown that correlation between CT-derived FFR and invasive FFR is high. [2, 3] The non-randomised PLATFORM study showed that in patients referred for invasive angiography due to chest pain (predominantly atypical angina) and intermediate pre-test probability of CAD, assessment with CT and CT-derived FFR reduced the number of patients with subsequently normal invasive coronary angiograms compared with standard care.[4] Currently, clinical trial data with CT-derived FFR is insufficient to make a recommendation for use in clinical practice.

3.1.2 Assessment of myocardial viability in patients with heart failure and CAD

In patients with regional wall motion abnormalities or ventricular dysfunction, heart failure can be caused by stunned or hibernating myocardium and may be reversed by revascularisation. Assessment of myocardial viability may be done in order to select patients more likely to benefit from myocardial revascularisation and can be achieved with several imaging modalities: myocardial contrast echocardiography, SPECT, and late gadolinium enhancement CMR (LGE-CMR) all assess cellular integrity; positron emission tomography (PET) assesses cellular metabolism; and dobutamine techniques assess contractile reserve.[1, 5] Assessment of ischaemia provides incremental benefit over viability in mild to moderate CAD, but with extensive CAD, viability assessment is sufficient.[6] Patients with advanced heart failure (HF) and viable myocardium should first undergo revascularisation with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) before being considered for mechanical circulatory support (MCS) or heart transplantation.[7, 8]

The PARR-2 trial (PET and Recovery following Revascularisation) included patients with severe left ventricular dysfunction being considered for revascularisation or heart failure/transplantation work-ups and randomised to management assisted by fluorodeoxyglucose positron emission tomography (FDG PET) or standard care.[6] The primary outcome of cardiac death, myocardial infarction (MI), or recurrent hospital stay for cardiac cause at 1 year was not improved in the group managed by FDG-PET (relative risk 0.82, 95% confidence interval [CI] 0.59 to 1.14; p = 0.16), though the rate of compliance with the treatment recommended by FDG-PET was variable.

The viability substudy of the STICH trial (Surgical Treatment for Ischemic Heart Failure) found viable myocardium in 487/601 patients (81%) and none in 114 (19%).[9] There was a significant association between myocardial viability and outcome by univariate analysis but not on multivariable analysis. The lack of correlation between myocardial viability and benefit from revascularisation indicates that this strategy should not be the only test in selecting the optimal therapy.

Recommendations for noninvasive imaging in patients with CAD and HF

Recommendations	Class[a]	Level[b]

Non-invasive stress imaging (CMR, stress echocardiography, SPECT, PET) may be considered for the assessment of myocardial ischaemia and viability in patients with HF and CAD (considered suitable for coronary revascularisation) before the decision on revascularisation[9-11]	IIb	B

CAD = coronary artery disease; CMR _ cardiac magnetic resonance; HF = heart failure; PET = positron emission tomography; SPECT = single photon emission computed tomography

[a]Class of recommendation.

[b]Level of evidence.

3.2 Invasive diagnostic tools

3.2.1 Pressure-derived fractional flow reserve

3.2.1.1 Use of FFR in patients with intermediate grade coronary stenosis including left main stenosis

Coronary pressure-derived FFR is the current standard of care for the functional assessment of lesion severity in patients with intermediate grade stenosis (typically around 40-80% stenosis) without evidence of ischaemia in non-invasive testing, or in those with multivessel disease.

Multiple studies have shown that PCI can be safely deferred if FFR > 0.75.[12-15] The DEFER trial enrolled 325 patients scheduled for PCI of an intermediate stenosis. [15] If FFR was >or =0.75, patients were randomly assigned to deferral (Defer group; n = 91) or performance (Perform group; n = 90) of PCI. The composite rate of cardiac death and acute myocardial infarction in the Defer and Perform groups was 3.3% vs. 7.9% (p = 0.21).

Most contemporary studies however use an FFR cut off of 0.80. A recent large-scale observational study supports the use of FFR > 0.80 rather than 0.75 as a cut off.[16] Indeed, the two largest studies in this field, DEFINE-FLAIR (Define Functional Lesion Assessment of Intermediate Stenosis to Guide Revascularisation DES drug-eluting stent) [17] and iFR-SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies)[18] used the 0.80 cut-off for lesion selection by FFR resulting in favourable event rates at 1 year. Thus, 0.80 is the accepted FFR threshold for defining haemodynamically relevant lesions.

Haemodynamic relevance, as defined by FFR ≤ 0.80, correlates poorly with diameter stenosis by visual assessment. In the FAME trial, only 35% of the 50% to 70% stenoses were haemodynamically relevant and of the 71% to 90% stenoses 20% were not. Only an estimated diameter stenosis > 90% predicted haemodynamic relevance with high accuracy (96% correct classification). A number of studies have shown that utilization of an FFR-based assessment strategy at the time of angiography results in reclassification of the revascularisation strategy (PCI, bypass surgery or medical therapy) in a high proportion of patients with intermediate grade lesions (>40% of patients are reclassified).[19-21] [22] In addition, separate and pooled analysis of the patients included in those studies have shown that the end results of "FFR-based reclassification" in patients investigated at time of diagnostic angiography is overall neutral on the number of patients indicated to revascularisation.[23]

A patient-level and study-level meta-analysis of 9,173 lesions demonstrated that with lesions with FFR < 0.75 revascularisation reduced the 1-year risk of major adverse cardiac events (MACE) including a reduction in the composite risk of death and myocardial infarction. [24] Thus, the FFR threshold of 0.75 is used to define more severe ischaemia that is of prognostic relevance.

The presence of intermediate grade left main stem disease is not infrequent and angiographic evaluation may be challenging. Assessment using pressure-derived FFR is more challenging in comparison with non-left main stem stenosis due to requirement for disengagement of the guiding catheter and inability to administer intracoronary adenosine. Some observational data exist to support the use of FFR in order to decide if revascularisation should be deferred or performed.[25] In the largest study including 230 patients with intermediate grade left main stem stenosis, only 23% showed FFR <0.80. Treatment was deferred in patients with an FFR ≥0.80 and bypass surgery was done in patients with an FFR <0.80.[26] Clinical outcomes at 5 years were similar in both groups. It is important however to consider the potential influence of any untreated downstream disease in the left anterior descending or left circumflex arteries, which may be associated with an increased risk of a false negative FFR.[27]

The value of FFR to evaluate intermediate stenosis and guide selection of lesions for

revascularisation at the time of bypass surgery has been shown in an observational study.[28] Of 627 patients with intermediate stenosis evaluated, 429 had bypass without FFR, 198 had bypass with FFR: In the latter group the proportion of patients with three-vessel disease was re-classified from 94 to 86%. Outcomes were similar in both groups at 3 years (hazard ratio [HR] for death/MI/target vessel revascularisation [TVR] = 1.03 (0.67-1.69) though the group with FFR guidance was associated with a lower number of graft anastomoses and a lower rate of on-pump surgery compared with angiography-guided coronary artery bypass graft surgery.

3.2.1.2 Use of FFR to identify lesion-requiring revascularisation in patients with multivessel CAD undergoing PCI

FFR may also be useful to select lesions requiring revascularisation in patients with multivessel CAD. The FAME trial (Fractional Flow Reserve vesus Angiography for Multivessel Evaluation) showed that in patients with multivessel disease randomised to an FFR-guided PCI strategy (using a cut-off ≤ 0.80 to indicate requirement for PCI) outcomes at 12 months in terms of death, non-fatal MI and repeat revascularisation were superior compared with angiography-guided PCI and utilized less resources.[29] In addition, the 2-year composite risk of death or myocardial infarction was significantly lower with the FFR-guided PCI strategy.[30] Long-term follow-up at 5 years showed broadly consistent findings although differences between groups in relation to the primary endpoint were no longer significant.[31] This suggests that FFR-guided PCI should be the preferred management strategy in these patients.

3.2.1.3 FFR-guided management versus medical therapy in patients with CAD

In patients with stable CAD and at least one stenosis with FFR ≤ 0.80, the FAME-2 trial showed that PCI using drug-eluting stent (DES) implantation improved the primary endpoint of death, non-fatal MI, or urgent revascularisation within 2 years compared with medical treatment alone, which was driven by a lower need for urgent revascularisation.[32] The advantage of FFR-guided PCI over medical therapy alone was maintained at 3 years.[33]

3.2.2 Other pressure-derived indexes

FFR evaluation requires maximal and stable hyperaemia—usually obtained by

administration of intravenous (i.v.) adenosine. Recently there has been renewed interest in resting indices derived from resting gradients alone (Distal coronary to aortic pressure [Pd/Pa] or instantaneous wave-free ratio [iFR]). Two recent large-scale randomised trials showed broadly comparable results between FFR-guided and iFR-guided revascularisation strategies in patients with intermediate grade stenosis. [17, 18] Revascularisation was indicated in both trials if FFR was 0.80 or lower or if iFR was 0.89 or lower. In the DEFINE-FLAIR trial the primary end point of major adverse cardiac events (MACE) at 1 year occurred in 6.8% in patients randomised to iFR-guided revascularisation vs. 7.0% in patients randomised to FFR-guided revascularisation (*P* <0.001 for non-inferiority; HR 0.95, 95% CI 0.68 to 1.33; *P* =0.78). [17] In the iFR-SWEDEHEART trial, the primary endpoint of death from any cause, non-fatal MI, or unplanned revascularisation was 6.7% in the iFR group and 6.1% in the FFR group (*P* =0.007 for non-inferiority; HR 1.12, 95% CI 0.79 to 1.58; *P* =0.53). [18] In iFR-SWEDEHEART 17.5% had acute coronary syndrome at the time of presentation. There was no interaction with outcomes. Both trials are limited by having a follow-up duration of only 1 year.

The SYNTAX II study (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery), a single arm, prospective study in patients with multivessel disease incorporating a management strategy including iFR assessment of stenosis severity in addition to intravascular ultrasound (IVUS) guided stent implantation, and guideline-directed medical therapy showed encouraging outcomes compared with a historical cohort enrolled in the SYNTAX trial.[34]

Randomised trials comparing iFR-guided revascularisation with angiography-guided revascularisation or medical therapy are not available. iFR has not been extensively validated for patients with left main stem stenosis.

There is no adequate randomised controlled trial (RCT) data to support the use of whole cardiac cycle Pd/Pa for guidance of revascularisation decisions.

3.2.3 Use of FFR and pressure-derived indexes in patients with severe aortic stenosis

In patients with intermediate coronary stenosis and concomitant severe aortic stenosis, although some observational studies exist (see **chapter 11** of this document) there is no

adequate RCT data to support the use of FFR or iFR for guidance of revascularisation decisions.

3.2.4 Use of intravascular imaging for diagnostic assessment of stenosis

IVUS is an ultrasound-based modality of intravascular imaging with an axial resolution of ca. 150 µm. IVUS imaging allows a real-time, tomographic assessment of vessel size, lumen area, and plaque composition and volume. In comparison with optical coherence tomography (OCT) it has more limited spatial resolution but better penetration depth and potential advantage in terms of vessel sizing. OCT is a light-based modality of intravascular imaging with higher axial resolution compared with IVUS (15 vs. 150 µm). Disadvantages of OCT imaging are that it requires complete blood clearance from the lumen for imaging and that it has more limited penetration, which can limit assessment of complete plaque burden and may impair accurate vessel sizing.

Potential clinical uses of intravascular imaging for diagnostic assessment in patients being considered for myocardial revascularisation are evaluation of stenosis severity in lesions with intermediate grade stenosis, evaluation of lesion morphology in lesions ambiguous with angiographic assessment, and characterization of plaque composition. The majority of existing clinical trial data relate to the use of intravascular imaging-guidance during PCI and are discussed in **chapter 16** of this document. Use of intravascular imaging to evaluate patients with stent failure is discussed in chapter **chapter 13** of this document.

Regarding the assessment of intermediate-grade stenosis, a number of studies have evaluated the optimal cut-off of minimal lumen area for identifying haemodynamically relevant lesions. One prospective registry showed overall moderate correlation of minimal lumen area with FFR values, with cut-off values for detecting haemodynamically-relevant stenosis (< 2.4 mm^2, < 2.7 mm^2, < 3.6 mm^2) dependent on vessel size (reference vessel diameters < 3.0 mm, 3.0–3.5 mm, > 3.5 mm, respectively).[35] Generally, haemodynamic assessment with FFR should be preferred for this indication.

The presence of intermediate grade left main stem disease is not infrequent and angiographic assessment may be challenging. Assessment using IVUS-evaluation of intermediate grade left main stem disease in patients being considered for bypass surgery or PCI is supported by data from a number of observational studies.[35-38] In a multicentre,

prospective study, revascularisation was mainly deferred if the minimal luminal area (MLA) was ≥6 mm^2 and performed if the MLA was <6 mm^2.[37] After two-year follow-up, cardiac death-free survival was similar in both groups (98 percent and 95 percent, respectively). Another study suggested that deferral of intervention in 131 patients with an MLA ≥7.5 mm^2 showed favourable clinical outcomes.[36] In Asian patients with generally smaller heart size, minimum studies have suggested that an IVUS MLA of 4·5–4·8 mm^2 may be the most appropriate.[38]

Recommendations on functional testing and intravascular imaging for lesion assessment

Recommendations	Class[a]	Level[b]
When evidence of ischaemia is not available, FFR or iFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis [15, 17, 18, 39]	I	A
FFR-guided PCI should be considered in patients with multivessel disease undergoing PCI [29, 31]	IIa	B
IVUS should be considered to assess severity of unprotected left main lesions [35-37].	IIa	B

FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; IVUS = intravascular ultrasound.

[a]Class of recommendation.

[b]Level of evidence.

3.3 Gaps in evidence

Further studies investigating the role of novel combined non-invasive anatomical and functional imaging are needed, such as Randomised clinical trials with CT-FFR in patients with suspected and known CAD, as well as further clinical investigation of perfusion CT.

Randomised trials comparing iFR-based management of patients with intermediate grade stenosis compared with medical therapy are missing. Further study of whole cardiac cycle Pd/Pa for guidance of revascularisation in the setting of randomised clinical trials is also required.

Further studies including randomised trials are needed to assess the value of functional versus anatomical guidance for CABG.

4. Process for decision making and patient information

4.1 Patient information and informed consent

Informed consent requires transparency, especially if there is debate over various treatment options. Active patient participation in the decision-making process should be encouraged. Patient information needs to be unbiased, evidence-based, up-to-date, reliable, accessible, relevant, and consistent with legal requirements. Use of terminology that the patient understands is essential. Short-term procedure-related and long-term risks and benefits—such as survival, relief of angina, quality of life, potential need for late re-intervention, the need for prevention measures and uncertainties associated with different treatment strategies—should be thoroughly discussed. Although current recommendations are mostly based on the ability of treatments to reduce adverse events including mortality, there is a growing interest in patient-reported outcome measures (PROM).[40, 41] Patients are not only interested to know how recommended treatment impacts on prognosis but also on their life quality in the way they perceive it. A written evidence-based patient information document should be provided, potentially with decision aids.

Patients must have the time to reflect on the trade-offs imposed by the outcome estimates. In order to seek a second opinion or to discuss the findings and consequences with referring physicians, enough time should be allowed—up to several days, as required—between diagnostic catheterization and intervention. These recommendations pertain to patients in stable condition, for whom various treatment options exist and who can make a decision without the constraints of an urgent or emergent situation (**Table 3**). The patient's right to decline the treatment option recommended by the Heart Team has to be respected. Patient refusal of a recommended treatment should be acknowledged in a written document after the patient has received the necessary information by the Heart Team members. In this case, the

patient may be offered an alternative treatment option by the Heart Team.

The patient has the right to obtain information on the level of expertise of the operator, the workload of the centre, whether all treatment options—including surgery—are available on-site and local results in the performance of percutaneous and surgical myocardial revascularisation procedures. Patients considered for revascularisation should also be clearly informed of the continuing need for medical therapy, as well as lifestyle modification and other secondary prevention strategies (see **Chapter 19**).[42]

4.2 Multidisciplinary decision-making (Heart Team)

The Heart Team—comprising clinical or non-invasive cardiologists, cardiac surgeons, interventional cardiologists, and other specialists if deemed necessary—should provide a balanced, multidisciplinary decision-making process.[43] Additional input may be needed from other specialties involved in the care of the patient. The Heart Team should meet on a regular basis to analyse and interpret the available diagnostic evidence, determine the need for myocardial revascularisation and assess the relative short- and long-term safety and effectiveness of the percutaneous and surgical options. *Ad hoc* meetings of the Heart Team should facilitate and support efficient clinical workflows.

The need for an interdisciplinary approach is underlined by reports on (i) underuse of revascularisation procedures in 18–40% of patients with CAD,[44] and (ii) inappropriate use of revascularisation strategies with a lack of case discussions.[45] The marked variability in PCI-to-CABG ratios between European countries (ranging from 2.4 to 7.6 in 2013, for example) has raised concerns regarding the appropriate selection of revascularisation strategies.[46] Rates for the inappropriate use of PCI (10–15%) [43, 47, 48] and for CABG (1–2%) are reported. Multidisciplinary decision-making in a Heart Team can minimize specialty bias and prevent self-referral from interfering with optimal patient care.[49]

Several reports from different centres have established that the treatment

recommendations made in multidisciplinary Heart Team discussions are reproducible and implemented in the vast majority of cases (93–95%).[50, 51]

Interdisciplinary institutional protocols should be developed for common case scenarios, to avoid the need for the systematic case-by-case review of all diagnostic angiograms. However, complex cases—defined by the protocols—should be discussed individually. In these cases, revascularisation should not be performed at the time of diagnostic angiography, to allow sufficient time to assess all available information, and clearly explain and discuss the findings with the patient. The rationale for a decision and consensus on the optimal revascularisation treatment should be documented in the patient's chart. For institutions without an on-site cardiac surgery unit, Heart Team discussion, and protocols defining when multidisciplinary discussion is needed, should be done in collaboration with an external cardiac surgery unit.

4.3 Timing of revascularisation

Patients in need for myocardial revascularisation may be at increased risk for adverse events during the waiting period.[52] A recent meta-analysis of observational studies calculated that a waiting period of 3 months for surgical myocardial revascularisation may be associated with the risk of one death among 80 patients.[53] **Table 3** shows the preferred timing of revascularisation depending on the clinical presentation and extent and localization of CAD.[54] **Chapters 7 and 8** show additional and more specific information in this regard for patients with acute coronary syndromes (ACS).

Ad hoc PCI is defined as a therapeutic intervention performed within the same procedure as the diagnostic coronary angiography. *Ad hoc* PCI is convenient, often cost-effective and safe, and is associated with fewer access site complications and lower radiation exposure.[55, 56] In the USA, however, up to 30% of patients undergoing *ad hoc* PCI are potential candidates for CABG.[56] This number may be lower in Europe.[45] Although it is not advisable for *ad hoc* PCI to represent the default approach for complex SCAD, it may be justified if a full diagnostic work-up, including functional testing, is available and the patient is adequately informed on both percutaneous and surgical myocardial

revascularisation options (see **Chapter 4.1**) Institutional protocols developed by the Heart Team in accordance with current guidelines should define specific anatomical criteria and clinical subsets that may be—or should not be—treated *ad hoc*. Stable patients with complex CAD, as reflected by a high SYNTAX score should, in general, be discussed by the Heart Team and not be treated *ad hoc.*

Table 3 **Multidisciplinary decision pathways, patient informed consent, and timing of revascularisation**

	ACS			SCAD without ad-hoc PCI indication according to Heart Team protocol	SCAD with ad-hoc PCI indication according to Heart Team protocol
	Shock	STEMI	NSTE-ACS		
Multidisciplinary decision making	Not mandatory during the acute phase. Mechanical circulatory support according to Heart Team protocol	Not mandatory during the acute phase	Not mandatory during the acute phase. After stabilization, recommended as in SCAD	Required	Not required
Informed consent	Witnessed verbal informed consent or family consent if possible without delay	Witnessed verbal informed consent may be sufficient unless written consent is legally required	Written informed consent[a] In emergency cases witnessed verbal informed consent may be sufficient	Written informed consent	Written informed consent[a]
Time to revascularisation	Emergency: no delay	Emergency: no delay	Urgency: within 2 hours to within 72 hours depending on the risk criteria	Within 2 weeks for high-risk patients[b] and within 6 weeks for all other patients	Ad hoc
Procedure	Proceed with intervention based on best evidence/availability. Ad-hoc treatment of culprit lesion, staged treatment non-culprit lesions according to institutional protocol or Heart Team decision.	Proceed with intervention based on best evidence/availability. Non-culprit lesions treated according to institutional protocol or Heart Team decision	Proceed with intervention based on best evidence/availability. Non-culprit lesions treated according to institutional protocol or Heart Team decision	Allow for enough time from diagnostic catheterization to decide on the appropriate intervention	Proceed with intervention according to institutional protocol defined by Heart Team

ACS = acute coronary syndromes; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; STEMI = ST-segment elevation myocardial infarction.

[a]This may not apply to countries that are not legally required to ask for written informed consent. ESC and EACTS advocate documentation of patient consent for all revascularisation procedures.

[b]Severe symptoms (CCS class 3), anatomy (left main disease or equivalent, three-vessel disease or proximal left anterior descending artery), or depressed ventricular function.

Recommendations for decision-making and patient information in the elective setting

Recommendations	Class[a]	Level[b]
It is recommended that patients undergoing coronary angiography are informed about benefits and risks as well as potential therapeutic consequences ahead of the procedure.	I	C
It is recommended that patients are adequately informed about short- and long-term benefits and risks of the revascularisation procedure with the local experience and allowed enough time for informed decision making.	I	C
It is recommended that institutional protocols are developed by the Heart Team to implement the appropriate revascularisation strategy in accordance with current guidelines.	I	C
In PCI centres without on-site surgery, it is recommended that institutional protocols are established with partner institutions providing cardiac surgery.	I	C

CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

[c] See chapter 3

5. Revascularisation for stable coronary artery disease

5.1 Rationale for revascularisation

The indications for revascularisation in patients with stable CAD who receive guideline-recommended medical treatment are persistence of symptoms despite medical treatment and/or improvement of prognosis.[1]

Several studies have shown that myocardial revascularisation by PCI or CABG more effectively relieves angina, reduces the use of anti-anginal drugs, and improves exercise capacity and quality of life compared with a strategy of medical therapy alone during short- and long-term follow-up (**Supplementary Table 1**).[32, 33, 57-62] Recently, the Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina (ORBITA) trial for the first time randomly compared PCI with placebo (sham-procedure) in patients with stable CAD due to single vessel CAD (diameter stenosis >70%) and preserved left ventricular (LV) function in the presence of moderate symptoms of angina (CCS II in 59% of patients, duration 9 months).[63] After 6 weeks of medication optimization (mean number of anti-anginal drugs of 3) and baseline cardiopulmonary exercise testing, 200 patients were randomised (105 PCI, 95 placebo). Following a 6-week post-randomisation period, the primary endpoint of increment in exercise time was not significantly different, but estimates were imprecise (PCI minus placebo 16.6 sec, 95% CI -8.9-42.0, p=0.20). The dobutamine stress echocardiography peak stress wall motion score index improved with PCI (-0.09, 95% CI -0.15 to -0.04, p=0.001). ORBITA raises the issue whether the symptom relief of PCI in the specific setting of stable single vessel CAD may be related at least in part to a placebo effect. Limitations of the study, as acknowledged by the investigators and outlined elsewhere, include the short observation period (6 weeks), the inclusion of patients with mild symptoms pre-randomisation (CCS Class 0-1 in 25% of patients), the group imbalance in ostial and proximal lesions (37% vs 57%, p=0.005), loss to follow-up after randomisation, and the insufficient power to detect a true difference. [64] This precludes definite conclusions at this stage. Nevertheless, the ORBITA study underlines the value of optimal medical therapy in the management of stable CAD.

Three-year follow-up of FAME-2 indicates yearly and sustained improvement of angina (10.2% vs 28.5% at 1 month, 5.2% vs 9.7% at 3 years) in favour of FFR-guided PCI despite considerable cross-over in the medical therapy arm. [33] Among patients with multivessel disease, assessment of frequency of angina and quality of life measures in SYNTAX, FREEDOM, and EXCEL consistently show early and sustained improvement for both PCI and CABG during long-term follow-up.[65-67]

5.2 Evidence basis for revascularisation

The indications for revascularisation in patients with stable angina or silent ischaemia are summarized in the **recommendation table**.

Indications for revascularisation in patients with stable angina or silent ischemia

Extent of CAD (anatomical and/or functional)		Class[a]	Level[b]
For prognosis	Left main disease with stenosis > 50%[c] [68-71]	I	A
	Proximal LAD stenosis > 50%[c] [62, 68, 70, 72]	I	A
	Two-vessel or three-vessel disease with stenosis > 50%[c] with impaired LV function (LVEF ≤ 35%) [61, 62, 68, 70, 73-83]	I	A
	Large area of ischaemia detected by functional testing (> 10% LV) or abnormal invasive FFR[d] [5959595959595959595824, 84-90]	I	B
	Single remaining patent coronary artery with stenosis > 50%[c]	I	C
For symptoms	Haemodynamically significant coronary stenosis[c] in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical	I	A

	therapy[e]. [24, 63, 68, 91-97]		

CAD = coronary artery disease; FFR = fractional flow reserve; iFR = instantaneous wave-free ratio; LAD = left anterior descending coronary artery; LV = left ventricular; LVEF = left ventricular ejection fraction.

[a]Class of recommendation.

[b]Level of evidence.

[c]With documented ischaemia or haemodynamically relevant lesion defined by FFR ≤ 0.80 or iFR ≤ 0.89 (see section 3.2.1.1) or >90% stenosis in a major coronary vessel.

[d]Based on FFR < 0.75 indicating a prognostically relevant lesion (see section 3.2.1.1)

[e] in consideration of patient compliance and wishes in relation to intensity of antianginal therapy

5.2.1 Revascularisation with the use of percutaneous coronary intervention

Several meta-analyses comparing a strategy of PCI with initial medical therapy among patients with SCAD found no or only modest benefits in terms of survival or MI for an invasive strategy taking into account that up to 40% of patients crossed-over after to revascularisation during longer term follow-up.[91, 98, 99] A network meta-analysis of 100 trials with 93 553 patients and 262 090 patient-years of follow-up comparing a strategy of initial medical therapy with revascularisation reported improved survival using PCI with new generation DES (everolimus: 0.75, 0.59 to 0.96; zotarolimus: 0.65, 0.42 to 1.00) compared with initial medical treatment.[100]

In the FAME-2 trial (Fractional Flow Reserve versus Angiography for Multivessel Evaluation)[32] patients with SCAD and at least one functionally significant stenosis (invasive fractional flow reserve (FFR) ≤ 0.80) were randomly assigned to medical therapy or medical therapy plus FFR-guided PCI using new generation DES. The 3-year report of FAME-2 reported a lower incidence of the primary composite endpoint death, myocardial infarction (MI), and urgent revascularisation (10.1% vs. 22.0%; *P* <0.001) driven by a lower incidence of urgent revascularisation in the PCI group (4.3% vs. 17.2%; *P* <0.001) and without significant differences in the rates of death and MI.[33] At 2 years of follow-up, the rate of death or MI was lower in the PCI than the medical therapy group (4.6% vs. 8.0%; HR 0.56, 95% CI 0.32 to 0.97, *P* =0.04) in a landmark analysis between 8 days and 2 years of follow-up, whereas event rates were higher during days 0-7 due to peri-procedural MI. (For overview of studies see **Supplementary Table 2**) [97]

5.2.2 Revascularisation with the use of coronary artery bypass grafting

The superiority of CABG over a strategy of initial medical therapy was established in a meta-analysis of seven RCTs[68] more than two decades ago, demonstrating a survival benefit of CABG in patients with SCAD and LM or three-vessel SCAD, particularly when the proximal LAD coronary artery was involved and has been corroborated in more recent studies. [100, 101] A network meta-analysis of 100 trials with 93,553 patients comparing a strategy of initial medical therapy with revascularisation reported improved survival (RR 0.80, 95%CI 0.63-0.99) and a reduced risk of myocardial infarction (RR 0.79, 95%CI 0.83-0.99) among patients undergoing CABG compared with initial medical treatment. [100]

In the STICH trial, 1212 patients with CAD and a left ventricular ejection fraction (LVEF) ≤ 35% were randomised to initial medical therapy or CABG. The extended 10-year follow-up of STICH reported a significant reduction in all-cause (59% vs. 66%; HR 0.84, 95% CI 0.73 to 0.97; *P* =0.02) and cardiovascular mortality (41% vs. 49%; HR 0.79, 95% CI 0.66 to 0.93; *P* =0.006).[81] (For overview of studies see **Supplementary Table 2**)

5.3 Percutaneous coronary intervention vs. coronary artery bypass grafting

The recommendation for the type of revascularisation (CABG or PCI) in patients with SCAD with suitable coronary anatomy for both procedures and low predicted surgical mortality are summarized in the **recommendation table**. The Heart Team should take into consideration the individual cardiac and extracardiac characteristics, in addition to patient preference, in the overall decision-making process (**Figure 3**). A summary of trials comparing outcomes of patients treated with angioplasty versus CABG and BMS versus CABG is shown in **Supplementary Table 3** and of studies comparing DES and CABG **Table 6**.

5.3.1 Criteria for decision making

Predicted surgical mortality, anatomical complexity of CAD, and the anticipated completeness of revascularisation are important criteria for decision making with respect to the type of revascularisation (CABG or PCI). Whether conservative therapy, PCI, or CABG is preferred should depend on the risk-benefit ratios of these treatment strategies, weighting the risks of periprocedural complications (e.g., cerebrovascular events, blood transfusions, renal failure, new onset arrhythmias, wound infections) against improvements in health-related quality of life, as well as long-term freedom from death, myocardial infarction or repeat revascularisation.

5.3.1.1 Predicted surgical mortality

To assess the predicted surgical mortality, the European System for Cardiac Operative Risk Evaluation (EuroSCORE II) (www.euroscore.org/calc.html) and the Society of Thoracic Surgeons (STS) score (http://riskcalc.sts.org) were both developed based on clinical variables to estimate the operative in-hospital or 30-day mortality risk. [102-104] (**Supplementary Table 4)** Both scores have demonstrated their

value in specific cohorts of patients undergoing CABG.[105] Calibration of the STS score is updated on a regular basis. It has been suggested that the STS score outperforms the EuroSCORE II when compared directly in a cohort of CABG patients,[106] although other studies have found a comparable performance of both models.[107, 108]

There are no established cut-offs for low predicted surgical mortality based on EuroSCORE II or STS score. Thus, individualised treatment decisions are needed. These decisions should respect the range of predicted surgical risks in the major RCTs which inform the choice of revascularisation modality (**Table 4**). In these studies, the predicted surgical risk was assessed by the logistic EuroSCORE. Compared with the more recent EuroSCORE II, the logistic EuroSCORE has similar discrimination, but poorer calibration and, thus, overestimates surgical mortality by roughly two-fold.[109]

Despite the usefulness of these scores, there is not a single risk model that provides perfect risk assessment because the scores are limited by (i) the specific definitions used or the methodology applied, (ii) absence of important variables such as frailty, (iii) practicability of calculation, (iv) failure to reflect all relevant mortality and morbidity endpoints, and (v) limited external validation. Decision-making should not be solely dependent on risk scores. These scores should be used as a guide within the multidisciplinary Heart Team discussion.

Table 4. Logistic EuroSCOREs in major randomised trials comparing PCI with CABG

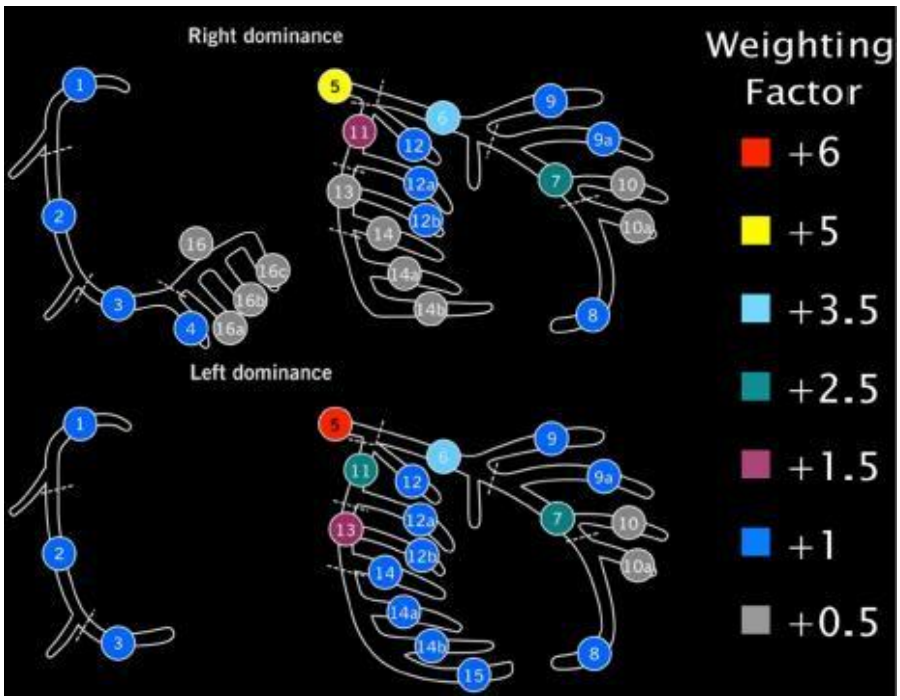
Trial	EuroSCORE PCI	EuroSCORE CABG
SYNTAX	3.8 ± 2.6	3.8 ± 2.7
BEST	2.9 ± 2.0	3.0 ± 2.1
FREEDOM	2.7 ± 2.4	2.8 ± 2.5
PRECOMBAT	2.7 ± 1.8	2.8 ± 1.9
EXCEL	not reported	not reported
NOBLE	2 [2-4]	2 [2-4]

Numbers are mean ± standard deviation or median [interquartile range]

5.3.1.2 Anatomical complexity of CAD

The SYNTAX score (http://www.syntaxscore.com) was prospectively developed for the SYNTAX trial to grade the anatomical complexity of coronary lesions in patients with LM or three-vessel disease (**Table 5, Supplementary Table 4**).[110] In the cohort of the SYNTAX trial and subsequently in external validation cohorts, the SYNTAX score was found to be an independent predictor of long-term major adverse cardiac and cerebrovascular events (MACCE) and of death in patients treated with PCI but not CABG.[111-114]

Table 5. Guide to calculate the SYNTAX score

Steps	Variable assessed	Description
Step 1	Dominance	The weight of individual coronary segments varies according to coronary artery dominance (right or left). Co-dominance does not exist as an option in the SYNTAX score.
Step 2	Coronary segment	The diseased coronary segment directly affects the score as each coronary segment is assigned a weight depending on its location, ranging from 0.5 (ie, posterolateral branch) to 6 (ie, left main in case of left dominance). 
Step 3	Diameter stenosis	The score of each diseased coronary segment is multiplied by x2 in case of a stenosis 50-99% and by x5 in case of total occlusion. In case of total occlusion, additional points will be added as follows:

		- Age >3 months or unknown +1 - Blunt stump +1 - Bridging +1 - First segment visible distally +1 per non visible segment - Side branch at the occlusion +1 if <1.5mm diameter +1 if both <1.5 and ≥1.5mm diameter +0 if ≥1.5mm diameter (ie, bifurcation lesion)
Step 4	Trifurcation lesion	The presence of a trifurcation lesion adds additional points based on the number of diseased segments: - 1 segment +3 - 2 segments +4 - 3 segments +5 - 4 segments +6
Step 5	Bifurcation lesion	The presence of a bifurcation lesion adds additional points based on the type of bifurcation according to the Medina classification:[115] - Medina 1,0,0–0,1,0–1,1,0 +1 - Medina 1,1,1–0,0,1–1,0,1–0,1,1 +2 Moreover, the presence of a bifurcation angle <70° adds 1 additional point.
Step 6	Aorto-ostial lesion	The presence of aorto-ostial lesion segments adds 1 additional point
Step 7	Severe tortuosity	The presence of severe tortuosity proximal of the diseased segment adds 2 additional points
Step 8	Lesion length	Lesion length >20mm adds 1 additional point
Step 9	Calcification	The presence of heavy calcification adds 2 additional points
Step 10	Thrombus	The presence of thrombus adds 1 additional point
Step 11	Diffuse disease/small vessels	The presence of diffusely diseased and narrowed segments distal to the lesion (ie, when at least 75% of the length of the segment distal to the lesion has a vessel diameter of <2mm) adds 1 point per segment number

In the SYNTAX trial, tertiles of SYNTAX score with low, intermediate and high anatomical complexity stratified patients into those similar outcomes with both, PCI and CABG, and those who derived significant benefit from CABG.[116-118] In subsequent RCTs, the interaction of the strata of SYNTAX score with the effect of the randomised treatment was less pronounced and did not reach statistical significance.[119-121] However, in a recent collaborative individual patient pooled analysis of randomised trials including 11,518 patients the test for trend across ordered tertiles of SYNTAX score of the SYNTAX study was positive at p=0.0011, confirming the strata of SYNTAX score as an effect modifier to be considered.[122] There is concern about bias and inter-individual variability in calculating the SYNTAX score.[123] This should be minimized by adequate training.

To combine clinical and anatomical risk estimation, the SYNTAX II score was retrospectively derived from the SYNTAX cohort [124] and subsequently externally validated.[114, 125, 126] Nevertheless, compared with SYNTAX score its value in assigning patients to PCI or CABG is less well investigated. The fact that the SYNTAX II score failed to predict the outcome of the EXCEL trial (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularisation) raises additional concern.[127]

5.3.1.3 Completeness of revascularisation

The aim of myocardial revascularisation is to minimise residual ischaemia. In support of this concept, the nuclear substudy of the COURAGE trial (Clinical Outcomes Utilizing Revascularisation and Aggressive Drug Evaluation) demonstrated an incremental benefit in reducing the risk of death and MI by reducing residual stress-induced ischaemia from > 10% of the myocardium to ≤ 5%.[86]

In the SYNTAX trial, anatomical complete revascularisation was defined as PCI or bypass of all epicardial vessels with a diameter exceeding ≥ 1.5 mm and a luminal reduction of ≥ 50% in at least one angiographic view.[128] A meta-analysis of 89,883 patients enrolled in RCTs and observational studies revealed a lower long-term mortality (relative risk (RR): 0.71, 95% CI 0.65 to 0.77; $p < 0.001$), myocardial infarction (RR: 0.78, 95% CI: 0.68 to 0.90; $p = 0.001$), and repeat myocardial revascularisation (RR: 0.74, 95% CI: 0.65 to 0.83; $p < 0.001$) by complete revascularisation (based on anatomical definition in 87% of the patients) as compared with incomplete revascularisation.[129] The benefit of complete revascularisation was independent of the treatment modality. A more recent meta-analysis suggested enhanced benefit of when performed with state-of-the-art techniques in high-risk patients.[122] Likewise, in a post-hoc analysis of the SYNTAX trial, anatomical incomplete revascularisation was associated with inferior long-term outcomes after both CABG and PCI.[128] A residual SYNTAX score > 8 after PCI was associated with significant increases in the 5-year risk of death and of the composite of death, MI and stroke, and any residual SYNTAX score > 0 was associated with the risk of repeat intervention.[130] In an observational study from the New York State registry that compared CABG with PCI using new generation DES (Everolimus-

eluting stent [EES]) in 9223 pairs of propensity matched patients with multivessel CAD, the significantly higher risk of MI associated with PCI as compared to CABG was not seen among matched pairs of patients in which the PCI group had complete revascularisation (P = 0.02 for interaction). [131] Consistent findings were obtained in a pooled analysis of 3,212 patients of the SYNTAX, BEST and PRECOMBAT trials.[132] A mean SYNTAX score of 27 and a LVEF of 59%. In a propensity matched analysis mortality and the composite risk of death, MI and stroke were significantly lower after PCI with complete versus incomplete revascularisation. After PCI with complete revascularisation the risk of death or of the composite of death, MI or stroke was not significantly different from that after CABG with complete revascularisation (adjusted HR [95%-CI] 1.16 [0.83 to 1.63], p=0.39 and 1.14 [0.87 to 1.48], p=0.35; respectively), whereas these risks were significantly elevated after PCI with incomplete revascularisation.

Functional complete revascularisation is achieved, when all lesions causing resting or stress-induced ischaemia are bypassed or treated by PCI. Given the limitations of non-invasive imaging techniques (see Chapter 3), these lesions are best identified by FFR or iFR during diagnostic angiography. For PCI, the FAME study demonstrated that the more restrictive selection of target lesions by functional guidance conferred superior long-term outcomes than anatomically guided lesion selection (see **Chapter 3**).[133] Vice versa, leaving functionally relevant lesions untreated resulted in a high rate of re-interventions in FAME-2.[33] Based on the data of FAME and FAME II complete revascularisation based on the functional definition is the preferred strategy for PCI.

The role of functional guidance for CABG is less clear. [28, 134] One of the potential benefits of CABG is protection against disease progression in proximal segments, which may be diminished by restricting the bypass targets to functionally relevant lesions. This has to be weighed against the risk of bypass closure, when native vessel flow is high. Thus, for ambiguous lesions functional testing may also help guide the surgical revascularisation strategy.

Recommendations on criteria for the choice between CABG and PCI

Recommendations	Class[a]	Level[b]
Assessment of surgical risk[c]		
It is recommended to calculate the STS score to assess in-hospital or 30-day mortality, and in-hospital morbidity after CABG.[106, 108, 135]	I	B
It may be considered to calculate the EuroSCORE II to assess in-hospital mortality after CABG[106] [102]	IIb	B
Assessment of CAD complexity		
In patients with LM or multivessel disease it is recommended to calculate the SYNTAX score to assess the anatomical complexity of CAD and the long-term risk of mortality and morbidity after PCI. [116, 122]	I	B
When considering the decision between CABG and PCI, completeness of revascularisation should be prioritized [128]	IIa	B

[a]Class of recommendation.

[b]Level of evidence.

[c]Level of evidence refers to prediction of outcomes

Table 6 Randomised clinical trials comparing PCI with DES versus surgical revascularisation trials

Stent type and Year of publication	Study	N	Baseline characteristics					Primary endpoint[c]			Secondary endpoints[c]				
			Age (y)	Women (%)	Diabetes (%)	MV disease (%)	EF (%)	Definition	Y	Results	Y	Death	MI	Revasc	Stroke
DES															
PES 2009	SYNTAX[136]	1800	65	22	25	MV 61 LM 39	-	Death, MI, stroke, or repeat revasc	1	17.8% vs. 12.4%	5	13.9% vs. 11.4%	9.7% vs. 3.8%*	25.9% vs. 13.7%*	2.4% vs. 3.7%
SES 2011	Boudriot[137]	201	68	25	36	LM 100	65	Death, MI, or repeat revasc	1	13.9% vs. 19%	1	2% vs. 5%	3% vs. 3%	14% vs. 5.9%	-
SES 2011	PRECOMBAT[138]	600	62	24	32	LM 100	61	Death, MI, stroke, or TVR	1	8.7% vs. 6.7%[a]	2	2.4% vs. 3.4%	1.7% vs. 1.0%	9.0% vs. 4.2%*	0.4% vs. 0.7%
EES 2015	BEST[119]	880	64	29	41	MV 100	60	Death, MI or TVR	2	11.0% Vs. 7.9%	5	6.6% vs. 5.0%	4.8% vs. 2.7%	13.4% vs. 6.6%	2.9% vs. 3.3%
BES 2016	NOBLE [120]	1201	66	22	15	LM 100	60	Death, MI or TVR	5	15.4% vs. 7.2%	5	11.6% vs. 9.5%	6.9% vs. 1.9%*[b]	16.2% vs. 10.4%*	4.9% vs. 1.7%
EES 2016	EXCEL[121]	1905	66	24	30	LM 100	57	Death, MI or stroke	3	15.4% vs. 14.7%[a]	3	8.2% vs. 5.9%	8.0% vs. 8.3%	13.4% vs. 6.6%*	2.3% vs. 2.9%

BES = biolimus-eluting stents; DES = drug-eluting stents; EES = everolimus-eluting stent; EF = left ventricular ejection fraction; LM = left main coronary artery disease; MI = myocardial infarction; MV = multivessel coronary artery disease; PES = paclitaxel-eluting stents; SES = sirolimus-eluting stents; TVR = target vessel revascularisation; Y = years.

*P <0.05.

[a]Non-inferiority met.

[b]Non-procedural MI (exclusion of peri-procedural MI).

[c]Results are reported as PCI vs. CABG
Age and ejection fraction are reported as means.

Recommendation for the type of revascularisation in patients with stable coronary artery disease in the absence of diabetes with suitable coronary anatomy for both procedures and low predicted surgical mortality*

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	**Level[b]**	**Class[a]**	**Level[b]**
One-vessel CAD				
Without proximal LAD stenosis	IIb	C	I	C
With proximal LAD stenosis [68, 101, 139-143 144]	I	A	I	A
Two-vessel CAD				
Without proximal LAD stenosis	IIb	C	I	C
With proximal LAD stenosis [68, 70, 73]	I	B	I	C
Left main CAD				
Left main disease with low SYNTAX score 0-22 [69, 116, 117, 122, 145-148]	I	A	I	A
Left main disease with intermediate SYNTAX score 23-32 [69, 116, 117, 122, 145-148]	I	A	IIa	A
Left main disease with high SYNTAX score ≥33 [c] [116, 117, 122, 146-148]	I	A	III	B
Three-vessel CAD				
Three-vessel disease with low SYNTAX score 0-22 [116, 118, 131, 136, 149, 150 119, 122]	I	A	I	A
Three-vessel disease with intermediate and high SYNTAX score > 22[c] [116, 118, 119, 122, 131, 136, 149, 150]	I	A	III	A

CABG = coronary artery bypass grafting; CAD = coronary artery disease; LAD = left anterior descending coronary artery; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.

Syntax score calculation http://www.syntaxscore.com

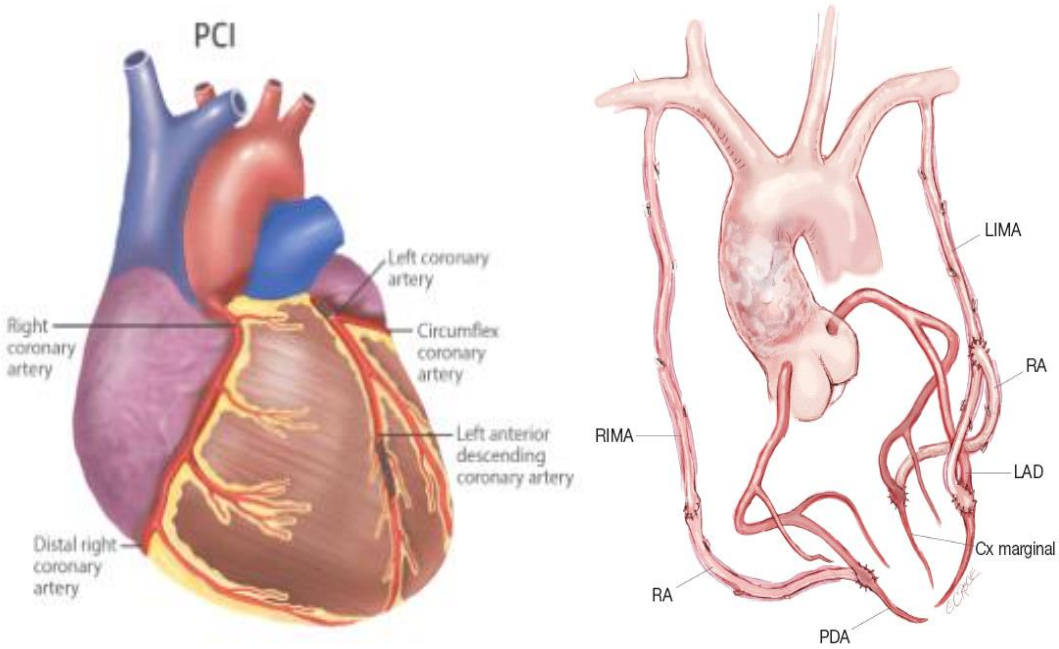
[a]Class of recommendation

[b]Level of evidence

[c]PCI should be considered, if the heart team is concerned about the surgical risk or if the patient refuses CABG after adequate counselling by the heart team including a cardiac surgeon

*eg. absence of previous cardiac surgery, severe morbidities, frailty, immobility, precluding CABG (also see **Table 4**)

Figure 3 – Aspects to be considered by the Heart Team for the decision making between percutaneous coronary intervention and coronary artery bypass grafting among patients with stable multivessel and/or left main coronary artery disease [Pictograms to be redrawn by medical artist]



Favours PCI
Clinical Characteristics
Presence of severe co-morbidity (not adequately reflected by scores)
Advanced age/frailty/ reduced life expectancy
Restricted mobility and conditions that affect the rehabilitation process
Anatomical and technical aspects
MVD with SYNTAX score 0-22
Anatomy likely resulting in incomplete revascularisation with CABG due to poor quality or missing conduits
Severe chest deformation or scoliosis
Sequelae of chest radiation
Porcelain aorta*

Favours CABG
Clinical Characteristics
Diabetes
Reduced LV function (EF≤35%)
Contraindication to DAPT
Anatomical and technical aspects
MVD with SYNTAX score ≥23
Anatomy likely resulting in incomplete revascularisation with PCI
Severely calcified coronary artery lesions limiting lesion expansion
Need for concomitant interventions
Ascending aortic pathology with indication for surgery
Concomitant cardiac surgery

CABG = coronary artery bypass grafting; DAPT = dual antiplatelet therapy; LV= left ventricular; EF = ejection fraction; MVD = multivessel coronary artery disease; PCI = percutaneous coronary intervention; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.

*consider no-touch off-pump CABG in case of porcelain aorta

5.3.2 Isolated proximal left anterior descending coronary artery disease

Comparing CABG and PCI among patients with isolated proximal LAD disease, available evidence suggests similar outcomes in terms of death, MI and stroke but a higher risk of repeat revascularisation with PCI.

5.3.3 Left main coronary artery disease

Available evidence from RCTs and meta-analyses comparing CABG with PCI using DES among patients with LM disease suggests equivalent results for the safety composite of death, MI and stroke up to 5 years of follow-up.[148] A significant interaction with time is notable providing early benefit for PCI in terms of MI and peri-interventional stroke, which is subsequently offset by a higher risk of spontaneous MI during long-term follow-up. The need for repeat revascularisation is higher with PCI than with CABG.

The EXCEL trial compared CABG with PCI using new generation DES (EES) among 1905 patients with significant LM disease.[121] At 3 years of follow-up, the primary endpoint of death, stroke or MI occurred with similar frequency in the CABG and PCI group (14.7% vs. 15.4%; HR 1.00, 95% CI 0.79 to 1.26; *P* =0.98).The preplanned landmark analysis from 30 days to 3 years showed a significant difference for the primary endpoint in favour of surgery (7.9% vs. 11.5%; *P* =0.02).

The NOBLE (Nordic-Baltic-British Left Main Revascularisation Study) trial compared CABG with PCI using new generation DES (biolimus-eluting stent, BES) among 1201 patients with significant LM disease (mean SYNTAX score of 23).[120] At a median follow-up of 3.1 years, the primary endpoint of death, non-procedural MI, stroke and repeat revascularisation occurred more frequently in the PCI than the CABG group (29% vs. 19%; HR 1.48, 95% CI 1.11 to 1.96; *P* =0.007).

A recent collaborative individual patient pooled analysis of randomised trials including 11,518 patients reviewed currently available evidence from randomised trials comparing CABG with PCI for left main or multivessel disease.[122] Primary outcome was all-cause mortality. In the overall cohort, CABG was associated with a significant survival benefit during a mean follow-up of 3.8±1.4 years (5 year all-cause mortality 11·5% after PCI vs 8·9% after CABG; HR 1·28, 95% CI 1·09–1·49; p=0·0019). There

was a linear trend for hazard ratios of death increasing with increasing SYNTAX tertiles (p for trend=0.00114). Among 4478 patients with LM disease, however, those randomly assigned to CABG or PCI with a mean follow-up of 3.4±1.4 years reported similar risks for the primary outcome all-cause mortality (PCI: 10.7% vs CABG 10.5%, HR=1.07, 95% CI 0.87.-1.33, P=0.52) at 5 years. There were no significant differences in mortality between PCI and CABG in subgroup analyses according to SYNTAX score. Nevertheless, in patients with high SYNTAX score a trend towards better survival with CABG was noted. The proportion of patients with high SYNTAX score was limited in view of the inclusion criteria of the respective studies.

Current evidence indicates that PCI is an appropriate alternative to CABG in LM disease and low-to-intermediate anatomical complexity. Among patients with LM disease and low anatomical complexity, there is evidence that the outcomes with respect to major clinical endpoints are similar for PCI and CABG, resulting in a class I recommendation. Among patients with LM disease and high anatomical complexity, the number of patients studied in RCTs is low due to exclusion criteria and the risk estimates and confidence intervals are imprecise, but suggest a trend towards better survival with CABG. Therefore, PCI in this setting cannot be endorsed as reflected by a class III recommendation. For PCI in LM with intermediate anatomical complexity, the previous class IIa recommendation was maintained in view of the incomplete 5-year follow-up of the two largest RCTs in this setting.

5.3.4 Multivessel coronary artery disease

The observation of a survival advantage of CABG over PCI has been consistent among patients with severe three-vessel CAD (intermediate to high SYNTAX score) and has been attributed at least in part to the placement of bypass grafts to the mid coronary vessels providing prophylaxis against the development of new proximal disease.

The BEST (Randomised Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease) trial comparing CABG with PCI using new generation DES (EES) among patients with multivessel CAD (77% three-vessel CAD, 23% two-vessel disease, mean SYNTAX score 24) prematurely stopped enrolment after inclusion of

880 patients due to slow recruitment.[119] At a median follow-up of 4.6 years, PCI was associated with a higher incidence of the primary endpoint (death, MI, and TVR) (15.3% vs. 10.6%; HR 1.47, 95% CI 1.01 to 2.13; *P* =0.04) than CABG. The risk of death, MI and stroke was not statistically different between the two treatment groups (11.9% vs. 9.5%; HR 1.26, 95% CI 0.84 to 1.89; *P* =0.26), whereas repeat revascularisation of any vessel (11.0% vs. 5.4%; HR 2.1, 95% CI 1.28 to 3.41; *P* =0.003) but not target lesion revascularisation (5.7% vs. 3.8%; HR 1.51, 95% CI 0.82 to 2.80; *P* =0.19) was more frequent in the PCI group. CABG resulted in more complete revascularisation (71.5% vs. 50.9%; *P* <0.001) and a lower incidence of revascularisation for new lesions (5.5% vs. 2.3%; HR 2.47, 95% CI 1.18 to 5.17; *P* =0.01).

Consistent with findings in the overall cohort (see section 5.3.3), the collaborative individual patient pooled analysis found that in 7040 patients with multivessel disease disease those assigned to CABG had a significantly lower 5-year all-cause mortality than those assigned to PCI (PCI: 11.5% vs CABG 8.9%, HR=1.28, 95% CI 1.09.-1.49, P=0.0019).[122] Outcomes for the endpoint all-cause mortality were modified by two variables: diabetes and disease complexity as assessed by the SYNTAX score. As compared to patients without diabetes (8.7% vs 8.0%, HR=1.08, 95% CI 0.86-1.36, P=0.49), mortality was higher after PCI than CABG in patients with diabetes (15.5% vs. 10.0%, HR=1.48, 95% CI 1.19-1.84, P=0.0004, P for interaction =0.045). There was a gradient of risk with a stepwise increase in mortality for PCI according to SYNTAX score tertile (SYNTAX score 0-22; 10.5% vs 8.4%, HR=1.11, 95% CI 0.77-1.62, P=0.57; SYNTAX score 23-32; 14·0% vs 9·5%; HR=1·50, 95% CI 1·09-2·08; P=0·0129; SYNTAX score >23: 19·2% vs 11·2%; HR=1·70, 95% CI 1·13-2·55; P=0·0094).

An individual patient data pooled analysis of SYNTAX and BEST comparing CABG with PCI using DES among 1,275 patients with multivessel disease in the absence of diabetes (89% three-vessel CAD, mean SYNTAX score 26) reported a lower risk of death (6.0% vs 9.3%, HR 0.65, 95% CI 0.43-0.98, P=0.04) and myocardial infarction 3.3% vs 8.3%%, HR 0.40, 95% CI 0.24-0.65, P<0.001) in the CABG group at a median follow-up of 61 months.[150] The risk of death was not significantly different among patients with low (0-22) Syntax score (6.0% vs 7.5%, P=0.66), whereas the

benefit of CABG over PCI was greater in patients with intermediate to high (>22) Syntax Score (7.1% vs 11.6%, P=0.02). Another individual patient data pooled analysis of SYNTAX and BEST comparing CABG with PCI using DES among 1,166 patients with multivessel disease involving the proximal LAD (88% three-vessel CAD, mean Syntax score 28) reported a higher risk of the composite of death, myocardial infarction and stroke (16.3% vs 11.5%, HR 1.43, 95% CI 1.05-1.96, P=0.02), cardiac death, myocardial infarction and repeat revascularisation in the PCI group at 5 years of follow-up.[147] Of note, outcomes were not significantly different for CABG and PCI for all endpoints except myocardial infarction among the subgroup of patients with low Syntax score (0-22).

Available evidence suggests that in multivessel CAD without diabetes and low anatomical complexity PCI and CABG achieve similar long-term outcomes with respect to survival and the composite of death, MI and stroke, justifying a class I recommendation for PCI. In patients with multivessel CAD and intermediate-to-high anatomical complexity the two large trials using DES, SYNTAX and BEST, found a significantly higher mortality and a higher incidence of death, MI and stroke with PCI in the absence of diabetes. Consistent results were also obtained for patients with multivessel CAD in the recent individual patient-level meta-analysis.[122]] Thus, the previous class III recommendation for PCI in multivessel CAD and intermediate-to-high complexity was maintained.

5.4 Gaps in evidence

It remains to be determined whether revascularisation by PCI improves prognosis in patients with SCAD. The ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) study (NCT01471522) is currently recruiting 5000 patients with SCAD and evidence of moderate to severe ischaemia detected by non-invasive imaging, who are randomised before coronary angiography to medical therapy or an invasive strategy to detect differences in the primary endpoint of death or MI. Current techniques rely on coronary angiography and detection of ischaemia-producing lesions. However, future adverse events are related at least in part to non-flow limiting, vulnerable plaques. Identification of vulnerable plaques and appropriate treatment strategies require further development. Along the same lines, completeness and timing of revascularisation is not well

defined and neither is the role of residual ischaemia and lesions. Very long-term, extended follow-up (10 years) of trials comparing PCI and CABG particularly in the setting of LM disease will provide further insights into the relative merits of both revascularisation techniques.

6. Revascularisation in non-ST-elevation acute coronary syndrome

Myocardial revascularisation in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is addressed by a prior guideline that is endorsed by the current task force.[151] In the present guideline, we discuss new evidence where previous recommendations require an update.

6.1 Early invasive vs. conservative strategy

An invasive strategy has become the standard of care for high-risk patients.[151] This approach allows prompt diagnosis of the underlying CAD, identification of the culprit lesion, guidance for antithrombotic management, and the assessment of the suitability of coronary anatomy for PCI or CABG. Numerous factors interplay in the decision-making process including clinical presentation, comorbidities, risk stratification (**Figure 4)**, high-risk features specific for a revascularisation modality such as frailty, cognitive status, estimated life expectancy and functional and anatomical severity of CAD.

Up to 40% of NSTE-ACS patients with obstructive CAD present with multiple complex plaques[152-155] and 25% with an acute occluded coronary artery,[156] so that identification of the culprit lesion may be challenging. Correlation with ECG or echo changes and the use of OCT in the 25% of NSTE-ACS patients with angiographically normal epicardial coronary arteries[157-159] may be helpful for identifying the culprit lesion or rule-out other mechanisms such as dissection or haematomas (myocardial infarction with non-obstructive coronary arteries [MINOCA]).[160-162]

A routine invasive strategy in NSTE-ACS has been shown to improve clinical outcomes[163], a benefit was mainly confined to biomarker-positive patients[164] and patients with other high-risk features as defined in **Figure 4**. Of importance, the use of radial approach, new-generation DES as well as more effective P2Y12 inhibitors were not available or broadly implemented in these trials and led to a magnified benefit in frail ACS populations.[165, 166]

6.2 Timing of angiography and intervention

The current recommendations on timing of angiography and intervention as defined in **Figure 4** are based on evidence discussed in detail by the prior guideline on NSTE-ACS.[151] Specifically, a reduction in recurrent or refractory ischaemia and length of hospital stay was found with early intervention.[167, 168] More recently, an updated collaborative meta-analysis on individual published and unpublished data (n=5324 patients with a median follow-up of 180 days) suggested that early intervention might also be associated with decreased mortality.[169] This meta-analysis showed a statistical trend towards decreased mortality with an early invasive strategy as compared with a delayed invasive strategy in unselected patients with NSTE-ACS (HR 0·81, 95% CI 0·64–1·03; p=0·0879). The survival benefit of the early invasive strategy appeared more pronounced in high risk subsets, including elevated cardiac biomarkers at baseline (HR 0·761, 95% CI 0·581–0·996), diabetes (HR 0·67, 95% CI 0·45–0·99), a GRACE risk score more than 140 (HR 0·70, 95% CI 0·52–0·95), and age 75 years older (HR 0·65, 95% CI 0·46–0·93), although tests for interaction were inconclusive.

6.3 Type of revascularisation

6.3.1 Percutaneous coronary intervention

6.3.1.1 Technical aspects

Implantation of new generation DES is the standard treatment strategy even when dual antiplatelet therapy (DAPT) cannot be sustained beyond one month post intervention [166, 170-172] (see **Chapter 17**) and the radial approach has also become the standard of care[165]. DAPT is recommended for 12 months irrespective of stent type, while in patients at high ischaemic risk not experiencing bleeding events, DAPT may be extended (see **Chapter 17**). There is no evidence for any additional benefit of thrombectomy in patients undergoing PCI in the setting of NSTE-ACS.[173] While FFR is considered the invasive gold standard for the functional assessment of lesion severity in stable CAD, it has been shown to be feasible, reliable, safe and effective in NSTE-ACS patients with multivessel disease although its prognostic value is unclear yet.[22, 134, 174]

6.3.1.2 Revascularisation strategies and outcomes

Complete revascularisation of significant lesions should be attempted in multivessel disease NSTE-ACS patients, given that it was mandated in trials testing early vs. late intervention[164, 175, 176] and that the prognosis of patients with incomplete revascularisation is known to be worse.[128, 177] In addition, it seems that complete one stage revascularisation is associated with better clinical outcome than multistage PCI.[178] Periprocedural complications of PCI defined as MI or myocardial injury as well as the long-term ischaemic risk remains higher in NSTE-ACS than in stable patients[179, 180] For ACS patients who underwent PCI, revascularisation procedures represent the most frequent, most costly and earliest cause for rehospitalization.[181, 182] As in STEMI, routine treatment of non-culprit lesions during the primary intervention by PCI is harmful in NSTE-ACS with cardiogenic shock, as shown by the recently published Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial (see section 7.3).[183]

6.3.2 Coronary artery bypass grafting

Approximately 5% up to 10% of NSTE-ACS patients require CABG[184] and represent a challenging subgroup given their high-risk characteristics compared with patients undergoing elective CABG.[185] In the absence of randomised data, optimal timing for non-emergent CABG in NSTE-ACS patients should be determined individually. The risk of ischaemic events possibly related to suboptimal antiplatelet therapy while awaiting surgery is less than 0.1% while perioperative bleeding complications associated with platelet inhibitors is higher than 10%.[186] In patients with ongoing ischaemia or haemodynamic instability and with an indication for CABG, emergency surgery should be performed and not postponed as a consequence of antiplatelet treatment exposure.

6.3.3 Percutaneous coronary intervention vs. coronary artery bypass grafting

There is no randomised comparison of PCI vs. CABG in the specific setting of NSTE-ACS. Currently available evidence indirectly suggests that the criteria applied in patients with stable CAD to guide the choice of revascularisation modality should be applied to stabilized patients with NSTE-ACS.[100, 116, 149 187] A recent individual-patients data analysis from BEST, PRECOMBAT and SYNTAX compared the outcome of CABG with that of PCI in 1246 patients with stabilised NSTE-ACS and multivessel or left main disease. [187] The 5-year incidence of the primary outcome, the

composite of death, MI or stroke, was significantly lower with CABG than with PCI (13.4% vs 18%, p = 0.036). The findings of this meta-analysis were consistent with the main findings of the studies included, thus supporting the concept that the principles of SCAD should apply to stabilised patients with NSTE-ACS as well. For complex cases, Heart Team discussion and use of the SYNTAX score are recommended,[188] in particular given its ability to predict death, MI and revascularisation in multivessel disease NSTE-ACS patients undergoing PCI where recent evidence suggests a greater benefit of CABG versus PCI.[189]

Recommendations for invasive evaluation and revascularisation in non-ST-elevation acute coronary syndrome

Recommendations	Class[a]	Level[b]
Urgent coronary angiography (< 2 hours) is recommended in patients at very high ischaemic risk (Figure 3).[190]	I	B
An **early** invasive strategy (< 24 hours) is recommended in patients with at least one high-risk criterion (Figure 3). [157, 167, 169]	I	A
An invasive strategy (< 72 hours after first presentation) is indicated in patients with at least one intermediate-risk criterion (Figure 3) or recurrent symptoms. [163 164]	I	A
It is recommended to base the revascularisation strategy (*ad hoc* culprit-lesion PCI/multivessel PCI/CABG) on the **clinical status** and comorbidities as well as the **disease severity**, i.e. distribution and angiographic lesion characteristics (e.g. SYNTAX score), according to the principles for SCAD*.[187]	I	B
In cardiogenic shock, routine revascularisation of non-IRA lesions is not recommended during primary PCI.[183]	III	B

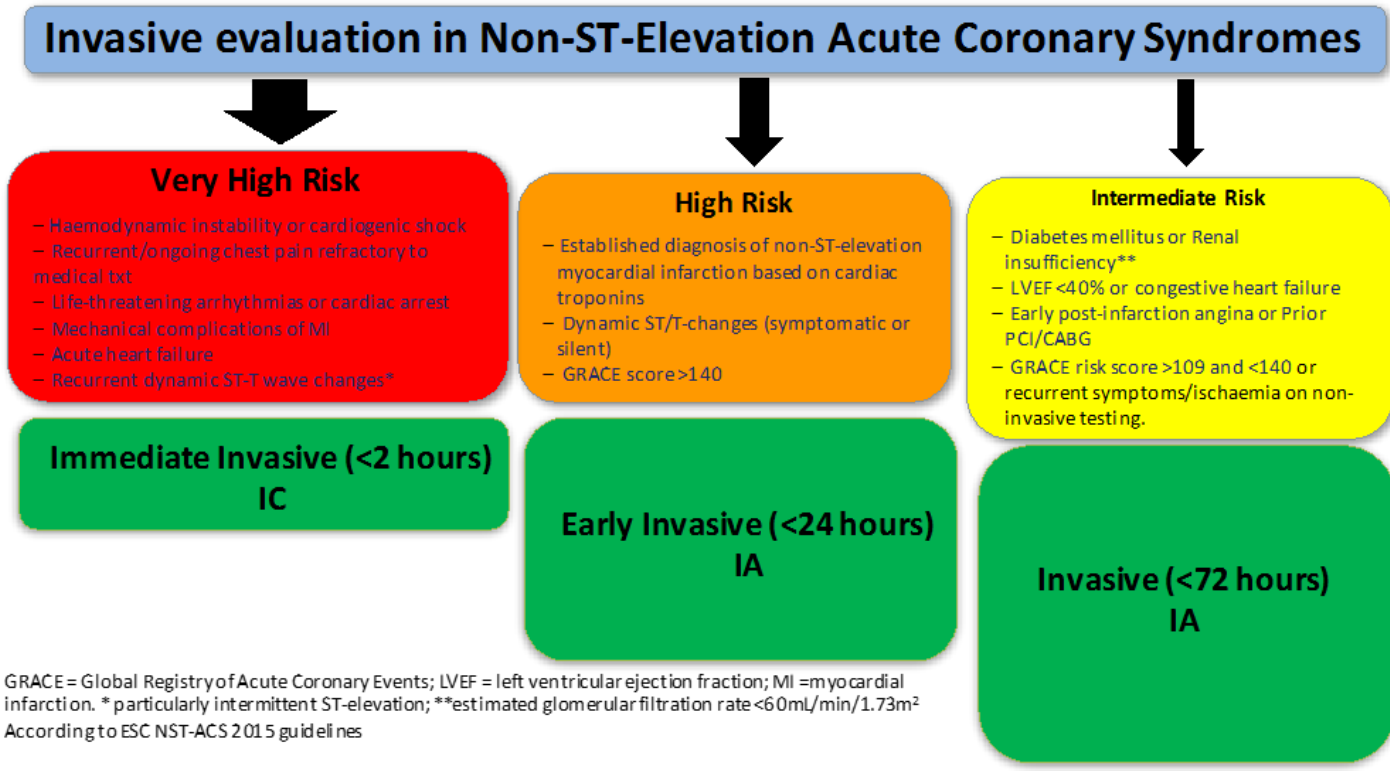
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease; SYNTAX = SYNergy between percutaneous coronary intervention with TAXus.

[a]Class of recommendation

[b]Level of evidence

*may apply to stabilised NSTE-ACS patients

Figure 4 Selection of non-ST-elevation acute coronary syndrome (NSTE-ACS) treatment strategy and timing according to initial risk stratification.



6.4 Gaps in evidence

In the setting of NSTE-ACS, there are no dedicated prospective studies on the revascularisation strategy with multivessel disease. Thus, current recommendations on choice of lesions to be treated and treatment modality (PCI or CABG) are based on an analogy to findings obtained in stable CAD or STEMI. Likewise, the prognosis role of FFR and iFR in guiding myocardial revascularisation needs additional clarification.

7. Revascularisation in ST-segment elevation myocardial infarction

Myocardial revascularisation in patients with STEMI is addressed by the 2017 ESC guidelines on STEMI. After reviewing the subsequent literature, the current task force endorses most recommendations of this guideline.[191]

7.1 Time delays

Delays in the timely implementation of reperfusion therapy are key issues in the management of STEMI. Detailed recommendations on time lines, logistics and prehospital management have been provided in the recent ESC STEMI guidelines (**Figure 5**).[191]

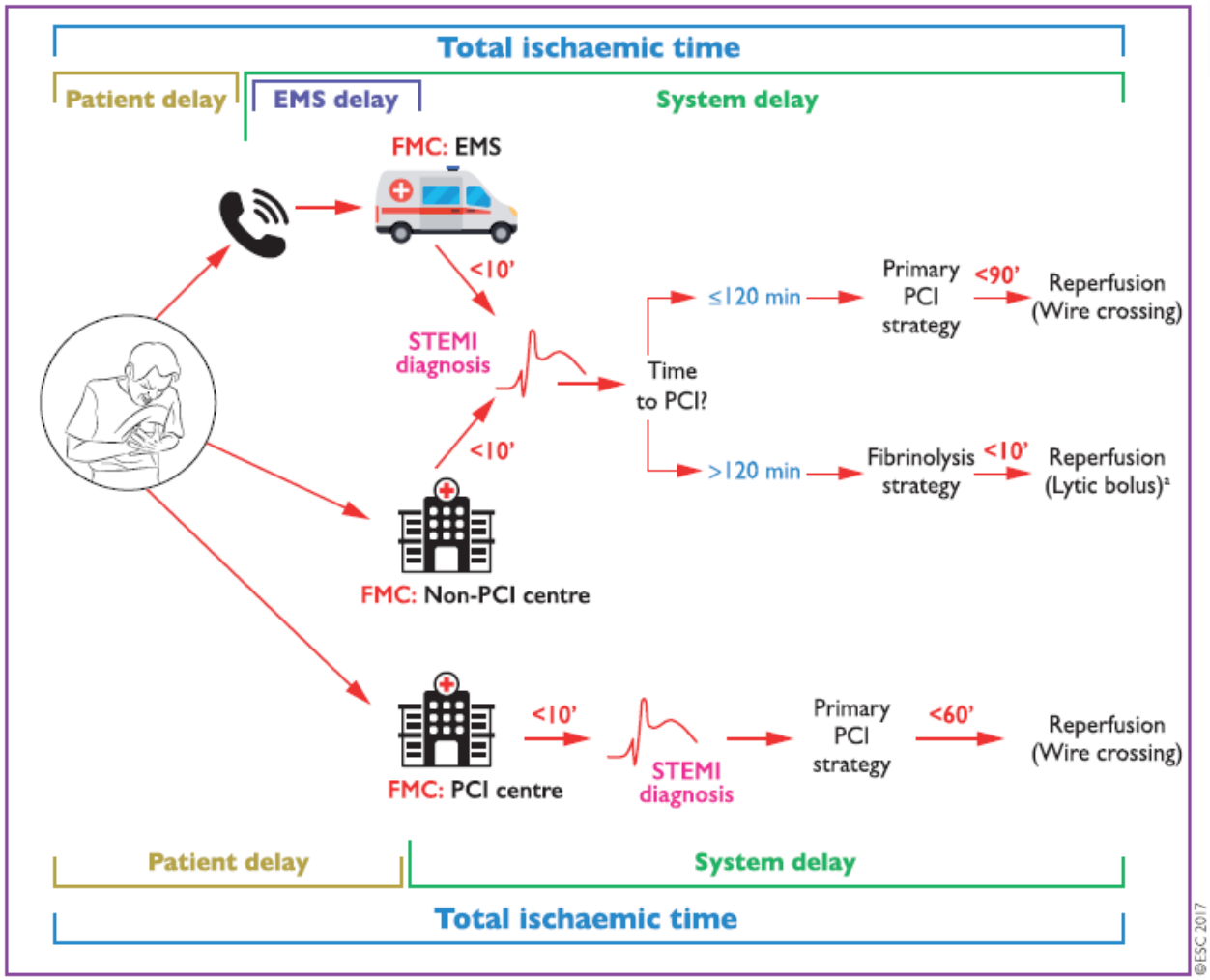
A recent analysis of 12,675 STEMI patients of the Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction (FITT-STEMI) trial emphasizes the strong impact of time delays on mortality, particularly in STEMI patients with cardiogenic shock or out-of-hospital cardiac arrest.[192] In shock without out-of-hospital cardiac arrest, every 10-min treatment delay between 60 and 180 min from the first medical contact resulted in 3.3 additional deaths per 100 PCI-treated patients and in 1.3 additional deaths after out-of-hospital cardiac arrest without cardiogenic shock. In stable STEMI patients time delays were substantially less relevant (0.3 additional deaths per 100 PCI-treated patients for every 10-min delay between 60 to 180 min from the first medical contact). Thus, the high-risk STEMI patients with cardiogenic shock or out-of-hospital cardiac arrest are those whose benefit most from expediting all steps of the care pathway.

7.2 Selection of reperfusion strategy

Primary PCI, defined as percutaneous catheter intervention in the setting of STEMI without previous fibrinolysis, is the preferred reperfusion strategy. It has replaced fibrinolysis in patients with STEMI, provided it can be performed in a timely manner in high-volume PCI centres with experienced operators and 24-hour, 7-day catheterization laboratory activation.[191, 193, 194] In settings where primary PCI cannot be performed in a timely fashion, fibrinolysis should be administered as soon as possible. If FMC is out of hospital lysis should be implemented pre-hospital (e.g. in the ambulance). (**Figure 5**).[195-199] It should be followed by transfer to PCI-capable centres for routine coronary angiography in all patients, and should be performed without delay for rescue PCI in the case of unsuccessful fibrinolysis or within 2 to 24 hours after the bolus administration.[191] Emergency CABG may be indicated in selected STEMI patients unsuitable for PCI.

Figure 5 Modes of patient's medical contact, components of ischaemia time and

flowchart for reperfusion strategy selection.



EMS = Emergency Medical System; FMC = First Medical Contact; PCI = Percutaneous Coronary Intervention; STEMI = ST-segment elevation myocardial infarction. The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the choice of reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when EMS arrives to the scene. ' denotes minutes. [a]Patients receiving fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.

7.3 Primary percutaneous coronary intervention

Key points for optimizing and guiding primary PCI are summarized below.

The infarct-related artery (IRA) should be systematically treated during the initial intervention. Patients with extensive CAD in vessels remote from the IRA have an

adverse prognosis following primary PCI.[200] Staged PCI in patients with multivessel disease and no haemodynamic compromise is an independent predictor of survival, and more frequent ischaemic events have been reported in direct vs. staged revascularisation of STEMI patients with multivessel disease.[201-203]

Four major randomised trials (Preventive Angioplasty in Acute Myocardial Infarction [PRAMI] [204], Complete Versus Lesion-Only Primary PCI trial [CvLPRIT],[205] complete revascularisation versus treatment of the culprit lesion only in patients with STEMI and multivessel disease [DANAMI-3−PRIMULTI],[206] and Compare-Acute[207]) have consistently shown a benefit of complete revascularisation (performed immediately or staged) as compared to IRA-only PCI in patients with STEMI and multivessel disease (for details see web addenda). A recent meta-analysis of 10 trials has shown that complete revascularisation was associated with a lower risk of MACE (RR 0.57, 95% CI 0.42 to 0.77), due to a lower risk of urgent revascularisation (RR 0.44, 95% CI 0.30 to 0.66), with no significant difference in mortality (RR 0.76, 95% CI 0.52 to 1.12) or MI (RR 0.54, 95% CI 0.23 to 1.27).[208] This meta-analysis did not include Compare-Acute. Yet, similar to earlier studies the benefit of complete revascularisation over culprit-only revascularisation seen in Compare-Acute was driven by a lower need for unplanned re-intervention, whereas the incidences of death and recurrent MI were similar between the two strategies. [207]

Most of the studies support the concept of full revascularisation either during the initial hospital stay for STEMI or a staged admission,[208] but it remains to be determined how clinicians can identify lesions that should be revascularised beyond the culprit lesion and whether complete revascularisation should be performed in single- or multi-stage procedures. Moreover, there is lack of evidence on optimal timing of staged procedures. In most of the studies, staged procedures were performed during the initial hospital stay. At present, one-stage multivessel PCI during STEMI without cardiogenic shock should be considered in patients in the presence of multiple, critical stenoses or highly unstable lesions (angiographic signs of possible thrombus or lesion disruption), and if there is persistent ischaemia after PCI on the supposed culprit lesion.

In patients with multivessel disease and acute myocardial infarction with cardiogenic

shock, the recently published CULPRIT-SHOCK trial showed that a strategy with PCI of culprit lesion only with possible staged revascularisation determined a lower 30-day risk of the composite of all-cause mortality or severe renal failure as compared to immediate multivessel PCI.[183] This was driven by a significant risk reduction in 30-day all-cause mortality by the culprit only strategy as compared with immediate multivessel PCI (43.3% vs. 51.6%; HR 0.84, 95% CI 0.72-0.98; P=0.03). These findings need to be interpreted in light of a low 12.5% (43 out of 344 patients) cross-over rate from culprit only to immediate multivessel PCI based on physician´s judgment. Based on these findings, culprit only PCI is recommended as the default strategy in patients with acute myocardial infarction with cardiogenic shock. A more detailed discussion of the revascularisation strategy in MI with cardiogenic shock is found in the web addenda.

In patients with STEMI, DES, in particular new generation DES, have demonstrated better efficacy as compared to bare-metal stent (BMS) and should be used as the default strategy in STEMI patients, even when DAPT cannot be sustained beyond 1 month.[170, 171, 209-211] (see **Chapter 16.1.2**). As discussed in **Chapter 16.4**, the radial access is preferred over the femoral access.

Delaying stenting in primary PCI has been investigated as an option to reduce microvascular obstruction (MVO) and preserve microcirculatory function in two small trials with conflicting results.[212, 213] More recently, in the larger Deferred versus conventional stent implantation in patients with STEMI (DANAMI 3-DEFER) trial in 1215 STEMI patients, there was no effect on the primary clinical outcome (composite of death, non-fatal MI, or ischaemia driven revascularisation of non-IRA lesions) over a median follow-up of 42 months.[214] Routine deferred stenting was associated with a higher risk of TVR.

Thrombus aspiration has been proposed as an adjunct during primary PCI, to further improve epicardial and myocardial reperfusion by the prevention of distal embolization of thrombotic material and plaque debris.[215] Two landmark randomised controlled trials adequately powered to detect superiority of routine manual thrombus aspiration vs. conventional PCI showed no benefit on clinical outcomes of the routine aspiration strategy overall or in any subgroup of patients indicating high thrombotic risk.[216-219] A

safety concern emerged in the Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI (TOTAL) with an increase in the risk of stroke.[218, 220] Taken together, these results suggest that the routine use of thrombus aspiration is not indicated. In the high thrombus burden subgroup, the trend towards reduced cardiovascular death and increased stroke/transient ischaemic attack (TIA) provides a rationale for future trials of improved thrombus aspiration technologies in this high-risk subgroup (although statistical tests did not support significant subgroup interaction).[221]

7.4 Percutaneous coronary intervention after thrombolysis and in patients with late diagnosis

The benefits of early, routine PCI after thrombolysis were seen in the absence of an increased risk of adverse events (stroke or major bleeding). Based on data from the four most recent trials, all of which had a median delay between start of thrombolysis and angiography of 2–6 hours, a time-frame of 2–24 hours after successful lysis is recommended.[199, 222-224] In cases of failed fibrinolysis, or if there is evidence of re-occlusion or re-infarction with recurrence of ST segment elevation, the patient should undergo immediate coronary angiography and rescue PCI.[225] Patients presenting between 12 and 48 hours after onset of symptoms, even if pain-free and with stable haemodynamics, may still benefit from early coronary angiography and possibly PCI.[226, 227] In patients presenting days after the acute event with a completed MI, only those with recurrent angina or documented residual ischaemia—and proven viability on non-invasive imaging in a large myocardial territory—may be considered for revascularisation when the infarct artery is occluded. Routine late PCI of an occluded IRA after MI in stable patients has no incremental benefit over medical therapy.[228]

7.5 Gaps in evidence

Patients undergoing primary PCI benefit from full revascularisation but the optimal timing of treatment of the non-culprit lesion is not known. More studies evaluating the use the non-culprit lesions by FFR or IFR at the time of acute PCI and studies investigating whether intravascular imaging guidance of primary PCI can improve outcomes of STEMI patients are needed. Future trials of improved thrombus aspiration technologies may address role of this strategy in patients with high-risk features, such large thrombus burden.[221]

Primary percutaneous coronary intervention for myocardial reperfusion in ST-elevation myocardial infarction: indications and logistics

Recommendations	Class[a]	Level[b]
Indication		
Reperfusion therapy is indicated in all patients with time from symptom onset < 12 hours duration and persistent ST-segment elevation[193, 194, 229].	I	A
In the absence of ST-segment elevation, a primary PCI strategy is indicated in patients with suspected ongoing ischaemic symptoms suggestive of MI and at least one of the following criteria present: - haemodynamic instability or cardiogenic shock - recurrent or ongoing chest pain refractory to medical treatment - life-threatening arrhythmias or cardiac arrest - mechanical complications of MI - acute heart failure - recurrent dynamic ST-segment or T-wave changes, particularly with intermittent ST-segment elevation	I	C
A primary PCI strategy is recommended over fibrinolysis within indicated timeframes[230, 231].	I	A
In patients with time from symptom onset >12 h, a primary PCI strategy is indicated in the presence of ongoing symptoms or signs suggestive of ischaemia, haemodynamic instability, or life-threatening arrhythmias.	I	C
A routine primary PCI strategy should be considered in patients presenting late (12–48 h) after symptom onset [226, 227, 232].	IIa	B
Logistics		
It is recommended that the prehospital management of	I	B

STEMI patients be based on regional networks designed to deliver reperfusion therapy timely and effectively, and to offer primary PCI to as many patients as possible [233, 234].		
It is recommended that all EMSs, emergency departments, coronary care units, and catheterization laboratories have a written updated STEMI management protocol, preferably shared within geographic networks.	I	C
It is recommended that primary PCI-capable centres deliver a 24-hour/7-day service and ensure for primary PCI to be performed as fast as possible [235-237].	I	B
It is recommended that patients transferred to a PCI-capable centre for primary PCI bypass the emergency department and CCU/ICCU and are transferred directly to the catheterization laboratory [238-240].	I	B

CCU = coronary care unit; ECG = electrocardiogram; EMS = emergency medical service; ICCU = intensive coronary care unit; LBBB = left bundle branch block; RBBB = right bundle branch block, PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation.

[b]Level of evidence.

Primary percutaneous coronary intervention for myocardial reperfusion in ST-elevation myocardial infarction: procedural aspects (strategy and technique)

Recommendations	**Class[a]**	**Level[b]**
Strategy		
Routine revascularisation of non-IRA lesions should be considered in patients with multivessel disease before hospital discharge. [204], [205] [206, 207].	IIa	A
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardised myocardium if PCI of the IRA cannot be performed.	IIa	C
In cardiogenic shock, routine revascularisation of non-IRA lesions is not recommended during primary PCI.[183]	III	B

Technique		
Routine use of thrombus aspiration is not recommended [216-219, 221]	III	A

CABG = coronary artery bypass grafting; IRA = infarct-related artery; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

[a]Class of recommendation.

[b]Level of evidence.

8. Myocardial revascularisation in patients with heart failure

8.1 Chronic Heart Failure

8.1.1 Recommendations for myocardial revascularisation in patients with chronic heart failure

When compared to medical therapy alone, coronary revascularisation is superior in improving survival in patients with heart failure (HF) of ischaemic origin and is recommended in clinical practice. [81, 241] However, the optimal revascularisation strategy is not defined. The choice between CABG and PCI should be made by the Heart Team after careful evaluation of the patient's clinical status and coronary anatomy, expected completeness of revascularisation (see **section 5.3.1.3**), myocardial viability, coexisting valvular disease and co-morbidities. Considerations relating to the need for viability testing prior to revascularisation are discussed in **chapter 3** of this document.

Randomised clinical trial data comparing revascularisation with medical therapy exists only for CABG in the setting of the Surgical Treatment for Ischemic Heart Failure (STICH) trial[81]. One analysis from this trial showed that CABG can be performed with acceptable 30-day mortality rates (5.1%) in patients with left ventricular dysfunction (LVEF≤ 35%).[242] Extended follow-up in the STICH Extension Study (STICHES) support a significant survival benefit of CABG combined with medical therapy versus medical therapy alone in a 10-year observation.[81]

There are currently no dedicated randomised clinical trials comparing PCI vs. medical therapy in patients with HFrEF (Heart Failure with Reduced Ejection Fraction). In addition, CABG vs. PCI randomised trials have excluded patients with severe HF. In one prospective registry including 4616 patients with multivessel disease and severe HFrEF, propensity-score matched comparison revealed similar survival (mean follow-

up 2.9 years) with PCI (using EES) versus CABG.[243] PCI was associated with a higher risk of MI, particularly in patients with incomplete revascularisation, and repeat revascularisation. CABG was associated with higher risk of stroke. The conclusion of the study was that multivessel PCI can be a valuable option in HF patients, if complete revascularisation is possible. A systematic review of studies comparing revascularisation with medical therapy in patients with an ejection fraction ≤ 40% showed that there was a significant mortality reduction with CABG (hazard ratio, 0.66; 95% confidence interval, 0.61-0.72; P<0.001) and PCI (hazard ratio, 0.73; 95% confidence interval, 0.62-0.85; P<0.001) versus medical therapy, though these finding are limited by the predominantly observational nature of the included studies and missing information on completeness of revascularisation.[241]

A recent observational study investigated outcomes with PCI or CABG for multi-vessel CAD and LV dysfunction in 1738 propensity-matched patients with diabetes mellitus.[244] Similar to the findings in absence of LV dysfunction, CABG as compared with PCI was associated with a significantly lower risk of MACE, which included a significant reduction in mortality. Event curves separated early during the first year and continued to separate out to 12 years.

In older patients without diabetes in whom complete revascularisation can be achieved PCI should be considered whereas in younger patients with more extensive CAD or those with diabetes CABG is preferred. In patients with diabetes and LV moderate or severe dysfunction (EF<50%) CABG is associated with better long term survival and reduced incidence of MACCE.[243, 244]

8.1.2 Ventricular reconstruction and aneurysm resection

The aim of surgical ventricular reconstruction (SVR) is to restore physiological volume, and achieve an elliptical shape of the LV, by scar resection and LV wall reconstruction on a mannequin of predefined size. The aim of ventricular aneurysmectomy is to remove fibrous scar in cases of severe dilatation, thrombus formation or as a source of life-threatening ventricular arrhythmias.

The STICH trial revealed no difference in the primary outcome (total mortality or cardiac hospitalization) between patients randomly allocated to CABG versus combined CABG and SVR.[245] Subgroup analyses of patients with a less dilated LV

and better LV ejection fraction showed benefit from SVR. [246] In the STICH trial, a postoperative LV end-systolic volume index of 70 mL/m^2 or lower, after CABG plus SVR, resulted in improved survival compared with CABG alone.[245] [247] In experienced centres, SVR may be done at the time of CABG if HF symptoms are more predominant than angina and if myocardial scar and moderate LV remodeling are present.

Recommendations on revascularisations in patients with chronic heart failure and systolic left ventricular dysfunction (ejection fraction ≤ 35%)

Recommendations	Class[a]	Level[b]
In patients with severe LV systolic dysfunction and coronary artery disease suitable for intervention, myocardial revascularisation is recommended [81, 243]	I	B
CABG is recommended as first revascularisation strategy choice in patients with multivessel disease and acceptable surgical risk. [68, 81, 241, 248]	I	B
In patients with 1 or 2 vessel disease, PCI should be considered as an alternative to CABG when complete revascularisation can be achieved	IIa	C
In patients with 3 vessel disease PCI should be considered based on the evaluation by the Heart Team of the patient's coronary anatomy, expected completeness of revascularisation, diabetes status, and co-morbidities.	IIa	C
Left ventricular aneurysmectomy during CABG should be considered in patients with NYHA class III/IV, large LV aneurysm, large thrombus formation or if the aneurysm is the origin of arrhythmias.	IIa	C
Surgical ventricular restoration during CABG may be considered in selected patients treated in centres with expertise [245-247, 249, 250].	IIb	B

CABG = coronary artery bypass grafting; LAD = left anterior descending; LV = left ventricular; LVESV = left ventricular end-systolic volume; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

8.2 Acute Heart Failure and Cardiogenic Shock

Acute myocardial ischaemia in the setting of AMI is the antecedent event for the majority of patients with cardiogenic shock undergoing percutaneous revascularisation. Mechanical complications, such as papillary muscle rupture with severe mitral valve regurgitation, ventricular septal defect, or free wall rupture, are additional precipitating causes.

8.2.1 Revascularisation

The SHOCK trial (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) demonstrated that in patients with cardiogenic shock complicating acute myocardial infarction, emergency revascularisation with PCI or CABG improved long-term survival when compared with initial intensive medical therapy. All-cause mortality at 6 months was lower in the group assigned to revascularisation than in the medically treated patients (50.3% vs. 63.1%, respectively; RR 0.80, 95% CI 0.65 to 0.98; P=0.03).[251]

The revascularisation strategy for patients with cardiogenic shock and multivessel disease is addressed in **chapter 7** of this document.

A sub-analysis of the SHOCK trial comparing patients treated with CABG or PCI showed similar survival rates between the two subgroups.[252] There were more patients with diabetes (48.9% versus 26.9%; P=0.02), 3-vessel disease (80.4% versus 60.3%; P=0.03), and left main coronary disease (41.3% versus 13.0%; P=0.001) in the CABG group. The findings of this non-randomised comparison suggest that CABG should be considered in patients with cardiogenic shock who have suitable anatomy, particularly if successful PCI is not feasible.

8.2.2 Mechanical circulatory support

Short-term MCS devices currently available are the intra-aortic balloon pump (IABP), veno-arterial extracorporeal membrane oxygenation (ECMO) and percutaneous left ventricular assist devices (pLVAD). Short-term MCS may be considered in refractory cardiogenic shock depending on patient age, comorbidities, neurological function, and prospects for long-term survival and quality of life.

8.2.2.1 Intraaortic Balloon Pump

IABP is a low cost device that is easy to insert and remove. It moderately increases cardiac output and coronary and cerebral perfusion while decreasing ventricular workload. In patients with cardiogenic shock complicating acute MI, the IABP-SHOCK II randomised trial (600 patients) showed that the use of IABP did not reduce 30-day mortality and that there was no evidence of long-term benefit.[253, 254] A recent Cochrane review of seven trials (790 patients) showed that IABP may have a beneficial effect on some haemodynamic parameters but did not result in survival benefits.[255] Thus, the routine use of IABP in patients in cardiogenic shock with cardiogenic shock complicating acute MI is not recommended.

8.2.2.2 Extracorporeal Membrane Oxygenation

Veno-arterial ECMO (VA-ECMO), also known as extracorporeal life support (ECLS), in its current form is a modified form of cardiopulmonary bypass. It decompresses the venous system, increases coronary, cerebral and peripheral perfusion, and also provides supplementary blood oxygenation. When performed percutaneously, it does not allow for left ventricular decompression, and leads to increasing LV afterload.

In patients with cardiac arrest, evidence from observational trials supports better survival in patients treated with VA-ECMO compared with those without.[256] When compared with IABP, VA-ECMO provides superior circulatory support. [257, 258] Moreover, a meta-analysis of observational studies suggested that in patients with cardiogenic shock post ACS, VA-ECMO showed a 33 % higher 30-day survival compared with IABP (95 % CI, 14–52 %; $p < 0.001$; NNT 13).[256] However, the low number of patients included in the analysed studies and the non-random treatment allocation are important limitations.

8.2.2.3 Percutaneous Left Ventricular Assist Devices

The majority of clinical experience with currently available pLVADs is limited to two types of devices: 1) transaortic microaxial pump (Impella) which directly unloads left ventricle providing 2,5-5l/min blood flow and 2) a transseptal centrifugal assist device (TandemHeart) which unloads the LV via a cannula introduced into left atrium through transseptal puncture.

A recent meta-analysis on MCS in cardiogenic shock included four randomised trials investigating the efficacy and safety of pLVADs vs IABP and demonstrated similar short-term mortality despite initial beneficial effects on arterial blood pressure and peripheral perfusion, measured by serum lactate levels.[259] In all trials, higher rate of bleeding from vascular access sites and a significantly higher incidence of limb ischaemia following pLVAD was noted. Similar outcomes were noted in a RCT in high-risk PCI in patients with impaired LV function. The 30-day incidence of major adverse events was not different for patients with pLVAD versus IABP.[260]

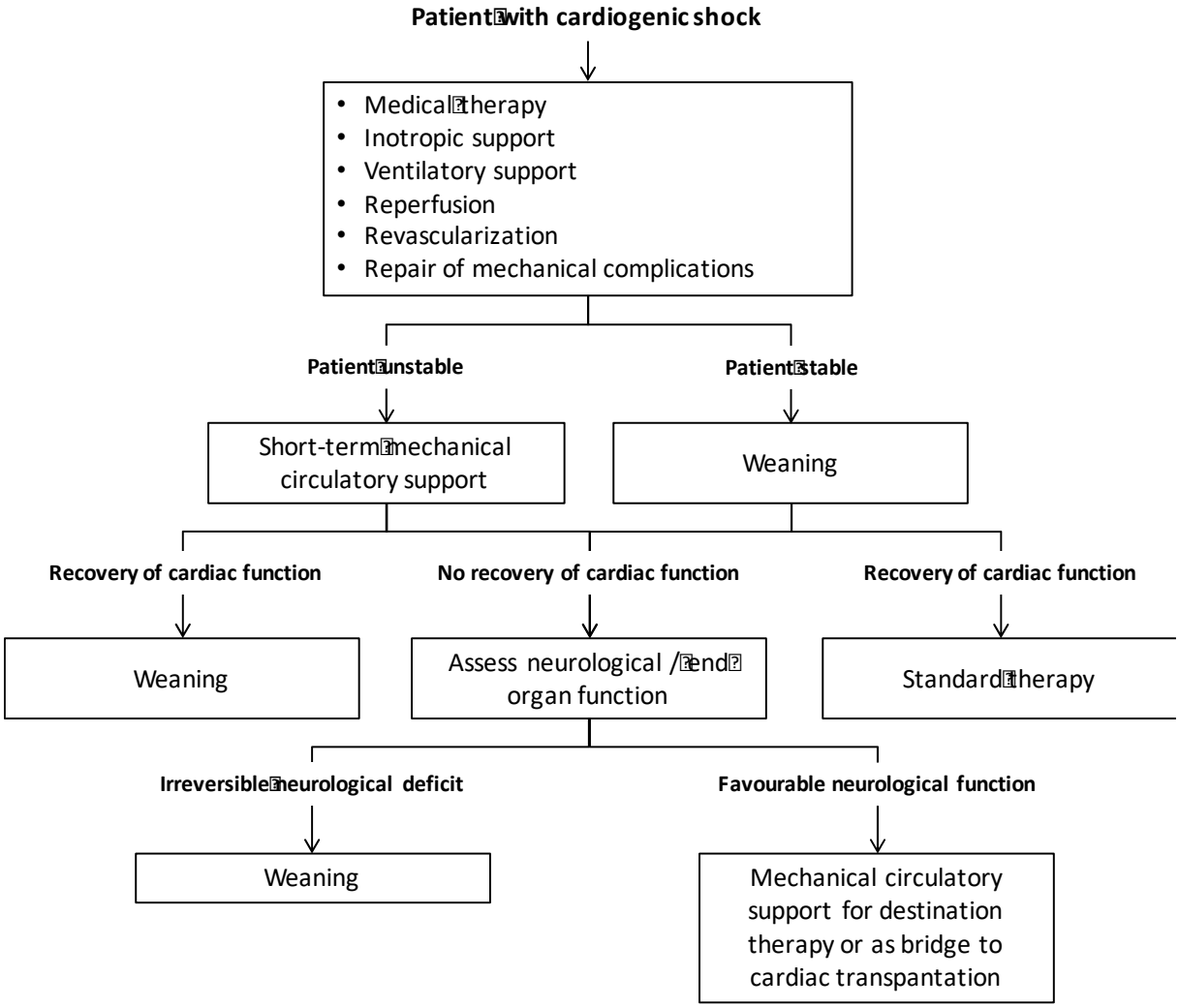
In summary, the evidence for pLVAD is insufficient to provide a recommendation on clinical use in cardiogenic shock.

8.2.2.4 Surgically implanted LVAD

There is limited data with surgically-implanted left ventricular assist device (LVAD) therapy in patients with AMI and cardiogenic shock. One multicentre registry showed that despite being more critically ill prior to implantation, patients with acute MI managed with LVAD had outcomes similar to other LVAD populations.[261]

A suggested algorithm for the management of patients with cardiogenic shock is shown in **Figure 6**.

Figure 6. Algorithm for management of patients with cardiogenic shock



8.3 Gaps in Evidence

There is no RCT comparing revascularisation with PCI vs CABG in patients with HF. There is limited evidence on the role of active MCS in patients with cardiogenic shock compared with standard therapy.

Recommendations for management of patients with cardiogenic shock

Recommendations	Class[a]	Level[b]
Emergency coronary angiography is indicated in patients with acute heart failure or cardiogenic shock complicating ACS [251, 262].	I	B
Emergency PCI of the culprit lesion is indicated for patients with cardiogenic shock due to STEMI or NSTE-ACS independent of time delay of symptom onset. if coronary anatomy is amenable to PCI [251].	I	B
Emergency CABG is recommended for patients with cardiogenic shock if the coronary anatomy is not amenable to PCI[251] .	I	B
In case of haemodynamic instability, emergency surgical or catheter-based repair of mechanical complications of ACS is indicated as decided by the heart team.	I	C
In selected patients with ACS and cardiogenic shock, short-term mechanical circulatory support may be considered, depending on patient age, comorbidities, neurological function and prospects for long-term survival and predicted quality of life.	IIb	C
Routine use of IABP in patients with cardiogenic shock due to ACS is not recommended [253-255].	III	B

ACS = acute coronary syndrome; CABG - coronary artery bypass grafting VA ECMO - veno-arterial extracorporeal membrane oxygenation. IABP = intra-aortic balloon pump; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-elevation myocardial infarction.

[a]Class of recommendation.

[b]Level of evidence

9. Revascularisation in patients with diabetes

Patients with diabetes mellitus have a higher prevalence of CAD which often manifests earlier in life and confers a substantially worse prognosis than for patients without diabetes.[263] Patients with diabetes who have suffered an MI have a worse prognosis, particularly those requiring treatment with insulin, and the presence of

diabetes amplifies the risk of any cardiovascular event.[264] Diabetes mellitus is present in 25–30% of patients admitted with ACS and in up to 40% of patients undergoing CABG.[265]

The anatomical pattern of CAD in patients with diabetes clearly influences their prognosis and response to revascularisation. Angiographic studies have demonstrated that patients with diabetes are more likely to have LM disease and multivessel coronary artery disease (MVD) with more diffuse disease involving smaller vessels.[266] In addition, patients with diabetes have a greater atherosclerotic burden and an increased number of lipid-rich plaques which are prone to rupture,[267, 268] and those with unstable angina have more fissured plaques and intracoronary thrombi.[269] Patients with diabetes undergoing revascularisation, either with CABG or PCI, are at greater risk for kidney injury than patients without diabetes.

9.1 Evidence for myocardial revascularisation

In patients with diabetes, the indications for myocardial revascularisation are the same as those in patients without diabetes (see **Chapters 5 to 7**). A meta-analysis of nine RCTs with 9904 ACS patients did not show an interaction between diabetic status and the benefit from invasive management and revascularisation.[270] Yet, absolute risk reductions were larger in the diabetic subsets as compared with non-diabetic subsets. Consistent with the findings in the absence of diabetes, the adverse impact of incomplete revascularisation in patients with diabetes was also demonstrated in the BARI-2D (Bypass Angioplasty Revascularisation Investigation 2 Diabetes) trial.[271]

Data from randomised trials on revascularisation in patients with diabetes are summarized in **Supplementary Table 5.**

9.2 Type of myocardial revascularisation

The selection of the optimal myocardial revascularisation strategy for patients with diabetes and MVD requires particular consideration. The recommendations are provided in **Chapter 5**.

9.2.1. Randomised clinical trials

The Future Revascularisation Evaluation in Patients with Diabetes Mellitus (FREEDOM) trial compared elective revascularisation with CABG or PCI with first generation DES (94%) in 1900 patients with diabetes (6% of the screened population) with multivessel disease but without LM stenosis.[149] The primary endpoint of any cause death, non-fatal MI, or stroke at 5 years occurred in 26.6% in the PCI group, as compared with 18.7% in the CABG group (absolute difference 7.9%, 95% CI 3.3% to 12.5%; *P* =0.005). The incidence of death (16.3% in the PCI group vs. 10.9% in the CABG group; absolute difference 5.4%, 95% CI 1.5% to 9.2%; *P* =0.049) and MI (13.9% in the PCI group vs. 6.0% in the CABG group; *P* <0.001) were higher in the PCI group but the incidence of stroke was lower (2.4% vs. 5.2%; *P* =0.03). Within the FREEDOM trial at 5 years, patients with diabetes treated with insulin had higher event rates, but there was no significant interaction of treatment and insulin requirement for the primary end point ($P_{interaction}$ =0.40) even after adjusting for SYNTAX score: the NNT with CABG vs. PCI to prevent 1 event was 12.7 for insulin treated patients and 13.2 in those not requiring insulin.[272]

The Veterans Affairs Coronary Artery Revascularisation in Diabetes Study (VACARDS) compared CABG with PCI in patients with diabetes and extensive CAD in the USA.[273] Only 198 patients with diabetes were randomised due to early termination of the study. The combined risk for death or non-fatal MI was 18.4% for the CABG arm and 25.3% for the PCI arm (HR 0.89, 95% CI 0.47 to 1.71, p<0.05).[273]

In the Coronary Artery Revascularisation in Diabetes (CARDia) trial, 510 patients with diabetes and multivessel or complex single-vessel CAD were randomly assigned to either CABG or PCI with use of either BMS or DES and routine use of abciximab.[274] There were no differences between CABG and PCI for the primary endpoint of 1-year composite of death, MI, or stroke at 1 year but the trial was underpowered to detect these differences. However, repeat revascularisation was more likely to occur in patients treated with PCI (*P* <0.001).[274]

In the subset of 452 patients with diabetes and multivessel CAD who were enrolled in the SYNTAX trial, there were no differences in the composite safety end-point of all-cause death/stroke/MI at 5-year follow-up.[275] However, the need for repeat revascularisation (HR 2.01, 95% CI 1.04 to 3.88; *P* <0.001) was significantly more

frequent in patients with diabetes treated with PCI than in those who underwent CABG. [275 275 275 275 275 275 275 275 275 275 269 269 269 269 269 269 269 270 272 272] Patients with diabetes had a higher rate of repeat revascularisation after PCI when compared with CABG in the low (≤ 22) (38.5% vs. 18.5% respectively, *P* =0.014) and intermediate (23−33) (27% vs. 13.4% respectively, *P* =0.049) SYNTAX score tertiles. Further analyses according to treatment with either oral hypoglycaemic agents or insulin showed that the MACCE rate was significantly greater after PCI in both the oral hypoglycaemic agent group (PCI 40.4% vs. CABG 26.4%, *P* =0.022) and the insulin dependent group (PCI 56.2% vs. CABG 32.6%, *P* =0.002). A higher incidence of cardiac death was noted in the insulin-dependent patients treated with PCI (PCI 18.8% vs. CABG 7.1%, *P* =0.023).

In the SYNTAX trial, diabetes was not an independent predictor of outcomes once the SYNTAX score was entered into the multivariable model. [124] Consequently the SYNTAX 2 score does not include diabetes as one of the eight variables that impacts on preferential selection of revascularisation modality.[124] Conflicting data were seen in a patient-level pooled analysis of 6081 patients treated with stents (75% newer generation DES), stratified according to diabetes status and SYNTAX score.[276] After Cox regression adjustment, that SYNTAX score and diabetes were both associated with MACE (*P* <0.001 and *P* =0.0028, respectively). At 2 years patients with diabetes had higher MACE (HR 1.25, 95% CI 1.03 to 1.53; *P* =0.026) and TVR and similar death and MI rates.[276]

In the BEST trial, patients with diabetes treated with PCI had a higher rate of the primary endpoint of death, MI, or TVR compared with CABG (EES: n=177; CABG: n=186), (19.2% vs. 9.1%, *P* =0.007) (see **Chapter 5**).[119]

9.2.2 Meta-analysis of CABG vs PCI in patients with diabetes

A meta-analysis—restricted to four RCTs covering 3052 patients, compared PCI with use of early-generation DES vs. CABG in patients with diabetes and multivessel CAD. It suggested a higher risk of death and MI with revascularisation by early-generation DES (RR 1.51, 95% CI 1.09 to 2.10; *P* <0.01) but a lower risk of stroke (2.3% vs. 3.8%; RR 0.59, 95% CI 0.39 to 0.90; *P* <0.01).[277] A sensitivity analysis revealed that this superiority of CABG over early-generation DES for the endpoint

MACCE was most pronounced among patients with a high SYNTAX score. A network meta-analysis had suggested that the survival benefit of CABG over PCI in patients with diabetes might be lost when using EES,[278] though this was not confirmed in a subsequent meta-analysis which also included the direct comparison between EES and CABG in the subset of BEST.[279]

In a collaborative individual patient-data pooled analysis of 11,518 patients with multivessel or LM disease randomised to CABG or PCI with stents, all-cause death was significantly different after CABG (9.2%) and PCI (11.2%) (P=0.0038), which was evident in patients with diabetes (10.7% versus 15.7%, resepectively; P=0.0001) but not in patients without diabetes (8.4% versus 8.7%, respectively; P=0.81) (P for interaction = 0.0077).[122]Similar results were found in the subgroup of 7040 patients with multivessel disease (P for interaction 0.0453), while the interaction with diabetes was not significant in the 4478 patients with LM disease (P for interaction 0.13).

A recent population based analysis has confirmed the benefit of CABG compared to PCI in patients with diabetes when patients present with an ACS. [189] Consequently overall current evidence continues to favour CABG as the revascularisation modality of choice for patients with diabetes and multivessel disease. When patients present with co-morbidity that increases surgical risk, the choice of revascularisation method is best decided by multidisciplinary individualised risk assessment.

9.3 Revascularisation with the use of percutaneous coronary intervention

For reasons discussed above, PCI in patients with diabetes is often more complex than PCI in the absence of diabetes. Nevertheless, irrespective of diabetic status, the same principles apply as discussed in **Chapter 16.** Placement of new generation DES is the default strategy.

9.4 Antithrombotic pharmacotherapy

In the current context of use of oral $P2Y_{12}$ inhibitors, there is no indication that antithrombotic pharmacotherapy should differ between diabetic and patients without diabetes undergoing revascularisation. For detailed discussion refer to **Chapter 17**.

9.5 Metformin

There is a theoretical risk of the risk of lactic acidosis and deteriorating renal function in patients treated with metformin who are exposed to iodinated contrast media. [280] Consequently, it is generally recommended that in elective cases metformin should be withheld before angiography or PCI for 48 hours, as the plasma half-life of metformin is 6.2 hours, [280] and reintroduced 48 hours later. However, clinical experience suggests that the actual risk of lactate acidosis is very small and checking renal function after angiography in patients on metformin and withholding the drug when renal function deteriorates appears to be an acceptable alternative. [280] In patients with renal failure, metformin should be stopped before the procedure. Accurate recognition of metformin-associated lactic acidosis based on arterial pH < 7.35, blood lactate > 5 mmol/L (45 mg/dL), and detectable plasma metformin concentration should prompt initiation of haemodialysis.

Recommendations for revascularisation in patients with diabetes

Recommendations	Class[a]	Level[b]
In patients with stable multivessel CAD and an acceptable surgical risk, CABG is recommended over PCI.[122]	I	A
In patients with stable multivessel CAD and SYNTAX Score ≤ 22, PCI may be considered as alternative to CABG.[122 277]	IIb	B
It is recommended to check renal function if patients have taken metformin immediately before angiography and withhold metformin if renal function deteriorates	I	C

[a]Class of recommendation.

[b]Level of evidence.

9.6 Gaps in evidence

Following successful revascularisation, the rate of events during follow-up remains high in patients with diabetes, independent of the mode of revascularisation. Future research should be focused on identifying new disease modifying therapies to influence the progression of vascular disease in this high-risk cohort.

10 Revascularisation in patients with chronic kidney disease

10.1 Evidence-base for revascularisation and recommendations

Myocardial revascularisation in patients with chronic kidney disease (CKD), specifically National Kidney Foundation stages 3 or higher, is addressed by the 2014 ESC/EACTS guidelines on myocardial revascularisation. After reviewing the subsequent literature, the current task force does not find evidence to support any major update. A recent post-hoc analysis of the SYNTAX trial on patients with chronic kidney disease confirms the principles for allocating patients to PCI or CABG,[281] as discussed in **Chapter 5** of this document.

10.2 Prevention of contrast-induced nephropathy

The risk of contrast-induced nephropathy (CIN) depends on patient related factors, such as CKD, diabetes mellitus, congestive HF, haemodynamic instability, reduced plasma volume, female sex, advanced age, anaemia and periprocedural bleeding, as well as on the type and volume of contrast administered.[282-288] When the ratio of total contrast volume (in ml) to glomerular filtration rate (GFR, in ml/min) exceeds 3.7, the risk of CIN increases significantly.[287, 288]

Adequate hydration remains the mainstay of CIN prevention.[289-294] High-dose statins as indicated for secondary prevention irrespective of the risk of CIN are also beneficial.[293] All other strategies for prevention of CIN do not have sufficient evidence to justify a recommendation in favour or against. [293 294] For more detailed discussion refer to the web addenda.

10.3 Gaps in evidence

Thus far, patients with CKD have been excluded from randomised trials on myocardial revascularisation, hence current data are based on observational studies only. A randomised trial on optimal long-term revascularisation strategies in patients with moderate to severe stress induced ischaemia and severe CKD is currently ongoing (ISCHEMIA-CKD https://clinicaltrials.gov/ct2/show/NCT01985360). Moreover, additional randomised evidence on optimal strategies for CIN prevention is needed.

Recommendations for prevention of contrast-induced nephropathy

Recommendations	Dose	Class[a]	Level[b]
Patients undergoing coronary angiography or MSCT			

It is recommended to assess all patients for the risk of contrast-induced nephropathy.		I	C
Adequate hydration is recommended.		I	C
Patients with moderate or severe CKD (National Kidney Foundation stages 3b and 4)			
Use of low-osmolar or iso-osmolar contrast media is recommended [284-286].		I	A
It is recommended to minimize volume of contrast media [287, 288].	total contrast volume/GFR < 3.7[c].	I	B
In statin-naïve patients, pretreatment with high-dose statins should be considered. [293]	Rosuvastatin 40/20mg or atorvastatin 80 mg	IIa	A
Pre- and post-hydration with isotonic saline should be considered if the expected contrast volume is > 100 mL .	1 mL/kg/h 12 hours before and continued for 24 hours after the procedure (0.5 mL/kg/h if LV EF ≤ 35% or NYHA > 2).	IIa	C
As an alternative to the pre- and post-hydration regimen tailored hydration regimens[d] may be considered [295, 296, 297].		IIb	B
Patients with severe CKD (National Kidney Foundation stage 4)			
Prophylactic haemofiltration 6 hours before complex PCI may be considered [298-300].	Fluid replacement rate 1000 mL/h without negative loss and saline hydration continued for 24 hours after the procedure.	IIb	B
Haemodialysis is not recommended as a preventive measure [300, 301].		III	B

CIN = contrast-induced nephropathy; CKD = chronic kidney disease; EF = ejection fraction; GFR = glomerular filtration rate; i.v. = intravenous; LV = left ventricular; MSCT = multi-slice computed tomography; NYHA = New York Heart Association; PCI = percutaneous coronary angiography.

[a]Class of recommendation.

[b]Level of evidence.

[c] Example: 370 ml of contrast medium in a patient with a GFR of 100 ml/min will yield a ratio of 3.7.

[d] Options are: infusion of normal saline adjusted to central venous pressure[295]; furosemide with matched infusion of normal saline [296, 297] (for details see web addenda)

11. Revascularisation in patients requiring valve interventions

11.1 Primary indication for valve interventions

Myocardial revascularisation in patients undergoing primary valve interventions either by surgery or transcatheter routes is addressed by the 2014 ESC/EACTS guidelines on myocardial revascularisation. After reviewing the subsequent literature, the current task force endorses the recommendations of the 2014 guidelines and does not find evidence to support any major update. These recommendations are included in the table below for ease of reference. Of note, available evidence on invasive functional assessment of CAD (with FFR or iFR) in patients with severe aortic stenosis (AS) is limited to few small-scale observational studies. These studies support the feasibility of FFR and iFR in this setting.[302-304] Notwithstanding, available evidence is insufficient to support the use of invasive functional assessment of coronary lesions in patients with AS, particularly in consideration of the altered hemodynamic condition related to the presence of AS. Therefore, the Task Force is in consensus to maintain indications for myocardial revascularisation based on angiographic assessment of CAD, consistent with 2014 ESC/EACTS guidelines on myocardial revascularisation and 2017 ESC/EACTS guidelines for the management of valvular heart disease.[305]

11.2 Primary indication for myocardial revascularisation

11.2.1 Aortic Valve Disease

The recommendations for patients undergoing CABG for the clinically leading problem of CAD, who also have coexisting severe aortic stenosis or regurgitation, remain unchanged from 2014 and support replacement of the aortic valve.[305] However, in the current era of rapid developments in transcatheter valve implantation technologies, decision regarding replacement of the aortic valve for moderate stenosis/regurgitation should be carefully considered on a case-by-case basis in discussion with the Heart Team. The patient's age, type of prosthesis, pathogenesis of aortic stenosis/regurgitation, aortic annular size, predicted size of implanted valve, transcatheter aortic valve implantation (TAVI) access routes and technical feasibility of a TAVI procedure in the future in case of disease progression should all be taken into account.[306]

11.2.2 Mitral Valve Disease

Patients with concomitant severe primary mitral regurgitation should undergo mitral valve repair at the time of CABG in keeping with guidance for surgical repair of primary MR.[305] There is also consensus based on expert opinion on surgical repair of severe secondary MR at the time of CABG.[307 305] Considerable controversy exists, however, about the treatment of moderate secondary or ischaemic MR in patients undergoing CABG. Until the publication of 2-year outcomes of the Cardiothoracic Surgical Trials Network (CTSN) randomised trial on treatment of “moderate” ischaemic MR, the literature in this field was limited to small single centre randomised trials, observational studies and case series and failed to provide clear direction. The CTSN trial showed that addition of surgical mitral valve repair to CABG made no significant difference to survival, overall reduction in adverse events or LV reverse remodelling at 2 years[308, 309]. Increased length of intensive care and hospital stay and perioperative morbidity, including neurological complications and supraventricular arrhythmias, were reported in the CTSN and other randomised trials in this group of patients.[308-310] Because the CTSN trial used a very broad definition of moderate MR, including an EROA ≤0.2 cm^2 plus additional criteria, no firm conclusions can be drawn concerning patients with an EROA >0.2 cm^2. Observational data suggest that in secondary MR, an EROA of >0.2 cm^2 and regurgitant volume of >30 ml indicates greater risk of cardiovascular events.[311, 312] In the absence of dedicated trials in this setting, the decision for combining mitral valve surgery with CABG in patients with an EROA of >0.2 cm^2 and regurgitant volume of >30 ml needs to be made on a case-by-case basis by the heart team. For a more detailed discussion of this issue, please refer to the web addenda.

11.3 Gaps in evidence

In patients with concomitant valvular and coronary disease, the possibility of future transcatheter therapy for the aortic and mitral valves has made a significant impact on decision making for patients with predominantly coronary disease with moderate valve lesions. There is, however, little evidence currently on this topic. Also, the need and timing of PCI in patients undergoing TAVI is an area with limited evidence. The long-term outcomes of patients with concomitant surgical repair of ischaemic MR are also awaited.

Recommendations for combined valvular and coronary interventions

	Class[a]	Level[b]
Primary valve intervention and coronary revascularisation		
CABG is recommended in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis > 70%.	I	C
CABG should be considered in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis 50–70%.	IIa	C
PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis > 70% in proximal segments.	IIa	C
PCI should be considered in patients with a primary indication to undergo transcatheter mitral valve interventions and coronary artery diameter stenosis > 70% in proximal segments.	IIa	C
Primary myocardial revascularisation and valve intervention		
SAVR is indicated in patients with severe AS undergoing CABG, or surgery of the ascending aorta or another valve.	I	C
Mitral valve surgery is indicated in patients with severe[c] secondary MR undergoing CABG, and LVEF > 30%.	I	C
Mitral valve surgery may be considered in symptomatic patients with severe[c] secondary MR, LVEF < 30% but with evidence of viability and option for surgical revascularisation.	IIa	C

AS = aortic stenosis; CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; PCI = percutaneous coronary intervention; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

[a]Class of recommendation

[b]Level of evidence

[c]Severe secondary MR was defined as an EROA > 0.40 cm^2

12. Associated peripheral artery diseases

12.1 Prevention of stroke associated with carotid artery disease and myocardial revascularisation

The early risk of stroke after myocardial revascularisation is higher after CABG as compared with PCI.[313] After 30 days, stroke rates between revascularisation techniques were similar in a recent individual patient-data meta-analysis of 11 randomised trials.

Ischaemic stroke after CABG is multifactorial: thrombo-embolism from the aorta, its branches or the heart, atrial arrhythmias, inflammatory pro-thrombogenic milieu, lower levels of antiplatelet therapy peri-operatively and haemodynamic instability. However, the most consistent predictor of peri-operative stroke is previous stroke or TIA. There is no strong evidence that carotid artery stenosis is a significant cause of peri-operative stroke except for bilateral severe carotid bifurcation stenosis.[314] Therefore, indications for pre-operative carotid bifurcation screening by duplex ultrasound are limited.[315] Also, there is no evidence that prophylactic revascularisation of unilateral asymptomatic carotid stenoses in CABG candidates reduce the risk of perioperative stroke. It may be reasonable to restrict prophylactic carotid revascularisation to patients at highest risk of postoperative stroke, i.e. patients with severe bilateral lesions or a history of prior stroke/TIA.[316] Hence, the indication for revascularisation and the choice between carotid endarterectomy or carotid artery stenting in these patients should be made by a multidisciplinary team including a neurologist.

The 2017 Guidelines on the diagnosis and treatment of peripheral arterial diseases in collaboration with the European Society of Vascular Surgery cover the screening for and management of carotid artery disease in patients scheduled for coronary artery bypass grafting including screening, indications, timing and type of carotid revascularisation.[317] Its recommendations are reproduced here.

Particularly for patients at high risk for peri-operative stroke risk after CABG, such as elderly patients or patients with previous TIA/stroke, specific preventive measures have been suggested. CT scan screening of the ascending aorta/arch atheroma has been proposed to better assess the risk stratification and guide surgical strategy in elderly patients.[318] It is recommended to restart acetylsalicylic acid 6 hours or at the latest 24 hours after surgery and add clopidogrel or ticagrelor in patients with ACS.

New onset atrial fibrillation (AF) is associated with a 2−3 times higher risk of stroke after CABG. Its management is discussed in **Chapter 14**.

12.2 Associated coronary and peripheral artery diseases

Seven to 16% of patients with CAD have lower extremity artery disease (LEAD), which is associated with a worse prognosis, even if it remains frequently asymptomatic, masked by cardiac symptoms. On the other hand, in patients with LEAD, CAD is present in up to 70% of patients.[317] The choice between CABG and PCI is controversial and in the absence of solid data, it should follow a multidisciplinary approach.[124] In patients undergoing CABG, the saphenous vein should be preserved or harvested guided by the results of clinical examination including ankle-brachial index. In addition, inter-arm blood pressure asymmetry should lead to investigation of subclavian artery stenosis.
Further details are provided in the 2017 PAD guidelines.[317]

Recommendations on the management of carotid stenosis in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients scheduled for CABG it is recommended that the indication (and if so the method and timing) for carotid revascularisation be individualised after discussion within a multidisciplinary team, including a neurologist.	I	C
In patients scheduled for CABG, with recent (< 6 months) history of TIA/stroke:		
- Carotid revascularisation should be considered in patients with 50−99% carotid stenosis[319, 320]	IIa	B
- Carotid revascularisation with CEA should be considered as first choice in patients with 50−99% carotid stenosis[319, 320]	IIa	B
- Carotid revascularisation is not recommended in patients with carotid stenosis < 50%.	III	C

In neurologically asymptomatic patients scheduled for CABG:		
- Routine prophylactic carotid revascularisation in patients with a 70−99% carotid stenosis is not recommended	III	C
- Carotid revascularisation may be considered in patients with bilateral 70−99% carotid stenosis or 70−99% carotid stenosis and contralateral occlusion	IIb	C
- Carotid revascularisation may be considered in patients with a 70−99% carotid stenosis, in the presence of one or more characteristics that may be associated with an increased risk of ipsilateral stroke,[c] in order to reduce stroke risk beyond the perioperative period.	IIb	C

CABG = coronary artery bypass grafting; CEA= carotid endarterectomy; TIA = transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

[c]Contralateral TIA/stroke, ipsilateral silent infarction on cerebral imaging, intraplaque haemorrhage or lipid-rich necrotic core on magnetic resonance angiography, or any of the following ultrasound imaging findings: stenosis progression (>20%), spontaneous embolization on transcranial Doppler, impaired cerebral vascular reserve, large plaques, echolucent plaques, increased juxta-luminal hypoechogenic area [317]

Preoperative strategies to reduce the incidence of stroke in patients undergoing coronary artery bypass grafting

Recommendations	Class[a]	Level[b]
In patients undergoing CABG, carotid DUS is recommended in patients with recent (< 6 months) history of stroke/TIA [321, 322].	I	B
In patients with no recent (< 6 months) history of TIA/stroke, carotid DUS may be considered before CABG in the following cases: age ≥ 70 years, multivessel coronary artery disease, concomitant LEAD, or carotid bruit[321, 322]	IIb	B
Screening for carotid stenosis is not indicated in patients requiring urgent CABG with no recent stroke/TIA.	III	C

CABG = coronary artery bypass graft surgery; DUS = duplex ultrasound; LEAD = lower extremity artery disease; TIA = transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

13. Repeat revascularisation and hybrid procedures

13.1 Early graft failure

Early graft failure after CABG is reported in up to 12% of grafts as evaluated by intraoperative angiography.[323] However, only a minority, around 3%, are clinically apparent. Graft failure can be due to conduit defects, anastomotic technical errors, poor native vessel run-off, or competitive flow with the native vessel. When clinically relevant, acute graft failure may result in MI with consequently increased mortality and major cardiac events. The suspicion of early graft failure should arise in the presence of ECG signs of ischaemia, ventricular arrhythmias, biomarker changes, new wall motion abnormalities, or haemodynamic instability. [324, 325] Owing to the low specificity of ECG changes and echocardiographic wall motion abnormalities during the postoperative course and the delay in appearance of biomarker changes, a careful assessment of all variables will influence the decision making for angiographic evaluation.

Perioperative angiography is recommended in cases of suspected severe myocardial ischaemia to detect its cause and aid decision making on the most appropriate treatment.[323, 325, 326] In symptomatic patients, early postoperative graft failure can be

identified as the cause of ischaemia in 40−80% of cases.[324, 326-328] The optimal treatment strategy in patients with acute graft failure should be decided by *ad hoc* consultation between the cardiovascular surgeon and the interventional cardiologist, on the basis of the patient's clinical condition and extent of myocardium at risk. In the case of early postoperative graft failure, emergency *ad hoc* PCI may limit the extent of infarction, if technically feasible. The target for PCI is the native vessel or the internal mammary artery (IMA) graft, while the acutely occluded saphenous vein graft (SVG) and any anastomotic site should be avoided, if possible, due to concerns regarding embolisation or perforation. Re-do surgery should be favoured if the anatomy is unsuitable for PCI, if several important grafts are occluded, or in the case of clear anastomotic errors. In asymptomatic patients, repeat revascularisation should be considered if the artery is of appropriate size and supplies a large territory of myocardium.

Further details on diagnosis and management of perioperative MI is provided in a recent ESC Position Paper.[329]

13.2 Acute percutaneous coronary intervention failure

The need for urgent surgery to manage PCI-related complications is uncommon (< 1%) and only required in patients with major complications that cannot be adequately resolved by percutaneous techniques.[330, 331] The need for emergency CABG is mainly confined to patients with a large, evolving MI due to iatrogenic vessel occlusion that cannot be salvaged percutaneously, or in patients with recurrent cardiac tamponade after pericardiocentesis following PCI-related vessel rupture.[330, 332, 333]

13.3 Disease progression and late graft failure

Ischaemia after CABG may be due to progression of disease in native vessels or *de novo* disease of bypass grafts.[334] Repeat revascularisation in these patients is indicated in the presence of significant symptoms despite medical treatment, and in asymptomatic patients with objective evidence of large myocardial ischaemia (> 10% of the LV).[32, 87]

Re-do coronary artery bypass grafting or percutaneous coronary intervention

PCI in patients with prior CABG has worse acute and long-term outcomes than in patients without prior CABG.[335, 336] Likewise, redo CABG has a two- to four-fold increased mortality compared with first-time CABG and repeat CABG is generally performed infrequently.[334, 337-339] There are limited data comparing the efficacy of PCI vs. redo CABG in patients with previous CABG. The proportion of patients undergoing PCI, redo CABG, or conservative treatment differs significantly between studies; in one study PCI was favoured in about 50% of patients with only 22% undergoing redo CABG, while another study favoured CABG in 67% of patients.[340, 341] In the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) RCT and registry, overall 3-year mortality was comparable between redo CABG and PCI.[341, 342] A more recent study also found comparable rates of death and MI between redo CABG and PCI, although there were significantly more repeat revascularisations with PCI.[341, 343]

In view of the higher risk of procedural mortality with redo CABG and the similar long-term outcome, PCI is the preferred revascularisation strategy in patients with amenable anatomy.[340] PCI via the bypassed native artery should be the preferred approach. If PCI in the native vessel fails or is not an option, PCI in the diseased SVG should be considered. CABG should be considered for patients with extensively diseased or occluded bypass grafts and diffuse native vessel disease, especially in the absence of patent arterial grafts.[340] The IMA is the conduit of choice for revascularisation during re-do CABG if not previously used, or can be salvaged and reused in specific cases.[344, 345]

Percutaneous coronary intervention for saphenous vein graft lesions

PCI in SVGs is associated with an increased risk of distal coronary embolisation, frequently resulting in periprocedural MI.[346] PCI of *de novo* SVG stenosis is considered a high-risk intervention because SVG atheroma is friable and more prone to distal embolisation. Several different approaches have been evaluated to prevent distal embolisation of particulate debris, including distal occlusion/aspiration, proximal occlusion, suction, filter devices or covered stents. Distal protection devices using filters have shown the most encouraging results. However, although a single Randomised trial supports the use of distal embolic protection during SVG PCI, observational studies including data from large-scale registries are conflicting.[347-349]

Outcomes from studies with other devices used for SVG PCI is not sufficient to recommend use. [350-353]

Based on data from a small number of randomised trials, implantation of DES in SVG lesions is associated with a lower risk of repeat revascularisation than with BMS at 1 year follow-up.[354-356] In the only trial powered for a clinical endpoint—the Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts (ISAR-CABG) trial[354]—the primary endpoint of death, MI and target lesion revascularisation was significantly reduced with DES vs. BMS. Longer-term follow-up of the two smaller trials is available; one suggested sustained superiority of DES over BMS, while the other suggested loss of efficacy advantage of the DES.[357, 358]

13.4 Repeat percutaneous coronary intervention

Recurrence of symptoms or ischaemia after PCI is the result of restenosis, incomplete initial revascularisation, or disease progression.[334] Patients may require repeat PCI due to late and very late stent thrombosis.

Restenosis

Restenosis associated with angina or ischaemia should be treated by repeat revascularisation, and repeat PCI remains the strategy of choice for most of these patients. In this setting, the results from DES are superior to those obtained with balloon angioplasty, BMS implantation or brachytherapy.[359-363]

For restenosis within BMS, drug-coated balloon (DCB) proved superior to plain balloon angioplasty[364-366] and comparable to first generation DES.[364, 365, 367-371] One trial showed inferior angiographic outcomes in comparison to new generation DES,[372] while a second trial showed comparable outcomes.[373] For restenosis within DES, DCB also proved superior to plain balloon angioplasty[366, 368, 370] and comparable to first generation DES.[370] In one study, DCB were inferior to new generation DES in terms of the primary angiographic outcome measure.[374] In a more recent study, including patients with any type of in-stent restenosis, outcomes between DCB and repeat stenting with new generation DES were comparable.[375] A single Randomised trial of patients undergoing DCB for restenosis within DES showed superior angiographic outcomes in patients who underwent lesion preparation with scoring

balloon versus standard angioplasty balloons.[376]

Network meta-analysis suggest that repeat stenting with new generation DES (with EES) and DCB are ranked first and second as the highest efficacy treatments.[377, 378] The superior angiographic anti-restenotic efficacy of new generation DES should be weighed against a possible excess of long-term adverse events with repeat stenting during longer-term follow-up of these trials.[379, 380] However, observations in relation to clinical events must be interpreted with caution as none of the trials were powered for clinical endpoints and the comparator stent in studies with long-term follow-up was an early generation DES.

The use of intracoronary imaging provides unique insights into the underlying mechanisms of in-stent restenosis (see **Chapter 16.2**). OCT is able to detect the presence of neoatherosclerosis in a significant number of these patients. Underexpanded stents should be aggressively tackled with high-pressure dilatations using non-compliant balloons. Optimising final results remains crucial during reinterventions for in-stent restenosis and, in this regard, the use of intracoronary imaging may be particularly helpful. Outcomes of patients with in-stent restenosis after DES are poorer than those in patients with BMS in-stent restenosis, independently of the therapeutic modality.[381] In patients with recurrent episodes of diffuse in-stent restenosis in large vessels—and in those with associated multivessel disease, especially in the presence of other complex lesions such as chronic total occlusions—CABG should be considered before a new PCI attempt.

Disease progression

Patients with symptomatic disease progression after PCI account for up to 50% of re-interventions.[382, 383] They should be managed using criteria similar to those applied to patients without previous revascularisation.

Stent thrombosis

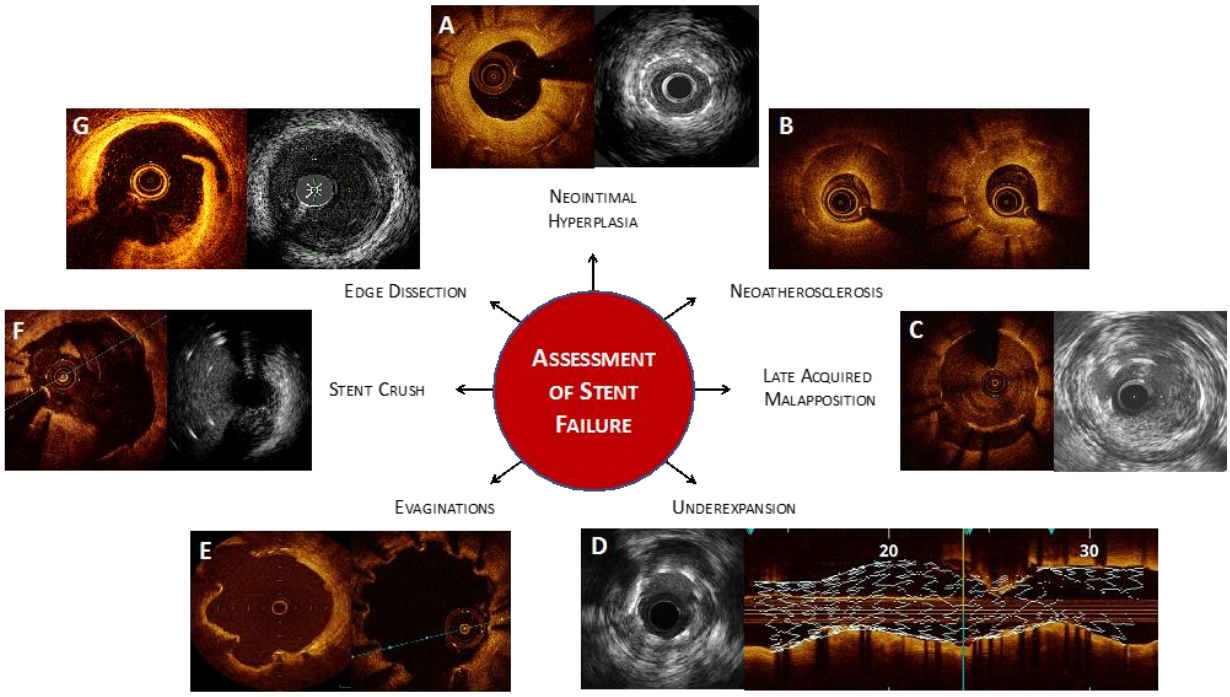
Although stent thrombosis is very rare, particularly since the advent of new-generation DES, it may have devastating clinical consequences. Stent thrombosis usually presents as a large MI and patients should be treated according to the principles outlined in **Chapter 8**.[384] Aggressive, high-pressure balloon dilation should

be used to correct underlying, stent-related, predisposing, mechanical problems.[385, 386] Liberal use of intracoronary imaging in order to detect and modify underlying mechanical factors is recommended (**Figure 7**)(see **Chapter 16.2**).

Although repeat stenting in patients with stent thrombosis may be avoided when satisfactory results are obtained with balloon dilation, a new stent may be required to overcome edge-related dissections and adjacent lesions or to optimise final results.[387]

There is no evidence that the post-interventional management of patients with stent thrombosis should differ from that of patients with thrombosis of a *de novo* lesion resulting in STEMI.

Figure 7 Intracoronary Imaging for the Assessment of Stent Failure



Recommendations on repeat revascularisation

Recommendations	Class[a]	Level[b]
Early postoperative ischaemia and graft failure		
Coronary angiography post-CABG is recommended for patients with: • symptoms of ischaemia and/or abnormal biomarkers suggestive of perioperative myocardial infarction • ischaemic ECG changes indicating large area of risk • new significant wall motion abnormalities • haemodynamic instability.	I	C
It is recommended to decide for either emergency reoperation or PCI by *ad hoc* consultation in the Heart Team and based on feasibility of revascularisation, area at risk, comorbidities and clinical status.	I	C
Disease progression and late graft failure		
Repeat revascularisation is indicated in patients with large area of ischaemia or severe symptoms despite medical therapy [32, 334].	I	B
If considered safe, PCI should be considered as first choice over CABG	IIa	C
CABG		
IMA is the conduit of choice for redo CABG in patients in whom the IMA was not used previously [344].	I	B
Redo CABG should be considered for patients without a patent IMA graft to the LAD [340, 341, 344].	IIa	B
PCI		
Distal protection devices should be considered for PCI of SVG lesions[348, 350, 351]	IIa	B
PCI of the bypassed native artery should be considered over PCI of the bypass graft.	IIa	C
Restenosis		
DES are recommended for the treatment of in-stent restenosis of BMS or DES. [372, 374, 377, 378]	I	A

Drug-coated balloons are recommended for the treatment of in-stent restenosis of BMS or DES. [372, 374, 377, 378]	I	A
In patients with recurrent episodes of diffuse in-stent restenosis, CABG should be considered by the Heart Team over a new PCI attempt.	IIa	C
IVUS and/or OCT should be considered to detect stent-related mechanical problems leading to restenosis.	IIa	C

BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; ECG = electrocardiogram; IMA = internal mammary artery; LAD = left anterior descending artery; PCI = percutaneous coronary intervention; SVG = saphenous vein graft. OCT = optical coherence tomography. IVUS = intravascular ultrasound.

[a] Class of recommendation

[b] Level of evidence.

14. Arrhythmias

14.1 Ventricular arrhythmias

14.1.1 Revascularisation for prevention of sudden cardiac death in patients with stable coronary artery disease and reduced left ventricular function

Revascularisation plays an important role in reducing the frequency of ventricular arrhythmias in patients with normal or mildly reduced LV function[388, 389] as well as the risk for sudden cardiac death in patients with CAD and LVEF ≤ 35%.[390] An indirect evidence for a protective effect of revascularisation is demonstrated in the MADIT II (Multicenter Automatic Defibrillator Implantation Trial II) and SCD HEFT studies (Sudden Cardiac Death in Heart Failure Trial), where the efficacy of cardioverter defibrillator implantation (ICD) is reduced if revascularisation is performed prior to implantation.[391, 392] Coronary artery bypass surgery in patients with reduced ejection fraction reduces cardiac and overall mortality for a follow-up of 10 years.[78, 81] In view of the protective effect of revascularisation on ventricular arrhythmias, patients with ischaemic LV dysfunction (LVEF ≤ 35%), who are considered for primary preventive ICD implantation should be evaluated for ischaemia and/or for potential revascularisation targets.

14.1.2 Revascularisation for treatment of electrical storm

Electrical storm is a life-threatening syndrome related to incessant ventricular arrhythmias, which is most frequently observed in patients with ischaemic heart disease, advanced systolic HF, valve disease, corrected congenital heart disease,

and genetic disorders such as Brugada syndrome, early repolarization and long QT syndromes.[393] Urgent coronary angiography and revascularisation should be part of the management of patients with electrical storm, as well as antiarrhythmic drug therapy and/or ablation of ventricular tachycardia.

14.1.3 Revascularisation after out-of-hospital cardiac arrest

Approximately 70% of survivors of out-of-hospital cardiac arrest have CAD, with acute vessel occlusion observed in 50%.[394] Multiple non-randomised studies suggest that emergency coronary angiography and, if appropriate, PCI after out-of-hospital cardiac arrest yields a favourable survival rate of up to 60% at 1 year, which is considerably higher than the 25% overall survival rate in patients with aborted cardiac arrest.[395, 396] More recent data suggest that almost one-quarter of patients, resuscitated from cardiac arrest but without ST-segment elevation, show a culprit lesion (either vessel occlusion or irregular lesion).[397-400] Recent, large-scale, observational studies have showed an impact on mortality of early angiography after out-of-hospital cardiac arrest.[401, 402] Thus, in survivors of out-of-hospital cardiac arrest, early coronary angiography and PCI, if appropriate, should be performed irrespective of the ECG pattern if no obvious non-cardiac cause of the arrhythmia is present.[403]

14.2 Atrial arrhythmias

The management of atrial fibrillation in patients with ischaemic heart disease is addressed by the 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS.[404] After reviewing the subsequent literature, the current task force endorses the Recommendations of the 2016 guidelines and does not identify the need for any major update. Accordingly, the current recommendations tables are taken from this guideline. For a detailed discussion, we refer to the previous guideline.[404]

14.2.1 Atrial fibrillation complicating percutaneous coronary intervention

New-onset AF in patients undergoing PCI occurs in 2–6% of procedures and increases with age, pre-existing HF, AMI and arterial hypertension.[405-408] Notably, new-onset AF (defined as change from sinus rhythm (SR) at admission to AF during/after PCI) typically occurs during the first 4 days after AMI and is associated

with impaired prognosis and a more than doubling the risk of death, CHF and stroke[403].

The use of oral anticoagulation (OAC) for stroke prevention in patients with AF occurring during or after PCI should follow the guidelines for antithrombotic treatment of AF that occurs outside the setting of PCI,[404] although prospective studies are scarce. The combination and duration of anticoagulation and antiplatelet therapy should be assessed according to the clinical situation, as outlined in **Chapter 17** as well as in the ESC Guidelines on Atrial Fibrillation[404] and ESC Focused Update on Dual Antiplatelet Therapy.[409]

14.2.2 Atrial fibrillation complicating coronary artery bypass grafting

Postoperative AF affects one-third of patients undergoing cardiac surgery[410-413] The main risk factor for postoperative AF is age, and it is associated with an increased immediate risk of stroke, increased morbidity and 30-day mortality.[414-416] In the long-term, patients with an episode of postoperative AF have a two-fold increase in cardiovascular mortality and a substantially increased risk of future AF and ischaemic stroke compared to patients who remain in SR after surgery. [415, 417-421]

Postoperative AF is a common complication, in which prophylactic treatment has a moderate effect. Preoperative anti-arrhythmic drug treatment may be initiated but will have to be weighed against side-effects. Beta-blockers decrease the incidence of postoperative AF after CABG.[411, 422-428]

14.2.3 Post-operative atrial fibrillation and stroke risk

Patients with postoperative AF have an increased stroke risk postoperatively as well as during follow-up,[418, 429] and warfarin medication at discharge has been associated with a reduced long-term mortality.[430] There are to date no studies indicating that postoperative AF is less harmful than any other form of AF, and good quality data are needed. Anticoagulation treatment with warfarin or non-vitamin K antagonist oral anticoagulants (NOAC) for stroke prevention in patients with postoperative AF should therefore follow the guidelines for antithrombotic treatment of AF occurring outside the setting of CABG using the CHA_2DS_2-VASc Score. The duration and timing of OAC in postoperative AF patients should be assessed individually.

Whether surgical left atrial appendage (LAA) obliteration reduces stroke risk has been studied in smaller trials and registry studies, with conflicting results, [431-433] and is currently under investigation in a large randomised trial.[434] Removal or closure of the LAA should be considered as an adjunct to anticoagulation and not as an alternative until more data are available.

Recommendations for prevention of ventricular arrhythmias by revascularisation

Recommendations	Class[a]	Level[b]
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an ECG consistent with STEMI.[394, 396, 435, 436]	I	B
Urgent angiography (and PCI if indicated) should be considered in patients with resuscitated cardiac arrest without diagnostic ST-segment elevation but with a high suspicion of ongoing myocardial ischaemia.	IIa	C
In patients with electrical storm urgent coronary angiography and revascularisation as required should be considered.	IIa	C

ECG = electrocardiogram; STEMI = ST-elevation myocardial infarction; PCI = percutaneous coronary intervention

[a]Class of recommendation.

[b]Level of evidence

Recommendations for prevention and treatment of atrial fibrillation in the setting of myocardial revascularisation

Recommendations	Class[a]	Level[b]
Peri-operative oral beta-blocker therapy is recommended for the prevention of postoperative AF after CABG surgery. [411, 437]	I	B

Restoration of sinus rhythm by electrical cardioversion or antiarrhythmic drugs is recommended in postoperative AF with haemodynamic instability.	I	C
Peri-operative amiodarone should be considered as prophylactic therapy to prevent AF after CABG surgery [411, 438].	IIa	A
Long-term anticoagulation should be considered in patients with AF after CABG or PCI at risk for stroke, considering individual stroke and bleeding risk [439, 440].	IIa	B
Asymptomatic postoperative AF should initially be managed with rate control and anticoagulation [441].	IIa	B
Antiarrhythmic drugs should be considered for symptomatic postoperative AF after CABG or PCI in an attempt to restore sinus rhythm.	IIa	C
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing CABG surgery [431-433]	IIb	B

AF = atrial fibrillation; CABG = coronary artery bypass grafting; LAA = left atrial appendage; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

14.3 Gaps in evidence

The duration of anticoagulation and the combination with antiplatelet therapy in patients with new onset AF after PCI or CABG has not been studied sufficiently. Likewise, the role of routine left atrial exclusion at surgery for the prevention of stroke is currently unclear.

15. Procedural aspects of coronary artery bypass grafting

CABG remains the most common cardiac surgery procedure, and the techniques have been refined during 50 years of evolution.[442] Perioperative medication and blood management are covered in separate guidelines.[409, 443]

15.1 Surgical techniques

15.1.1 Completeness of revascularisation

The current surgical practice is largely based on an anatomical definition of complete revascularisation, and aims to bypass all epicardial vessels with a diameter

exceeding ≥ 1.5 mm and a luminal reduction of ≥ 50% in at least one angiographic view.[128] Depending on the definition of completeness of revascularisation, the outcome after CABG in patients with incomplete revascularisation was either similar[444-448] or inferior[128, 129, 448-450] to that of patients with complete revascularisation. Certainly, in some patients with a stenosis in small vessels with little myocardium at risk, complete revascularisation may not be necessary.

FFR-guided surgical revascularisation has been associated with improved graft patency, but more studies are needed to investigate whether it improves clinical outcomes. [28, 451] Further discussion on FFR-guided revascularisation is provided in **sections 3.2.1.1 and 5.3.1.1**.

15.1.2 Conduit selection

In addition to patient related factors, the outcome following CABG is related to the long-term patency of grafts and therefore is maximized with the use of arterial grafts, specifically the internal mammary artery (IMA).[452, 453] Except in rare circumstances, all patients should receive at least one arterial graft—the LIMA— preferentially to the LAD.[452, 454] Saphenous vein graft (SVG) patency rates for non-LAD targets has been reported to be suboptimal.[455] Bilateral internal mammary artery (BIMA) and radial artery (RA) for non-LAD targets have been shown to provide better patency rates than SVG in particular for the left coronary artery system.[456] A second arterial graft should, therefore, be considered depending on patient's life expectancy, risk factors for sternal wound complications, coronary anatomy, degree of target vessel stenosis, graft quality and surgical expertise.

The question whether the use of additional arterial grafts can translate into prolonged survival remains debated. Data from non-randomised studies suggest that the use of BIMA over single internal mammary artery (SIMA) use is associated with improved long-term survival, as well as fewer non-fatal events such as MI, recurrent angina, and need for re-operation.[457-464] However, observational studies are subject to selection bias, despite propensity matching, and the effect of a prolonged survival with additional arterial grafts has not been confirmed in randomized trials.[465]

The ART trial has been designed to answer the question whether BIMA can improve

10-year survival when compared to SIMA. Interim analysis showed no difference at 5 years in the rate of death or the composite of death, myocardial infarction or stroke and 10-year results are warranted to draw final conclusions.[466] Limitations of the ART trial include a high cross over rate from the BIMA arm to the SIMA arm and a high rate of radial artery use in the SIMA arm that may have deluded the benefit of BIMA.[467-469] The use of BIMA grafting is associated with an increase in sternal dehiscence and increased rate of mediastinitis in obese patients and patients with diabetes.[457, 463, 470-474] In the ART trial the use of BIMA was associated with a 1.0%-1.5% absolute risk increase in the need for sternal would reconstruction and a subsequent sub-analysis has found that this risk is minimised with skeletonised harvesting.[475] Awaiting the 10-year data of the ART trial, currently, BIMA grafting should be considered in patients with a reasonable life expectancy and a low risk of sternal wound complication.

The radial artery constitutes an alternative as the second arterial graft in patients in whom BIMA grafting is not feasible, patients with a high risk of sternal wound complications, or as third arterial graft. There is a strong, adverse influence on radial artery patency when the native coronary artery stenosis is < 70% and therefore its use should be limited to coronary artery stenosis>70% and ideally >90%.[476] Use of the radial artery as the second conduit of choice has been linked to improved survival in registry studies,[477-479] Available RCTs testing the radial artery vs saphenous vein graft used angiographic patency as primary endpoint and none was powered to detect difference in clinical outcomes.[480] A recently published patient-level meta-analysis pooling all RCTs comparing radial artery vs saphenous vein graft showed that the use of radial artery was associated with a lower rate of adverse cardiac event at mid-term mainly driven by a significant reduction of need for reintervention and subsequent MI.[481]

15.1.3 Mammary artery harvesting

While the skeletonized technique of harvesting the IMA has a higher theoretical potential for injury, the potential benefits include a longer conduit, more versatility (sequential anastomosis), higher blood flow and fewer wound healing problems.[470, 482-487] Therefore, in patients at higher risk of sternal wound complications,

skeletonization is recommended.

15.1.4 Radial artery harvesting

RA harvesting is associated with negligible morbidity. Endoscopic radial harvesting is possible but robust evidence concerning its safety and efficacy is scarce.[488, 489] Use of the radial artery after recent coronary angiography with radial access should be discouraged due to potential endothelial damage.[490]

15.1.5 Saphenous vein harvesting

Saphenous vein harvest can be accomplished using open and minimally invasive techniques, which include interrupted incisions and partial or full endoscopic procedures. Endoscopic vein graft harvesting leads to a reduced rate of leg wound complications,[491-494] but the short- and long-term patency of endoscopically harvested vein grafts, compared with openly harvested grafts, has been challenged.[455, 495-497] Although there is no unequivocal evidence concerning patency rates, most data from meta-analyses and randomised and non-randomised trials do not demonstrate inferior clinical outcomes with endoscopic vein harvest.[491, 492, 498, 499] If an endoscopic vein graft harvest is performed, it should be undertaken by experienced surgeons or physician assistants with appropriate training and reasonable caseload.[500-502] If an open technique is used, the ‘no-touch’ technique has shown superior patency rates in multiple randomised trials,[503-506] with a patency rate >80% after 16 years.[506]

15.1.6 Construction of central anastomosis

A single cross-clamp technique may be preferred to multiple manipulations of the aorta, with the aim of reducing atheroembolic events, but a strict no-touch technique most effectively reduces embolization of atherosclerotic material.[507-509] In cases of off-pump surgery, devices that allow a clampless procedure may help reduce incidences of cerebral vascular complications.[510, 511]

15.1.7 Intraoperative quality control

Besides continuous ECG monitoring and transoesophageal echocardiography immediately after revascularisation, intraoperative quality control may also include graft flow measurement to confirm or exclude a technical graft problem.[512] Transit-time flow measurement is the most frequently used technique for graft assessment

and has been able to detect 2−4% of grafts that require revision. [512, 513] In observational studies, the use of intraoperative graft assessment has been shown to reduce the rate of adverse events and graft failure, although interpretation can be challenging in sequential and T-graft configurations.[512, 514-516]

15.1.8 On-pump and off-pump procedures

Two large, international, randomised trials have shown no difference in 30-day or 1-year clinical outcomes between on- and off-pump surgery, when performed by experienced surgeons.[517-519] There is also evidence to conclude that, for most patients and surgeons, on-pump surgery provides excellent short- and long-term outcomes.[517, 519-522] For some surgeons, off-pump surgery is associated with inferior early and late graft patency rates and possibly compromised long-term survival; however, aortic no-touch/clampless off-pump procedures in the hands of highly trained teams appear to be associated with a reduced risk of early morbidity, such as stroke, and fewer transfusions.[507-509, 523-527] In the subgroup of patients with end-stage CKD, there is some evidence that off-pump surgery is associated with lower in-hospital mortality and less need for new renal replacement therapy.[528]

15.1.9 Minimally invasive and hybrid procedures

Minimally invasive coronary surgery with LIMA, harvested either directly or under video-assisted vision, may represent an attractive alternative to a sternotomy.[529] It has a similar safety and efficacy profile to conventional on-pump and off-pump procedures, with markedly reduced postoperative length of stay and an early quality-of-life benefit, although spreading of the ribs is associated with increased postoperative pain.[530-532] It has been shown to be safe and effective in the treatment of proximal LAD stenosis or chronically occluded LAD arteries.[144] Moreover, when compared to PCI in a setting of single vessel proximal LAD disease, minimally invasive coronary surgery was associated with less need for coronary re-intervention.[143, 533, 534] When combined with PCI to non-LAD vessels, it provides the opportunity to perform hybrid coronary revascularisation in selected patients with multivessel disease.[535]

Hybrid revascularisation can be performed consecutively in a hybrid operating room, or sequentially on separate occasions in the conventional surgical and PCI

environments.[536-539] In a small randomised trial of 200 patients, 1-year and 5-year rates of death, MI, stroke and major bleeding or repeat revascularisation were not significantly different between hybrid revascularisation and CABG. [535] [540] Heart Team discussion and the prospective planning of a joint strategy are critical for the success of a hybrid revascularisation strategy.[541]

15.2 Reporting perioperative outcome

Perioperative reporting of outcome after CABG procedures should be done on a risk-adjusted basis. The early risk period after CABG extends up to 3 months, is multifactorial, and depends on the interface between technical variability and patient comorbidity.[542]

15.3 Gaps in evidence

The role of FFR and iFR in guiding surgical revascularisation needs further investigation whether it improves clinical outcomes. Likewise, there is insufficient data on the impact of intraoperative assessment of graft flow on outcomes.

In view of the limitations of observational studies comparing BIMA with SIMA and the limitations of the ART trial, the ROMA trial is recruiting to answer the question whether the use of additional arterial conduits (either BIMA or RA) translates into superior clinical outcomes when compared to SIMA supplemented by SVG only.

Hybrid procedures, which combine minimally invasive arterial grafting with percutaneous coronary intervention proved feasible and safe. However, multicenter studies are required to prove the efficacy and superiority of this approach in stable, multivessel coronary disease.

Recommendations on procedural aspects of coronary artery bypass grafting

Recommendations	**Class[a]**	**Level[b]**
GENERAL CONSIDERATIONS		
Minimization of aortic manipulation is recommended [507, 508, 543, 544].	I	B
CT scans of the ascending aorta should be considered in patients	IIa	C

over 70 years of age and/or with signs of extensive generalized atherosclerosis.		
Complete myocardial revascularisation should be considered[c] [128, 129].	IIa	B
Routine intraoperative graft flow measurement should be considered [515, 516].	IIa	B
Prior to aortic manipulation, epi-aortic ultrasound should be considered identify atheromatous plaques and select the optimal surgical strategy	IIa	C
CONDUIT SELECTION		
Arterial grafting with IMA to the LAD system is recommended [452, 453, 545].	I	B
An additional arterial graft should be considered in appropriate patients [546-551] [481, 547, 551, 552]	IIa	B
Use of the radial artery is recommended over saphenous vein in patients with high-degree stenosis [d] [481, 548, 549, 553, 554]	I	B
BIMA grafting should be considered in patients who do not have a high risk of sternal wound infection[d] [546, 547, 550, 551]	IIa	B
VESSEL HARVESTING		
Skeletonized IMA dissection is recommended in patients with a high risk of sternal wound infection[d] [470, 483, 484].	I	B
Endoscopic vein harvesting, if performed by experienced surgeons, should be considered to reduce the incidence of wound complications [489, 492, 493, 499, 555].	IIa	A
No-touch vein harvesting should be considered, when an open technique is used [505, 506, 556, 557].	IIa	B
MINIMALLY INVASIVE TECHNIQUES		
Off-pump CABG and preferably no-touch techniques on the ascending aorta, by experienced operators, are recommended in patients with significant atherosclerotic aortic disease [507, 508, 543, 558-560]	I	B
Off-pump CABG should be considered for subgroups of high-risk patients by experienced off-pump teams [524, 558-561].	IIa	B
Where expertise exists, minimally invasive CABG through limited thoracic access should be considered in patients with isolated LAD	IIa	B

lesions or in the context of hybrid revascularisation [143, 533, 534, 562].		
Hybrid procedures, defined as consecutive or combined surgical and percutaneous revascularisation, may be considered in specific patient subsets at experienced centres [562-565].	IIb	B

CABG = coronary artery bypass grafting; CT = computed tomography; IMA = internal mammary artery; BIMA = bilateral internal mammary artery. LAD = left anterior descending coronary artery.

[a]Class of recommendation.

[b]Level of evidence.

[c]Definitions of complete revascularisation are provided in section 5.3.1.3.

[d]Patients with diabetes mellitus, chronic pulmonary obstructive disease, previous mediastinal radiation, and obesity, particularly when multiple of these are present.

16. Procedural aspects of percutaneous coronary intervention

16.1 Percutaneous coronary intervention devices

16.1.1 Balloon angioplasty

Plain balloon angioplasty has been superseded in the treatment of *de novo* coronary lesions after demonstration of the superiority of stenting in terms of requirement for repeat revascularisation.[566] Balloon angioplasty might be considered for the treatment of selected patients in whom implantation of stents is not technically feasible, or in a vessel that is considered too small to be stented. Balloon angioplasty is no longer preferred to stenting with DES for patients who require urgent non-cardiac surgery as short duration DAPT may be reasonable with both strategies.[567, 568]

16.1.2 Choice of coronary stents

Stenting with BMS results in approximately 30% lower rate of restenosis in comparison with plain balloon angioplasty.[566] Although many efforts have been made to further reduce restenosis by modification of stent design and materials, reducing the thickness of stent struts has been the only proven modification capable of a reduction in restenosis of BMS.[569, 570]

A major reduction in the risk of restenosis has been achieved with DES technology. Early-generation DES released sirolimus[571] or paclitaxel[572] from a permanent

polymer matrix coating on a relatively thick strut (120–140 µm) stainless steel backbone. These devices reduced angiographic and clinical restenosis by approximately 50–70%, but increased the risk of very late stent thrombosis compared with BMS.[336, 573]

Early-generation DES have now been supplanted by new-generation DES. These stents represented an iterative development of early generation technology, including polymers with enhanced biocompatibility (permanent or biodegradable), exclusively sirolimus-analogue active drugs, and stent backbones with thin struts (50–100 µm) composed of stainless steel, cobalt chromium or platinum chromium. [574-579] New-generation DES have higher efficacy and safety in comparison with both early generation DES and BMS.[336, 573, 580] Although stenting with new-generation DES confers a similar risk of death or MI at mid- to long-term follow-up in comparison with BMS,[581] the risk of subacute and late stent thrombosis is significantly lower.[581, 582] Moreover, the risk of very late stent thrombosis is at least comparable to that of BMS and lower than that of early generation DES.[336, 573, 581, 582] These observations were conformed in a recent trial enrolling patients aged 75 years or older and demonstrating superior outcomes (composite of all-cause mortality, myocardial infarction, stroke, or ischaemia-driven target lesion revascularisation) with DES as compared with BMS with similar duration of intended DAPT (1 month or 6 month) in both treatment arms.[583] Similarly, there is no clear evidence of a difference between DES and BMS in the risk of stent thrombosis following unplanned disruption of DAPT.[567] Accordingly, new-generation DES should be preferred to BMS for routine use.

A large number of new-generation DES have received approval for use and CE mark in Europe.[580] **Supplementary Table 6** displays a list of new-generation DES with the CE mark, supported by evidence from large-scale clinical trials powered for clinical primary endpoints.

Biodegradable polymer and polymer-free DES offer the potential to reduce late adverse events after PCI by eliminating inflammatory reactions to permanent polymer coatings. A number of large-scale trials showed comparable efficacy and safety compared with permanent polymer stents.[577, 578, 584-592] However, at the moment,

there is no evidence of differential efficacy with new generation biodegradable polymer in comparison with new generation permanent polymer DES in large-scale randomised trials with follow-up out to 5 years. [593-596]

Regarding polymer-free DES, two large-scale trials with different devices showed comparable results with new generation DES and superior results to BMS.[166, 579] Long-term follow-up from randomised trials vs. new generation permanent polymer DES is only available for a single device and shows comparable outcomes between the devices.[593]

The high clinical efficacy and safety of new-generation DES support their preferred use in patients with an indication for PCI, including patients with diabetes, CKD, multivessel and left main stem (LMS) disease, AMI, vein grafts, restenotic lesions, and chronic total occlusions. New-generation DES should therefore be considered as the default stent type for PCI regardless of clinical presentation, lesion subtype, concomitant therapies or comorbidities.

16.1.3 Bioresorbable scaffolds

Completely bioresorbable scaffolds (BRS), which degrade to predominantly inert end products after fulfilling their scaffold function in the lesion site of the coronary vessel, have been developed with the goal of reducing or eliminating stent-related adverse events at long-term follow-up. Current scaffold platforms to have reached clinical testing are based on two different technologies: bioresorbable, polymer-based scaffolds (resorption up to 3–4 years) and resorbable, metallic (magnesium) scaffolds (resorption up to 1 year).[597] Although a number of devices have received approval for use in Europe (see **Supplementary Table 7**), randomised trial data are available only with the Absorb bioresorbable vascular scaffold (Absorb BVS, Abbott Vascular).

The safety and efficacy profile of Absorb BVS has been compared with contemporary DES in several trials. Findings of these trials as well as meta-analyses consistently indicate inferior efficacy and safety of Absorb BVS as compared with contemporary DES during long-term follow-up. Specifically, the Absorb BVS is associated with a significantly increased risk of target-lesion revascularisation and device thrombosis, with numbers needed to harm of 40–60.[598, 599] Of note, commercial use of Absorb

BVS was stopped in 2017 (for additional details see web addenda).

Available evidence on the magnesium scaffold is limited to small observational studies. Initial results appear encouraging, but further evaluation is needed. Therefore, the Task Force endorses the recommendation of the recent ESC/EAPCI document on bioresorbable scaffolds that any BRS should not be used outside well-controlled clinical studies. In patients who have been treated with BRS prolonged duration DAPT out to 3 years or longer may be considered.

16.1.4 Drug-coated balloons

The rationale for using DCB is based on the concept that with highly lipophilic drugs even short contact times between the balloon surface and the vessel wall are sufficient for effective drug delivery. There are various types of DCB approved for use in Europe and their main characteristics are listed in **Supplementary Table 8**. Although specifically designed comparative randomised trials are lacking, a class effect for all drug-coated balloons cannot be assumed.[600] Randomised trial data supporting the use of DCB angioplasty are limited to the treatment of in-stent restenosis (see **Chapter 13.4**). In terms of the use of DCB angioplasty for *de novo* disease, a number of small randomised trials have been reported with somewhat conflicting results.[601-603] At present, there are no convincing data to support the use of DCB angioplasty for this indication.

16.1.5 Devices for lesion preparation

Lesion preparation is critical for successful PCI. In addition to plain balloon angioplasty (with standard or non-compliant balloons), cutting or scoring balloon angioplasty or rotational atherectomy may be required in selected lesions—particularly those with heavy calcification—in order to adequately dilate lesions prior to stent implantation. However, studies investigating the systematic use of these adjunctive technologies such as rotational atherectomy have failed to show clear clinical benefit.[604]

16.2 Invasive imaging tools for procedural guidance

16.2.1 Intravascular ultrasound

The majority of existing clinical trial data relates to the use of IVUS guidance during

PCI. In the BMS era several RCTs addressed the potential of IVUS in reducing restenosis and adverse events after stenting, with somewhat conflicting results. Findings from one meta-analysis of randomised trials suggested better outcomes with IVUS guidance in terms of acute procedural results and reduced angiographic restenosis, repeat revascularisation and MACE, with no effect on death and MI.[605, 606] In the DES era, meta-analysis of randomised and observational studies also suggests better clinical outcomes with IVUS-guided vs. angiography-guided PCI.[607, 608] However, the contribution of findings from observational studies must be weighed against the likelihood of considerable residual confounding due to treatment selection bias. Similarly, findings of improved outcome in patients undergoing LM stem PCI with IVUS-guided PCI vs. angiography-guided PCI from a propensity-score matched analysis must be interpreted cautiously.[35]

In cases of stent failure, including restenosis and stent thrombosis, the use of IVUS should be considered in order to identify and correct underlying mechanical factors (see **Chapter 13**).[385]

16.2.2 Optical coherence tomography

A number of studies have assessed OCT imaging for PCI guidance. Two observational studies show that OCT imaging changes operator behaviour but its impact on clinical outcomes is unclear.[609, 610] Indeed OCT is more accurate than angiography or IVUS in detecting subtle morphological details including malapposition, residual thrombus, plaque prolapse, and residual dissections, although many of these additional findings may have a benign course.[611, 612] A single randomised trial compared OCT with IVUS and coronary angiography and showed that OCT-guided PCI was safe and resulted in similar minimum stent area to that of IVUS-guided PCI.[613] However, OCT-guidance was not superior to either IVUS or angiography alone. An additional randomised trial that enrolled patients with NSTE-ACSI compared OCT-guided PCI with angiography-guided PCI and found no signal of impact on clinical outcomes.[614]

A number of observational studies have shown that OCT is feasible and safe in the assessment of stent failure due to thrombosis and may yield information that may be clinically useful.[385, 386, 615, 616] Likewise, in cases of in-stent restenosis, intrastent

neointimal tissue may be characterized by OCT, enabling for example the detection of neoatherosclerosis.[385, 617, 618] In cases of stent failure, the use of OCT should be considered in order to identify and correct underlying mechanical factors (see **Chapter 13**).

16.3 Specific lesion subsets

16.3.1 Bifurcation stenosis

A number of RCTs have investigated the optimal intervention strategy in patients with bifurcation lesions and showed no benefit for the systematic two-stent approach vs. main branch only stenting with provisional stenting of the side branch in terms of clinical outcomes.[619] A recent pooled analysis of two RCTs showed lower 5-year survival in patients randomised to a systematic two-stent approach.[620] In addition, procedure time, contrast volume, radiation exposure, and cost are higher with a two-stent approach.[620] The EBC TWO (European Bifurcation Coronary TWO) trial found no difference between a provisional T-stent strategy and a systematic two-stent strategy (culotte technique) in terms of the composite endpoint of death, MI, and TVR at 12 months among 200 patients with large calibre true bifurcation lesions (side branch diameter ≥ 2.5 mm) and significant ostial disease length (≥ 5 mm).[621] Thus, main branch only stenting with provisional stenting of the side branch should be the preferred approach for most bifurcation lesions. Exceptions to this rule, where upfront side branch stenting may be preferable, include the presence of a large side branch (≥ 2.75 mm) with a long ostial side branch lesion (> 5mm) or anticipated difficulty in accessing an important side branch after main branch stenting, and true distal LM bifurcations. Recently, a multicentre trial conducted in China directly compared a double-kissing crush 2-stent strategy with provisional stenting of the main branch in 482 patients with distal LM bifurcation disease. Double-kissing crush resulted in a lower risk of the primary endpoint target-lesion failure at 1 year as compared with provisional stenting.[622]

When a two-stent strategy is necessary, it is debated which two-stent technique should be preferred. The three most widely-used contemporary two-stent techniques are culotte, crush (classic or double-kissing crush), and T and protrusion (TAP).[623, 624, 625 626] Several RCTs compared these techniques. In non-LM bifurcation lesions, there is no compelling evidence that one technique is superior to the others in terms

of major clinical endpoints. [623, 624], [625 626] In LM true bifurcation lesions, double-kissing crush has the most favourable outcome data.[627]

Final 'kissing' balloon dilation is generally recommended when two stents are eventually required, with no advantage from final kissing with the one-stent technique.[628, 629] Several stents, designed specifically for treatment of bifurcation lesions, have undergone extensive evaluation with promising angiographic and clinical results, though RCTs against current recommended therapy are limited.[630] Further technical details in relation to bifurcation PCI are described in the consensus document of the European Bifurcation Club.[631]

16.3.2 Chronic total coronary occlusion

Dedicated RCTs examining outcomes of patients with chronic total occlusion (CTO) allocated to revascularisation or conservative therapy are lacking. One recent trial randomised patients with STEMI and CTO in a non-culprit vessel to CTO-PCI vs. conservative therapy and found no difference in the primary endpoint of LVEF and LV end-diastolic volume at 4 months.[632] A systematic review of 25 observational studies showed that at median follow-up of 3 years, successful CTO-PCI was associated with improved clinical outcomes in comparison with failed revascularisation, including overall survival, angina burden and requirement for bypass surgery.[633] Broadly speaking, treatment of CTOs may be considered analogous to the treatment of non-CTO lesions (see recommendations in **chapter 5**). In cases of regional wall motion abnormalities in the territory of the CTO, objective evidence of viability should be sought. The decision to attempt CTO-PCI should be considered against the risk of greater contrast volume, longer fluoroscopy time and higher MACE rates in comparison with non-CTO PCI patients.[634] *Ad hoc* PCI is generally not recommended for CTOs, although it may be necessary in selected cases (e.g. acute bypass graft failure not amenable to recanalization of the bypass graft).

Recent developments in catheter and wire technology and increasing operator expertise with both antegrade and retrograde approaches as well as wire escalation and dissection/re-entry techniques have translated into increasing success rates of CTO-PCI with low rates of MACE.[634-636] Success rates are strongly dependent on

operator skills, depending on experience with specific procedural techniques, and the availability of dedicated equipment, and vary from 60–70% to > 90%.[634-636]

16.3.3 Ostial lesions

In ostial coronary lesions, additional judgement and caution is essential before proceeding to PCI. In particular, a catheter-induced coronary spasm must be rigorously excluded. Lesion assessment with IVUS may be helpful, particularly in LM ostial stenosis. FFR measurement may also be valuable in the assessment of ostial lesions of borderline significance,[637] taking special care to avoid a wedge position of the guiding catheter and using i.v., rather than intracoronary, adenosine. When performing intervention, due to interaction between the guide catheter and the proximal stent edge, the risk of longitudinal stent deformation must be considered[638] and avoided with careful catheter manipulation. The accurate positioning of the stent, precisely in the coronary ostium, may be technically challenging and some specialized techniques that may help to achieve the optimal stent placement have been described.[639, 640]

16.4 Vascular access

A number of RCTs have compared radial access with femoral access for diagnostic angiography and PCI. The two largest were RIVAL (Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes) and Minimizing Adverse Haemorrhagic Events by Transradial access Site and Systemic Implementation of AngioX (MATRIX).[165, 641] In the RIVAL trial, which enrolled 7021 patients, the primary outcome of death, MI, stroke, or non-CABG-related major bleeding at 30 days occurred at a similar rate in radial vs. femoral access (HR 0.92, 95% CI 0.72 to 1.17; *P* =0.50).[641] In the MATRIX trial, 8404 ACS patients were randomly allocated to radial or femoral access.[165] In terms of the first co-primary endpoint of 30-day MACE, there was no significant difference between radial access and femoral access (RR 0.85, 95% CI 0.74 to 0.99; two-sided *P* =0.031; non-significant at a pre-specified alpha of 0.025). The second co-primary outcome of 30-day net adverse clinical events (MACE or non-CABG BARC (Bleeding Academic Research Consortium) major bleeding) was significantly lower with radial access (RR 0.83, 95% CI 0.73 to 0.96; *P* =0.009). Major BARC 3 or 5 bleeding was significantly reduced in the radial group (1.6% vs. 2.3%; RR 0.67, 95% CI 0.49 to

0.92; *P* =0.013) and radial access was associated with a lower risk of all-cause mortality (1.6% vs. 2.2%; RR 0.72, 95% CI 0.53 to 0.99; *P* =0.045). However, the benefit of radial over femoral access depends upon the operator's expertise in the radial technique.[642]

Treatment of restenotic and saphenous vein graft lesions are discussed in **Chapter 13.3**.

Recommendations on choice of stent and access site

Recommendations	Class[a]	Level[b]
DES are recommended over BMS for any PCI irrespective of: clinical presentation lesion type planned non-cardiac surgery anticipated duration of DAPT concomitant anticoagulant therapy [100, 580, 643, 644]	I	A
Radial access is recommended as the standard approach, unless there are overriding procedural considerations [165, 641, 645].	I	A
BRS are currently not recommended for clinical use outside clinical studies [646-654]	III	C

BMS = bare-metal stents; BRS = bioresorbable scaffolds; DES = drug-eluting stents; DAPT = dual antiplatelet therapy; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

Recommendations on intravascular imaging for procedural optimisation

Recommendations	Class[a]	Level[b]
IVUS or OCT should be considered in selected patients to optimise stent implantation [605, 614, 655-657].	IIa	B
IVUS should be considered to optimise treatment of unprotected left main lesions [35].	IIa	B

IVUS = intravascular ultrasound; OCT = optical coherence tomography.

[a]Class of recommendation.

[b]Level of evidence.

Recommendations on specific lesion subsets

Recommendations	Class[a]	Level[b]
Stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch, is recommended for PCI of bifurcation lesions [658-662].	I	A
Percutaneous revascularisation of CTOs should be considered in patients with angina resistant to medical therapy or with a large area of documented ischaemia in the territory of the occluded vessel [663-667].	IIa	B
In true bifurcation lesions of the left main, double-kissing crush technique may be preferred over provisional T-stenting.[622]	IIb	B

CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

17. Antithrombotic treatments

Antithrombotic treatment is mandatory in CAD patients undergoing myocardial revascularisation. Its choice, the combination, the time point of initiation and the treatment duration depend on the patient´s characteristics, co-morbidities, the clinical setting (elective revascularisation vs. ACS), and the mode (PCI vs. CABG) of revascularisation. Both ischaemic and bleeding events significantly influence the outcome of CAD patients and their overall mortality risk during and after myocardial revascularisation.[668] Thus, the choice of treatment should reflect ischemic and bleeding risk. The recommended drugs **(Figure 8)** and doses **(Table 7)** for

anticoagulant and antiplatelet drugs used in conjunction with myocardial revascularisation are summarized below.

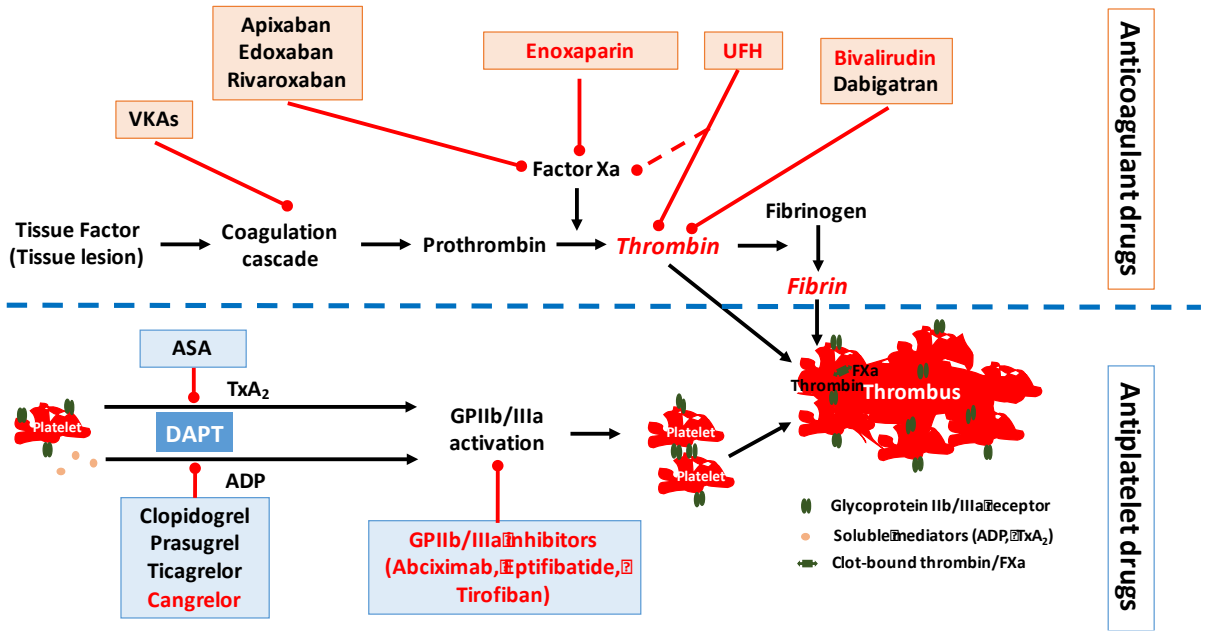


Figure 8: Antithrombotic treatment for myocardial revascularisation and its pharmacological targets. The figure illustrates anticoagulant and antiplatelet drugs being used during and after myocardial revascularisation (PCI or CABG). Drugs with oral administration are shown in black letters and drugs with preferred parenteral administration in red. ADP=adenosine diphosphate, ASA=acetylsalicylic acid, DAPT=dual antiplatelet treatment, FXa= Factor Xa, GP=glycoprotein, TxA2= Thromboxan A_2, UFH=unfractionated heparin.

Table 7 Doses of antiplatelet and anticoagulant drugs used during and after myocardial revascularisation

Antiplatelet drugs	
Aspirin	Loading dose of 150–300 mg orally or of 75–150 mg i.v. if oral ingestion is not possible, followed by a maintenance dose of 75–100 mg/day
Clopidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of 75 mg/day
Prasugrel	Loading dose of 60 mg orally, followed by a maintenance dose of 10 mg/day In patients with body weight <60 kg, a maintenance dose of 5 mg is recommended. In patients >75 years, prasugrel is generally not recommended, but a dose of 5 mg should be used if treatment is deemed necessary
Ticagrelor	Loading dose of 180 mg orally, followed by a maintenance dose of 90 mg b.i.d
Abciximab	Bolus of 0.25 mg/kg i.v. and 0.125 µg/kg/min infusion (maximum 10 µg/min) for 12 h
Eptifibatide	Double bolus of 180 µg/kg i.v. (given at a 10-min interval) followed by an infusion of 2.0 µg/kg/min for up to18 h
Tirofiban	Bolus of 25 µg/kg over 3 min i.v., followed by a an infusion of 0.15 µg/kg/min for up to 18 h
Cangrelor	Bolus of 30 µg/kg i.v. followed by 4 µg/kg/min infusion for at least 2 hours or duration of procedure, whichever is longer.
Anticoagulant drugs for PCI	
Unfractionated heparin (UFH)	70–100 U/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned 50–70 U/kg i.v. bolus with GP IIb/IIIa inhibitors
Enoxaparin	0.5 mg/kg i.v. bolus
Bivalirudin	0.75 mg/kg i.v. bolus followed by i.v infusion of 1.75 mg/kg/h for up to 4 h after the procedure as clinically warranted
Oral anticoagulant drugs (concomitant treatment after PCI)	
Vitamin K Antagonists (e.g. warfarin, phenprocoumon)	Dosing is based on INR value and the respective clinical indication
Apixaban	Maintenance doses of 5 and 2.5 mg b.i.d.
Dabigatran	Maintenance doses of 150 and 110 mg b.i.d.
Edoxaban	Maintenance dose of 60 and 30 mg/d
Rivaroxaban	Maintenance doses of 20 and 15 mg/d and 2.5 mg b.i.d (vascular dose)

17.1 Percutaneous coronary intervention in stable coronary artery disease

17.1.1 Choice of treatment and pretreatment

DAPT consisting of aspirin and a $P2Y_{12}$ receptor inhibitor represents the cornerstone of treatment in patients undergoing elective PCI.[669] The $P2Y_{12}$ receptor inhibitor

clopidogrel is recommended for elective stenting procedures. For a routine clopidogrel pretreatment (administration of the drug when the coronary anatomy is unknown), there is no compelling evidence for a significant clinical benefit in stable CAD patients.[670-672] Thus, pretreatment may only be an option in selected patients with high probability for PCI or before staged PCI procedures. **Figures 8 and 9** summarize the commonly used antiplatelet and anticoagulant drugs in stable CAD patients undergoing PCI.

17.1.2 Peri-interventional treatment

While aspirin and clopidogrel are indicated for elective stenting procedures, prasugrel or ticagrelor may only be considered in selected patients for specific high-risk situations of elective stenting (e.g. complex PCI procedures such as LM stenting, CTO procedures) or in patients with a history of stent thrombosis on clopidogrel treatment.

In parallel to antiplatelet treatment, the use of anticoagulants is standard of care during elective PCI to inhibit thrombin generation and activity. Different agents including unfractionated heparin (UFH) and bivalirudin have been evaluated for their use in clinical practice. The Randomised Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial demonstrated that the outcome with bivalirudin and provisional glycoprotein (GP) IIb/IIIa blockade is similar to that of UFH plus planned GP IIb/IIIa inhibition during elective PCI.[673] The ISAR-REACT (Intracoronary Stenting and Antithrombotic Regimen Rapid Early Action for Coronary Treatment) 3 trial also showed a similar outcome for bivalirudin vs. UFH treatment.[674] In ISAR REACT 3A[675], evaluating a lower dose of 100 U/kg UFH, this lower dose showed net clinical benefit compared to the historical control cohort and this benefit was mostly driven by a reduction in bleeding events. In view of the primary endpoint results of the randomised controlled trials and in view of a trend towards a lower risk of MI, UFH remains the standard anticoagulant for elective PCI. Based on the results of the Safety and Efficacy of Intravenous Enoxaparin in Elective Percutaneous Coronary Intervention Randomised Evaluation (STEEPLE) trial, enoxaparin should be considered as an alternative anticoagulant drug.[676]

Drugs for parenteral antiplatelet treatment include cangrelor and GP IIb/IIIa inhibitors. Cangrelor is a direct reversible, short-acting $P2Y_{12}$ inhibitor that has been evaluated during PCI for SCAD and ACS in clinical trials comparing cangrelor with clopidogrel, administered before PCI (CHAMPION (Cangrelor versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition) PCI) or after PCI (CHAMPION PLATFORM and CHAMPION PHOENIX).[677] A meta-analysis showed a benefit with respect to major ischaemic endpoints that is counter-balanced by an increase in relevant bleeding[677]. Moreover, the benefit of cangrelor with respect to ischaemic endpoints was attenuated in CHAMPION PCI with upfront administration of clopidogrel. Nevertheless, due to its proven efficacy in preventing intra-procedural and post-procedural stent thrombosis in $P2Y_{12}$-inhibitor naïve patients, cangrelor may be considered in $P2Y_{12}$ naïve patients undergoing PCI.

Available GP IIb/IIIa inhibitors include abciximab, eptifibatide and tirofiban. In a setting of elective PCI, clinical trials did not demonstrate an additional benefit of GP IIb/IIIa inhibitor administration in stable CAD patients in a setting of DAPT treatment that includes loading with clopidogrel.[678, 679] A meta-analysis on this topic revealed no mortality benefit of GP IIb/IIIa treatment and while non-fatal MIs were reduced, (minor) bleeding events were significantly higher when utilizing these agents.[680] Thus, GP IIb/IIIa inhibitors may only be considered in specific ‘bail-out’ situations including high intra-procedural thrombus burden, slow flow or no-flow with closure of the stented coronary vessel.

Algorithm for antithrombotic drugs in patients undergoing percutaneous coronary intervention is shown in **Figure 9**.

17.1.3 Post-interventional and maintenance treatment

Following elective stenting, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type. In specific clinical scenarios, this standard DAPT duration can be shortened (< 6 months) or extended (> 6–12 months). For a more detailed description of the pertinent clinical trials in the field of DAPT duration we may refer to the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease[681]. Following DAPT, a life-long single antiplatelet therapy (usually with aspirin) is recommended and patients should

be advised not to prematurely discontinue oral antiplatelet therapy after stenting due to the risks of stent thrombosis and recurrent MI.[682] Recently, the value of a vascular dose of rivaroxaban in conjunction with aspirin was demonstrated in the large-scale Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease (COMPASS trial)[683]. However, its utilization in stable CAD patients is a matter of secondary prevention and is not linked to myocardial revascularisation procedures.

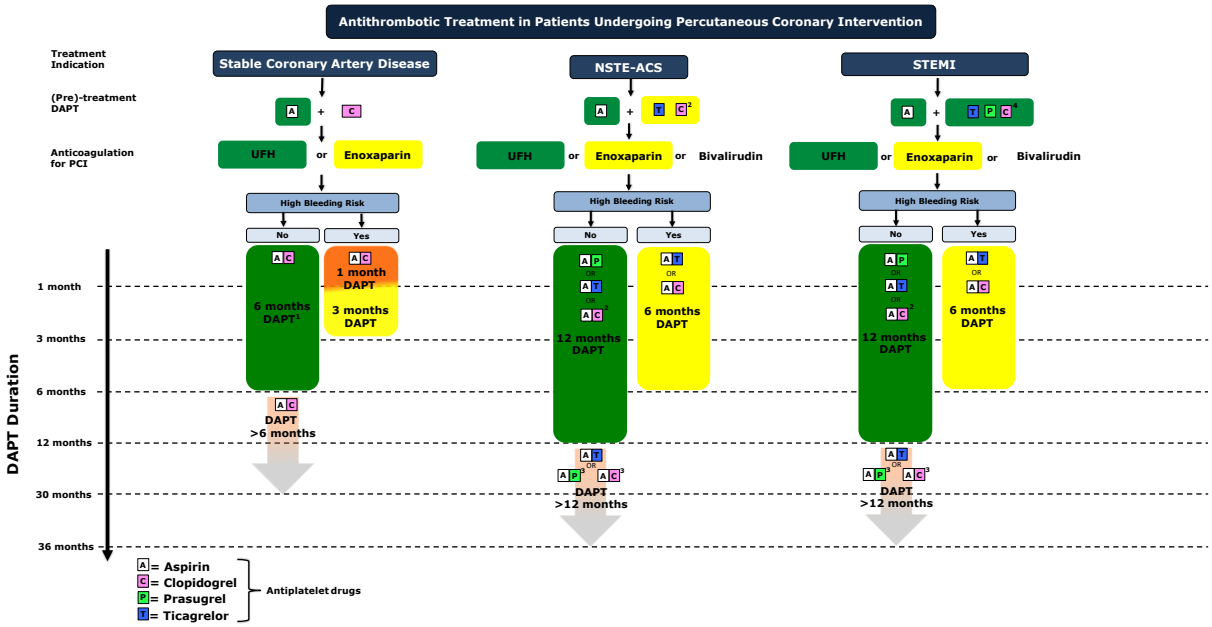


Figure 9. Algorithm for antithrombotic drugs in patients undergoing percutaneous coronary intervention. High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score >_25). Colour-coding refers to the ESC Classes of Recommendations (green = Class I; yellow = IIa; orange = Class IIb).
[1]After PCI with DCB 6 months DAPT should be considered (Class IIa)
[2]Clopidogrel if patient is not eligible for a treatment with prasugrel or ticagrelor; or in a setting of DAPT de-escalation (class IIb)
[3]Clopidogrel or prasugrel if patient is not eligible for a treatment with ticagrelor
[4]Pretreatment before PCI (or at the latest at the time of PCI); Clopidogrel if potent P2Y12 inhibitors are contraindicated or not available
(For scores see **Supplementary Table 4**)

Recommendations for antithrombotic treatment in stable coronary artery disease patients undergoing percutaneous coronary intervention

Recommendations for PCI	Class[a]	Level[b]
Pre-treatment and antiplatelet therapy		

Treatment with 600 mg clopidogrel is recommended in elective PCI patients once the coronary anatomy is known and a decision is made to proceed with PCI [671, 684, 685].	I	A
Pre-treatment with clopidogrel may be considered if the probability of PCI is high.	IIb	C
In patients on a maintenance dose of 75 mg clopidogrel, a new loading dose of 600 mg may be considered once the indication for PCI is confirmed.	IIb	C
Peri-interventional treatment		
Aspirin is indicated before elective stenting[686-688].	I	A
An oral loading dose of aspirin (150–300 mg p.o. or 75–250 mg i.v.) is recommended if the patient is not pretreated.	I	C
Clopidogrel (600 mg loading dose, 75 mg daily maintenance dose) is recommended for elective stenting [689-693].	I	A
Glycoprotein IIb/IIIa antagonists should be considered only for bail-out.	IIa	C
Prasugrel or ticagrelor may be considered in specific high-risk situations of elective stenting (e.g. history of stent thrombosis, left main stenting).	IIb	C
Unfractionated heparin is indicated as the standard anticoagulant (70–100 U/kg) [674, 675].	I	B
Bivalirudin (0.75 mg/kg bolus, followed by 1.75 mg/kg/h for up to 4 hours after the procedure) is indicated in the case of heparin-induced thrombocytopenia.	I	C
Enoxaparin (i.v. 0.5 mg/kg) should be considered as an alternative agent [676, 694].	IIa	B
Cangrelor may be considered in $P2Y_{12}$ inhibitor naïve patients undergoing PCI [677].	IIb	A
Post-interventional and maintenance treatment		
Life-long single antiplatelet therapy, usually aspirin, is recommended [686, 688].	I	A
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	I	C
In patients with SCAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type[c] [695-699].	I	A
In patients with SCAD treated with BRS, DAPT should be considered for at least 12 months and up to the presumed full absorption of the BRS based on an individual assessment of bleeding and ischaemic risk.	IIa	C
In patients with SCAD treated with DCB, DAPT should be considered for 6 months [370, 374].	IIa	B
In patients with SCAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥ 25), DAPT should be considered for 3 months[d] [700, 701].	IIa	A

In patients with SCAD who have tolerated DAPT without a bleeding complication and who are at low bleeding risk but high thrombotic risk, continuation of DAPT with clopidogrel for > 6 months and up to 30 months may be considered.[702-704]	IIb	A
In patients with SCAD in whom 3-month DAPT poses safety concerns, DAPT may be considered for 1 month.	IIb	C

BRS = bioresorbable scaffold; CAD = coronary artery disease; DAPT = dual antiplatelet therapy; DCB = drug-coated balloon; DES = drug-eluting stent; i.v. = intravenous; MI = myocardial infarction; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; SCAD = stable coronary artery disease.

[a]Class of recommendation.

[b]Level of evidence.

[c]These recommendations refer to stents which are supported by large-scale randomised trials with clinical endpoint evaluation leading to unconditional CE mark

[d]The evidence supporting this recommendation comes from two studies where zotarolimus-eluting Endeavour stent has been investigated in conjunction with a 3-month DAPT regimen.

17.2 Non-ST-segment elevation acute coronary syndrome

Activation of blood platelets and the coagulation cascade plays a key role in the initial phase and evolution of an ACS. Hence, sufficient platelet inhibition and anticoagulation is essential during ACS and especially in ACS patients undergoing PCI.

17.2.1 Choice of treatment and pretreatment

For NSTE-ACS patients, DAPT including aspirin and a potent $P2Y_{12}$ receptor inhibitor (prasugrel or ticagrelor) is recommended (see web addenda). [705] [706] Clopidogrel should only be used when prasugrel or ticagrelor are not available or are contraindicated. Based on the results of the ACCOAST (Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention or as Pretreatment at the Time of Diagnosis in Patients with Non-ST Elevation Myocardial Infarction) trial[158], it is not recommended to administer prasugrel in patients in whom coronary anatomy is not known. Nevertheless, pretreatment with ticagrelor was part of the Study of Platelet Inhibition and Patient Outcomes (PLATO) and was associated with an early benefit over clopidogrel.[706] For these reasons, pretreatment with ticagrelor can be used,

although there is no direct evidence from head-to-head comparison between pretreatment strategies.

17.2.2 Peri-interventional treatment

Anticoagulation is recommended for all patients in addition to antiplatelet therapy during PCI for NSTE-ACS.[707] In general, a crossover between anticoagulants should be avoided (especially between UFH and low-molecular-weight heparin (LMWH)), with the exception of adding UFH to fondaparinux when a patient proceeds to PCI.[708, 709] The respective agents should be discontinued after PCI except for specific clinical settings such as the presence of an LV aneurysm with thrombus or AF requiring anticoagulation.

A number of trials have compared bivalirudin with UFH in ACS patients undergoing PCI (see web addenda). Some of these trials pursued a balanced use of adjunctive GP IIb/IIIa inhibitors with both bivalirudin and heparin, whereas others, predominantly the older ones, had selective use of GP IIb/IIIa inhibitors in the heparin arm. These trials have been reviewed extensively in a number of meta-analyses[710].[711, 712] The more recent meta-analysis that also included MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) but not VALIDATE-SWEDEHEART (Bivalirudin versus Heparin in ST-Segment and Non–ST-Segment Elevation Myocardial Infarction in Patients on Modern Antiplatelet Therapy on the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) showed no significant benefit of bivalirudin as compared with UFH with respect to death, MACE and MI. [712] Nevrtheless, bivalirudin was associated with a significant increase in the risk of stent thrombosis and a significant decrease in the risk of bleeding. The reduction of bleeding risk was, however, linked to unbalanced use of GPI predominantly with UFH. Recently, VALIDATE-SWEDEHEART study[713] compared UFH vs. bivalirudin in a background of radial access and limited use of GP IIb/IIIa inhibitors. The study demonstrated similar risk patterns for both ischemia and bleeding when comparing the two drugs. Of note, while prior studies reported a reduced bleeding risk with bivalirudin vs. UFH, this was not confirmed in VALIDATE-SWEDEHEART and in a contemporary setting of preferred radial access and selective use of GPIIb/IIIa inhibitors.In summary and

based on the above-mentioned trials, UFH is primarily recommended as an anticoagulant for PCI. Due to its short half-life and favorable results in some of the studies, bivalirudin may be considered as an alternative to UFH in selected cases.

Patients may undergo cardiac catheterization after a conservative treatment phase and these patients are commonly treated with fondaparinux during the conservative treatment phase. This regimen is based on the Optimal Antiplatelet Strategy for Interventions (OASIS)-5 trial.[714] Of note, catheter thrombus formation was an issue with fondaparinux and therefore full-dose UFH must be added to prevent thrombus formation when the patient proceeds to PCI. Enoxaparin should be considered as anticoagulant for PCI in patients pretreated with subcutaneous enoxaparin. A benefit of enoxaparin over UFH to reduce mortality and bleeding complications was recently reported in a meta-analysis including NSTE-ACS patients.[694] Yet, this meta-analysis did not include a dedicated randomised study in NSTE-ACS and was largely based on non-randomised comparisons.

Most of the trials evaluating GP IIb/IIIa inhibitors in PCI-treated patients predated the era of routine oral DAPT treatment. These early trials demonstrated a reduction in the incidence of ischaemic events in favor of GP IIb/IIIa treatment in combination with UFH compared with UFH alone, primarily through a reduction in MI.[715] However, coronary angiography and PCI were delayed as compared to what is recommended now and a consistent major bleeding risk was observed. Overall, there is no compelling evidence for an additional benefit of routine upstream use of GP IIb/IIIa inhibitors in NSTE-ACS patients scheduled for coronary angiography and receiving DAPT treatment.[716, 717] Especially in a setting of potent platelet inhibition with ticagrelor or prasugrel, where randomised data on GP IIb/IIIa use is limited, routine use of these agents cannot be recommended. Nevertheless, it should be considered bail-out situations or thrombotic complications and may be used for high-risk PCI in patients without pretreatment with $P2Y_{12}$ inhibitors. Available evidence on cangrelor suggests that the potential benefit is independent of the clinical presentation. Thus, similar as to stable CAD patients, cangrelor may be considered in specific settings in $P2Y_{12}$-naïve patients undergoing PCI.

17.2.3 Post-interventional and maintenance treatment

Following PCI for NSTE-ACS, DAPT consisting of a $P2Y_{12}$ receptor inhibitor in addition to aspirin is generally recommended for 12 months, irrespective of the stent type. Recently, the SMART-DATE (Smart Angioplasty Research Team-safety of 6-month duration of Dual Antiplatelet Therapy after percutaneous coronary intervention in patients with acute coronary syndromes) prospective multicentre Randomised trial supported this notion in the setting of contemporary interventional practice. The study randomly assigned 2712 patients undergoing PCI for NSTE-ACS or STEMI to either the 6-month DAPT or 12-month or longer DAPT. Although the primary endpoint, a composite of all-cause death, myocardial infarction, or stroke, did not confirm the benefit of prolonged DAPT over 6-month DAPT (cumulative event rate 4.7% vs 4.2%; absolute risk difference 0.5%; upper limit of one-sided 95% CI 1.8%; $p_{non\text{-}inferiority}$=0.03 with a predefined non-inferiority margin of 2.0%), myocardial infarction occurred more frequently in the 6-month DAPT group than in prolonged DAPT group (1,8% vs 0,8%; p=0.02). The rate of BARC type 2-5 bleeding was not significantly affected by prolonged DAPT (HR 0.69 [95% CI 0.45-1.05]; p=0.09). The authors concluded that the increased risk of myocardial infarction with 6-month DAPT and the wide non-inferiority margin prevented concluding that short-term DAPT was safe in this setting and suggested that prolonged DAPT should remain the standard of care in patients with acute coronary syndrome without excessive risk of bleeding.[718]

In specific clinical scenarios, this standard DAPT duration can be shortened (< 12 months) or extended (> 12 months). Further on, switching and especially a de-escalation of DAPT (switch from potent $P2Y_{12}$ inhibitors to clopidogrel) was subject to a number of randomised clinical trials[719, 720]. Triggers for DAPT de-escalation include clinical (bleeding events or presumed high bleeding risk) and socio-economic factors[719]. Based on recent results from the randomised TROPICAL-ACS trial[720] (Testing responsiveness to platelet inhibition on chronic antiplatelet treatment for acute coronary syndromes), an approach of DAPT de-escalation guided by platelet function testing may be considered in ACS patients (NSTE-ACS and STEMI) as an alternative to 12 months potent platelet inhibition and especially for patients deemed unsuitable for maintained potent platelet inhibition. For a more detailed description of the pertinent clinical trials in the field of DAPT duration and switching antiplatelet drugs we may refer to the International Expert Consensus document on Switching

Platelet P2Y12 Receptor-Inhibiting Therapies[721] and the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease[681]. Following DAPT, a life-long single antiplatelet therapy (usually with aspirin) is recommended and patients should be advised not to prematurely discontinue oral antiplatelet therapy after stenting [682, 722].

Based on the results of the ATLAS-ACS 2–TIMI 51 (Anti-Xa Therapy to Lower cardiovascular events in Addition to Standard therapy in subjects with Acute Coronary Syndrome–Thrombolysis In Myocardial Infarction 51) trial in NSTE-ACS and STEMI patients,[723] a low-dose rivaroxaban may be considered after discontinuation of parenteral anticoagulation for patients with no prior stroke/TIA and at high ischaemic risk as well as low bleeding risk receiving aspirin and clopidogrel. Of note, rivaroxaban was not investigated in a background of potent $P2Y_{12}$ inhibitors.

Recommendations for antithrombotic treatment in patients with non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Pretreatment and antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term [686, 688, 724].	I	A
A $P2Y_{12}$ inhibitor is recommended in addition to aspirin, and maintained over 12 months unless there are contraindications such as excessive risk of bleeding [705, 706, 725] Options are:	I	A
• Prasugrel in $P2Y_{12}$-inhibitor naïve patients who proceed to PCI (60 mg loading dose, 10 mg daily dose) [705].	I	B
• Ticagrelor irrespective of the preceding $P2Y_{12}$-inhibitor regimen (180 mg loading dose, 90 mg b.i.d.) [706].	I	B
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated [725, 726].	I	B
GP IIb/IIIa antagonists should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C
For pretreatment in patients with NSTE-ACS undergoing invasive management, ticagrelor administration (180 mg loading dose, 90 mg b.i.d.), or clopidogrel (600 mg loading dose, 75 mg daily dose) if ticagrelor is not an option, should be considered as soon as the diagnosis is established.	IIa	C
GP IIb/IIIa antagonist may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI	IIb	C

Cangrelor may be considered in P2Y$_{12}$-inhibitor naïve patients undergoing PCI [677].	IIb	A
Pretreatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended [716, 717]	III	A
It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known [158].	III	B
Peri-interventional therapy		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy.[707, 727]	I	A
It is recommended to select anticoagulation according to both ischaemic and bleeding risks, and according to the efficacy–safety profile of the chosen agent.	I	C
UFH is recommended.	I	C
In patients on fondaparinux, a single bolus UFH (85 IU/kg, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) is indicated[728].	I	B
Enoxaparin should be considered in patients pretreated with subcutaneous enoxaparin[694].	IIa	B
Discontinuation of parenteral anticoagulation should be considered immediately after an invasive procedure.	IIa	C
Bivalirudin (0.75 mg/kg bolus, followed by 1.75 mg/kg/h for up to 4 hours after the procedure) may be considered as an alternative to UFH [156, 717, 729].	IIb	A
Crossover of UFH and LMWH is not recommended[709].	III	B

b.i.d. = twice daily; GP = glycoprotein; LMWH = low-molecular-weight heparin; NSTE-ACS = non-ST-segment elevation acute coronary syndromes; PCI = percutaneous coronary intervention; UFH = unfractionated heparin.
[a]Class of recommendation.
[b]Level of evidence.

Recommendations for post-interventional and maintenance treatment in patients with non-ST-elevation acute coronary syndromes and ST-elevation myocardial infarction undergoing percutaneous coronary intervention

Recommendations	**Class[a]**	**Level[b]**
In patients with ACS treated with coronary stent implantation, DAPT with a P2Y$_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥ 25) [730-732].	I	A
In patients with ACS and stent implantation who are at high risk of bleeding (e.g. PRECISE-DAPT ≥ 25), discontinuation of P2Y$_{12}$ inhibitor therapy after 6 months should be considered [733, 734].	IIa	B
In patients with ACS treated with BRS, DAPT should be considered for at least 12 months and up to the presumed full absorption of the BRS based on an individual assessment of bleeding and ischaemic risk.	IIa	C
De-escalation of P2Y$_{12}$ inhibitor treatment (e.g. with a switch from prasugrel or ticagrelor to clopidogrel) guided by platelet function testing may be considered as an alternative DAPT	IIb	B

strategy, especially for ACS patients deemed unsuitable for 12-month potent platelet inhibition[720].		
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered [735, 736].	IIb	A
In patients with MI and high ischaemic risk[c] who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg *b.i.d.* for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel [737-739].	IIb	B
In ACS patients with no prior stroke/TIA and at high ischaemic risk as well as low bleeding risk receiving aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg *b.i.d.* for approximately 1 year) may be considered after discontinuation of parenteral anticoagulation [723].	IIb	B

ACS = acute coronary syndrome; *b.i.d.* = twice daily; BRS = bioresorbable scaffold; DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; TIA = transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

[c]Defined as at least 50 years of age, and had one of the following additional high-risk features: age of 65 years or older, diabetes mellitus requiring medication, a second prior spontaneous MI, multivessel coronary artery disease, or chronic renal dysfunction, defined as an estimated creatinine clearance < 60 mL/min.

17.3 ST-segment elevation myocardial infarction

17.3.1 Choice of treatment and pretreatment

STEMI patients undergoing primary PCI should receive aspirin and a $P2Y_{12}$ receptor inhibitor as soon as the diagnosis of STEMI is established. In line with the treatment recommendations for NSTE-ACS patients, DAPT is the cornerstone of treatment for STEMI patients and includes aspirin and a potent $P2Y_{12}$ receptor inhibitor (prasugrel or ticagrelor).[705, 706] For both antiplatelet drugs, published subgroup analyses on STEMI patients are available (see web addenda). Randomised data on a comparison of ticagrelor vs. prasugrel in STEMI patients are limited, but the recently published randomised PRAGUE-18 (Comparison of Prasugrel and Ticagrelor in the Treatment of Acute Myocardial Infarction) trial[740] with limited statistical power found similar safety and efficacy profiles of ticagrelor and prasugrel in a setting of primary PCI. When potent $P2Y_{12}$ receptor inhibitors are contraindicated or are not available, clopidogrel should be given for primary PCI instead[726]. The value of pretreatment with

ticagrelor was addressed in the Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST-Elevation Myocardial Infarction to Open the Coronary Artery (ATLANTIC) trial.[741] No significant differences were observed on the level of the two co-primary surrogate endpoints measured before PCI (thrombolysis in myocardial infarction [TIMI] flow, ST segment resolution). Likewise, the incidence of a combined ischaemic endpoint (death, MI; stroke, stent thrombosis, urgent revascularisation) did not differ between the two treatment arms. Nevertheless, in both TRITON (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel–Thrombolysis In Myocardial Infarction) and PLATO pretreatment was part of the therapeutic regimen in STEMI.

17.3.2 Peri-interventional treatment

Immediate and sufficient anticoagulation is mandatory in the setting of primary PCI for STEMI and available options include UFH, bivalirudin and enoxaparin. A number of RCTs compared bivalirudin vs. UFH in different settings and with different utilization of GP IIb/IIIa inhibitors (see web addenda). The primary recommendation of UFH, reserving bivalirudin for selected cases, is essentially the same for primary PCI as for PCI in NSTE-ACS and is based on the same clinical trials[710, 713] (see **Chapter 17.2.2**).

Enoxaparin was compared with UFH in the randomised open-label Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischaemic and bleeding events at short- and Long-term follow-up (ATOLL) trial,[742] and based on the trial results enoxaparin should be considered as an alternative to UFH treatment in STEMI patients.

A number of clinical trials, performed at a time when pretreatment and potent platelet inhibition was not part of routine clinical practice, had documented clinical benefits of GP IIb/IIIa inhibitors as an adjunct to primary PCI performed with UFH.[743, 744] A meta-analysis showed a significant survival benefit especially in high-risk STEMI patients, but also a higher risk of bleeding with GP IIb/IIIa administration.[745] Dedicated trials have investigated the value of upstream treatment in the past.[746, 747] Based upon the available evidence, the routine use of i.v. or intracoronary GP IIb/IIIa inhibitor administration—regardless of whether treatment starts upstream or in the

catheterization laboratory—cannot be recommended. Especially in a setting where potent $P2Y_{12}$ inhibitors like prasugrel or ticagrelor are used, the value of GP IIb/IIIa inhibitors remains uncertain as these agents exhibit a fast onset of action (usually <1 hour). GP IIb/IIIa inhibitors remain an option as bail-out therapy or in high-risk PCI without pretreatment with $P2Y_{12}$ inhibitors. Of note, the bail-out scenarios have never been addressed in randomised controlled trials. For reasons discussed above (see **Chapters 17.1 and 17.2**), cangrelor may be considered in specific settings in $P2Y_{12}$-naïve patients undergoing PCI.

17.3.3 Post-interventional and maintenance treatment

Following PCI for STEMI, DAPT consisting of a $P2Y_{12}$ receptor inhibitor in addition to aspirin is generally recommended for 12 months. Recommendations for maintenance DAPT treatment are generally consistent with those for NSTE-ACS patients and are detailed in chapter 17.2.3.

Recommendations for antithrombotic treatment in ST-elevation myocardial infarction patients undergoing percutaneous coronary intervention

Recommendations	Class[a]	Level[b]
Pretreatment and antiplatelet therapy		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy [686, 688, 724].	I	A
A potent P2Y12 inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contraindicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding[705, 706, 725, 726, 748, 749]	I	A
GP IIb/IIIa inhibitors should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI [677].	IIb	A
GP IIb/IIIa antagonist may be considered in $P2Y_{12}$-inhibitor naïve patients undergoing PCI	IIb	C
Peri-interventional therapy		
Anticoagulation is recommended for all patients in addition to antiplatelet therapy during PCI. [707, 727]	I	A
Routine use of UFH is recommended.	I	C
Routine use of enoxaparin should be considered [742].	IIa	B
Routine use of bivalirudin may be considered [729, 750-752].	IIb	A

GP = glycoprotein; PCI = percutaneous coronary intervention; UFH = unfractionated heparin.

[a]Class of recommendation.

[b]Level of evidence.

17.4 CABG

Antithrombotic treatment before and after CABG is addressed in 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease.[681] After reviewing the subsequent literature, the current task force endorses the Recommendations of the Update on DAPT and does not identify the need for any major update. Accordingly, the current recommendation tables are taken from this guideline. For a detailed discussion, we refer to the previous document.

Dual antiplatelet therapy in patients undergoing cardiac surgery

Recommendations	Class [a]	Level [b]
It is recommended that the heart team estimates the individual bleeding and ischaemic risks and guide the timing of CABG as well as the anti-thrombotic management.	I	C
In patients on aspirin who need to undergo non-emergent cardiac surgery, it is recommended to continue aspirin at a low daily regimen throughout the perioperative period.	I	C
In patients treated with DAPT after coronary stent implantation who subsequently undergo cardiac surgery, it is recommended to resume $P2Y_{12}$ inhibitor therapy postoperatively as soon as deemed safe so that DAPT continues until the recommended duration of therapy is completed.	I	C
In patients with ACS (NSTE-ACS or STEMI) treated with DAPT and undergoing CABG and not requiring long-term OAC therapy, resumption of $P2Y_{12}$ inhibitor therapy as soon as deemed safe after surgery and continuation up to 12 months is recommended.	I	C
In patients on $P2Y_{12}$ inhibitors who need to undergo non-emergent cardiac surgery, it should be considered to postpone surgery for at least 3 days after discontinuation of ticagrelor, at	IIa	B

least 5 days after clopidogrel, and at least 7 days after prasugrel.[753-755]		
In CABG patients with prior MI who are at high risk of severe bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.	IIa	C
Platelet function testing may be considered to guide decision on timing of cardiac surgery in patients who have recently received $P2Y_{12}$ inhibitors.[186, 756-758]	IIb	B
In patients perceived at high ischaemic risk with prior MI and coronary artery bypass grafting who have tolerated DAPT without a bleeding complication, treatment with DAPT for longer than 12 and up to 36 months may be considered.	IIb	C

ACS = acute coronary syndrome; CABG = coronary artery bypass graft surgery; DAPT = dual antiplatelet therapy; NSTE-ACS = non-ST-elevation acute coronary syndrome; OAC = oral anticoagulant; STEMI = ST-elevation myocardial infarction. PRECISE DAPT= predicting bleeding complications in patients undergoing stent implantation and subsequent dual anti platelet therapy**.**

[a]Class of recommendation.

[b]Level of evidence.

17.5 Special conditions

17.5.1 Antithrombotic therapy after percutaneous coronary intervention in patients requiring oral anticoagulation

Compared with OAC therapy alone, the addition of DAPT to OAC therapy results in a two- to three-fold increase in bleeding complications suggesting that every effort should be undertaken to avoid bleeding **(Table 8)**.[759] Assessing the balance of ischaemic and bleeding risks of relatively short (i.e. 6 months or less) triple therapy duration as compared to double therapy consisting of clopidogrel and OAC requires a patient-by-patient decision. Of note, randomised studies evaluating the duration of triple therapy or the benefit of NOAC vs. vitamin K antagonist (VKA) were not adequately powered for assessing ischaemic events and data are lacking on the efficacy of dual therapy in patients at high risk for stroke or recurrent ACS.[760-763] In the major trials, there was no interaction between the duration of triple therapy and clinical presentation (ACS vs. no ACS). The rate of bleeding events peaked within the first 30 days of initiation of triple therapy and was twice as high when compared with

the rate of acute coronary events including recurrent MI and stent thrombosis. For these reasons, duration of triple therapy should be minimized depending on bleeding and ischaemic risks (see **Tables 8 to 10** for guidance in decision making). In stabilized event-free patients, discontinuation of any antiplatelet agent at 1 year after stenting is encouraged while dual therapy may be continued beyond 1 year according to the stent-driven risk shown in **Table 9**.

Based on the favorable bleeding risk in the large phase 3 studies a NOAC should be preferred over VKA. The PIONEER[762] (Prevention of bleeding in patients with AF undergoing PCI) trial discussed previously[681] and the more recent Randomised Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patientswith Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention (RE-DUAL)[763] trial compared a NOAC plus single antiplatelet therapy with triple therapy with VKA plus DAPT and consistently showed significantly lower bleeding risks with the dual antithrombotic regimen. In RE-DUAL both dosing regimens for dabigatran (150 mg and 110 mg b.i.d) vs. warfarin triple therapy were associated with a significant reduction of major or clinically relevant bleeding events. However, as compared with triple therapy an increase in both MI (4.5% vs. 3.0%, P = 0.09) and ST risk (1.5% vs. 0.8%, P = 0.15) was reported for the lower dabigatran dose (110 mg b.i.d.), but not for the higher dabigatran dose (150 mg b.i.d.). Although statistical significance was missed, these findings raise concern about the efficacy of the lower dabigatran dose in combination with single antiplatelet therapy in preventing coronary events. Thus, the 150 mg b.i.d. dose of dabigatran is preferred. At present, evidence for a dual treatment approach is available for VKA,[761] rivaroxaban[762] and dabigatran[763], but none of these studies were powered to assess the efficacy in preventing stent thrombosis or thromboembolic events and only RE-DUAL used a NOAC dose that was previously shown to be effective in the prevention of thromboembolic events. The ongoing AUGUSTUS trial (ClinicalTrials.gov Identifier: NCT02415400) will address the value of apixaban in a similar setting and with and without aspirin. Edoxaban is currently investigated in a setting of triple treatment in the ENTRUST-AF-PCI trial (ClinicalTrials.gov Identifier: NCT02866175).

Figure 10 illustrates applicable DAPT algorithms in patients with an indication for oral anticoagulation undergoing PCI with the respective classes of recommendations for

the different treatment regimens. For more details on the pertinent studies in the field of triple treatment (DAPT plus OAC) and the associated issues we may refer to and the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease[681].

Table 8 Strategies to avoid bleeding complications in OAC patients

– Assess ischaemic and bleeding risks using validated risk predictors (e.g. CHA_2DS_2-VASc, ABC, HAS-BLED) with a focus on modifiable risk factors.
– Keep triple therapy duration as short as possible; dual therapy after PCI (oral anticoagulant and clopidogrel) to be considered instead of triple therapy.
– One should consider the use of NOAC instead of VKA when NOACs are not contra-indicated.
– Consider a target INR in the lower part of the recommended target range and maximize time in therapeutic range (i.e. > 65%) when VKA is used.
– Clopidogrel is the $P2Y_{12}$ inhibitor of choice.
– Use low-dose (≤ 100 mg daily) aspirin.
– Routine use of PPIs.

Adapted from Valgimigli et al.[409]

ABC = Age, Biomarkers, Clinical history; CHA_2DS_2-VASc = Congestive heart failure, Hypertension, Age ≥ 75 years (doubled), Diabetes mellitus, prior Stroke or transient ischaemic attack or thromboembolism (doubled), Vascular disease, Age 65–74 years, Sex category; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; INR = international normalized ratio; NOAC = non-vitamin K antagonist oral anticoagulant; PPIs = proton pump inhibitors; VKA = vitamin K antagonist.

[a]Apixaban 5 mg twice daily (*b.i.d.*) or apixaban 2.5 mg *b.i.d.* if at least two of the following: age ≥ 80 years, body weight ≤ 60 kg or serum creatinine level ≥ 1.5 mg/dL (133 µmol/L); dabigatran 110 mg *b.i.d.*; edoxaban 60 mg once daily (*q.d.*) or edoxaban 30 mg *q.d.* if any of the following: creatinine clearance of 30–50 mL/min, body weight ≤ 60 kg, concomitant use of verapamil or quinidine or dronedarone; rivaroxaban 20 mg *q.d.* or rivaroxaban 15 mg *q.d.* if creatinine clearance 30–49 mL/min.

Table 9 High-risk features for ischaemic events

• Prior stent thrombosis on adequate antiplatelet therapy
• Stenting of the last remaining patent coronary artery

• Diffuse multivessel disease especially in diabetic patients
• Chronic kidney disease (i.e. creatinine clearance < 60 mL/min)
• At least three stents implanted
• At least three lesions treated
• Bifurcation with two stents implanted
• Total stented length > 60 mm
• Treatment of a chronic total occlusion
• History of STEMI

STEMI = ST-elevation myocardial infarction

Table 10 Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy

• Short life expectancy
• Ongoing malignancy
• Poor expected adherence
• Poor mental status
• End stage renal failure
• Advanced age
• Prior major bleeding/prior haemorrhagic stroke
• Chronic alcohol abuse
• Anaemia
• Clinically significant bleeding on dual antithrombotic therapy

Dual antiplatelet therapy duration in patients with indication for oral anticoagulation

Recommendations	Class[a]	Level[b]
It is recommended to administer periprocedural aspirin and clopidogrel in patients undergoing coronary stent implantation.	I	C
In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel and OAC should be considered for 1 month, irrespective of the type of stent used [761].	IIa	B
Triple therapy with aspirin, clopidogrel and OAC for longer than 1 month and up to 6 months should be considered in	IIa	B

patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk [761].		
Dual therapy with clopidogrel 75 mg/day and OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk [760, 762].	IIa	A
In patients with an indication for VKA in combination with aspirin and/or clopidogrel, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range > 65%.[760, 761]	IIa	B
In patients with non-valvular AF requiring anticoagulation and antiplatelet treatment, a NOAC should be preferred over VKAs[762, 763]	IIa	A
When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AF trials should be considered.[c]	IIa	C
When rivaroxaban is used in combination with aspirin and/or clopidogrel, rivaroxaban 15 mg *q.d.* may be used instead of rivaroxaban 20 mg *q.d.* [762].	IIb	B
When dabigatran is used in combination with aspirin and/or clopidogrel, the dose of 150 mg b.i.d may be preferred over the dose of 110 mg b.i.d. [763]	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and OAC.	III	C

ACS = acute coronary syndrome; AF = atrial fibrillation; *b.i.d.* = twice daily; INR = international normalized ratio; OAC = oral anticoagulant; NOAC = non-vitamin K oral anticoagulant; *q.d.* = once daily; VKA = vitamin K antagonist.

[a]Class of recommendation.

[b]Level of evidence.

[c]Apixaban 5mg b.i.d or apixaban 2.5 mg b.i.d. if at least two of the following: age >_80 years, body weight <_60 kg or serum creatinine level >_1.5 mg/dL (133 lmol/L); dabigatran 110 mg or 150 mg b.i.d.; edoxaban 60 mg q.d. or edoxaban 30 mg q.d. if any of the following: CrCl of

30–50 mL/min, body weight <_60 kg, concomitant use of verapamil, quinidine, or dronedarone; rivaroxaban 20 mg q.d. or rivaroxaban 15 mg q.d. if CrCl 30–49 mL/min.

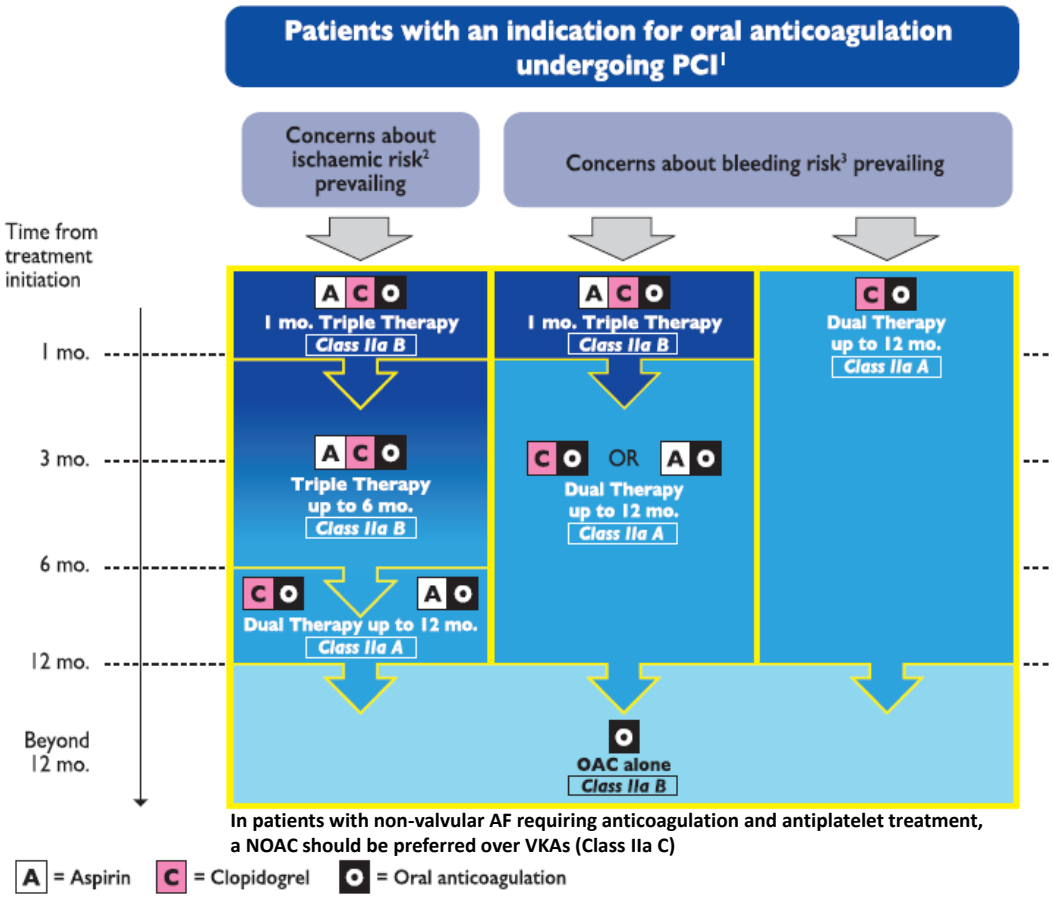


Figure 10: Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI). Colour-coding refers to the number of concomitant antithrombotic medication(s). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment with a single antiplatelet agent (aspirin or clopidogrel) plus OAC.

ABC = age, biomarkers, clinical history; ACS = acute coronary syndrome; mo. = month(s); PCI = percutaneous coronary intervention.

1: Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy.

2: High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.

3: Bleeding risk can be estimated by HAS-BLED or ABC score.

17.5.2 Revascularisation in patients with renal failure

See Web Addenda

17.5.3 Monitoring of antiplatelet drugs (platelet function testing and genotyping)

See Web Addenda

17.5.4 Surgery in patients on dual antiplatelet therapy

See 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease[681]

17.6 Gaps in evidence

- The value of pre-hospital pretreatment with prasugrel in STEMI patients, as well as the safety and efficacy of ticagrelor given at hospital admission in NSTE-ACS patients, has not been addressed in dedicated randomised studies.
- The safety and efficacy of short-term potent antiplatelet treatment with either prasugrel or ticagrelor in stable CAD patients is unknown and subject to ongoing clinical trials (ALPHEUS (Assessment of Loading With the $P2Y_{12}$ Inhibitor Ticagrelor or Clopidogrel to Halt Ischemic Events in Patients Undergoing Elective Coronary Stenting) trial: NCT02617290; SASSICAIA (Comparison of Loading Strategies With Antiplatelet Drugs in Patients Undergoing Elective Coronary Intervention) trial: NCT02548611).
- The clinical benefit of a short-term DAPT duration followed by long-term ticagrelor monotherapy (and stopping aspirin) remains unknown. The ongoing GLOBAL LEADERS (Long-term ticagrelor monotherapy versus standard dual antiplatelet therapy followed by aspirin monotherapy in patients undergoing biolimus-eluting stent implantation) and TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention) trials aim at closing this gap in knowledge (NCT01813435, NCT02270242).

18. Volume–outcome relationship for revascularisation procedures

Operator experience influences outcomes, particularly in critical, complex situations. The greater total experience of an entire hospital team—consisting of supporting members in the operating room or catheterization laboratory and those responsible for postoperative care—results in favorable outcomes.

18.1 Coronary artery bypass grafting

A number of studies have suggested that the CABG volume in a hospital significantly impacts in-hospital mortality, although no consistent cut-offs for volume are used in these studies. [764] [765] [766] This increase in mortality observed in lower volume centres seems to be attributable to so-called “failure to rescue”: although patients operated at low-volume centres are not at particularly higher risk of suffering a major complication, they are more likely to die from such a complication, should it occur.[767] Therefore, consideration should be given to performance of CABG in centres with an annual volume of at least 200 CABG cases. Apart from hospital volume, higher surgeon volume also appears to be inversely related to operative mortality. Birkmeyer and co-authors provided evidence suggesting that both hospital and surgeon have some impact on outcomes [768]

Several studies suggest that quality measures are more important than volume *per se*.[769, 770] Missing quality indicators in hospitals strongly predicted mortality, irrespective of surgeon or hospital case volume.[771] Therefore, it is recommended that such quality measures (see as an example **Supplementary Table 9**) are adopted and reported to facilitate focused quality improvement (see **Recommendation Tables**).[772]

18.2 Percutaneous coronary intervention

Numerous studies have investigated the relationship between volume of procedures and outcomes of PCI, suggesting a volume–outcome relationship at operator level, as well as at institutional level.[764, 773-777] A population-based study from the PCI reporting system of New York indicated that hospital case volumes < 400 PCIs per year and operator case volumes < 75 PCIs per year were associated with impaired outcomes.[773]

Among patients with ACS, particularly STEMI, operator and hospital volume play an important role. A large study in the USA reported that, in a cohort of 36 535 patients undergoing primary PCI, in-hospital mortality was significantly lower in institutions with higher primary PCI volumes (5.7% in hospitals performing >33 primary PCIs/year vs. 7.7% in hospitals performing <12 primary PCIs/year).[778]

Operator volume has also been shown to impact outcomes in LM PCI. A single-centre study of 1948 patients who underwent unprotected LM PCI, performed by 25 operators over a 7-year period, showed reduced 30-day and 3-year mortality for patients who had their PCI performed by a high-volume operator (defined as ≥ 15 LM PCI/year; mean 25/year) vs. a low volume operator (< 15 LM PCI/year).[779]

An example of quality measures for PCI is provided in **Supplementary Table 10**.

18.3 Training in cardiac surgery and interventional cardiology for myocardial revascularisation

A European training programme in interventional cardiology has been proposed by the European Association for Percutaneous Cardiovascular Interventions (EAPCI) in order to ensure high quality of patient care and clinical excellence.[780] The programme should last 1–2 years at high-volume institutions that handle at least 800 PCIs per year and that have established 24-hour/7-day service for the treatment of patients with ACS.

For CABG, no standardized European programme exists at this time. The pace at which proficiency reaches certain acceptable standards, however, differs from trainee to trainee. Therefore, although it is recommended that trainees perform at least 200 CABG procedures under supervision before becoming completely independent, a competency-driven residency programme with regular evaluation of progress is recommended over a volume-driven programme.

Recommendations for operator/institutional volume in myocardial revascularisation

Recommendations	Class[a]	Level[b]
CABG		
It should be considered that CABG is performed at institutions with an annual institutional volume of at least 200 CABG cases.	IIa	C
PCI		
It should be considered that PCI for ACS is performed by trained operators with an annual	IIa	C

volume of at least 75 procedures at institutions performing at least 400 PCIs per year with an established 24-hour/7-day service for the treatment of patients with ACS.		
It should be considered that PCI for SCAD is performed by trained operators with an annual volume of at least 75 procedures at institutions performing at least 200 PCIs per year.	IIa	C
It should be considered that institutions with an annual volume of fewer than 400 PCIs collaborate in networks with higher-volume institutions (more than 400 PCIs per year), with shared written protocols and exchange of operators and support staff.	IIa	C
It should be considered that PCI for LM is performed by trained operators with an annual volume of at least 25 LM PCI cases per year.	IIa	C
It should be considered that non-emergency high-risk PCI procedures, such as for LM disease, single remaining patent coronary artery, and complex chronic total occlusions, are only performed by adequately experienced operators at centres that have access to circulatory support and intensive care treatment.	IIa	C

ACS = acute coronary syndromes; CABG = coronary artery bypass grafting; ESC = European Society of Cardiology; LM = left main; PCI = percutaneous coronary intervention; SCAD = stable coronary artery disease.

[a]Class of recommendation.

[b]Level of evidence

Recommendations for training in myocardial revascularisation

Recommendations	**Class**[a]	**Level**[b]
Training in CABG		
It is recommended that trainees in cardiac surgery and interventional cardiology follow a competency-	I	C

driven residency programme with regular evaluation of progression.		
It should be considered that trainees in cardiac surgery perform at least 200 CABG procedures under supervision before being independent.	IIa	C
Training in PCI		
It should be considered that trainees in interventional cardiology perform at least 200 PCI procedures as first operator with one-third of PCI procedures in emergency or ACS patients under supervision before being independent.	IIa	C
It should be considered that trainees in interventional cardiology complete formal training according to a 1–2 year curriculum at institutions with at least 800 PCIs per year and an established 24-hour/7-day service for the treatment of patients with ACS.	IIa	C

ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

Recommendations for outcome registration, monitoring, and benchmarking

Recommendations	**Class**[a]	**Level**[b]
It is recommended that specific quality performance measures for CABG are adopted on a national level to allow outcome monitoring and benchmarking.	I	C
It is recommended that national societies establish national databases on CABG practice and outcomes.	I	C
It is recommended to report CABG outcome data by hospital to national databases.	I	C

CABG = coronary artery bypass grafting;

[a] Class of recommendation.

[b] Level of evidence.

19. Medical therapy, secondary prevention, and strategies for follow-up

Myocardial revascularisation must be accompanied by medical therapy and other secondary prevention strategies for risk factor modification and permanent lifestyle changes.[42] Secondary prevention and cardiac rehabilitation are an integral part of the management after revascularisation because such measures reduce future morbidity and mortality in a cost-effective way and can further improve symptoms. These measures are discussed in detail in the European Guidelines on Cardiovascular Disease Prevention published in 2016.[42]

The need to detect restenosis has been reduced in the DES era. Likewise, the durability of CABG results has increased with the use of arterial grafts, and ischaemia stems mainly from SVG attrition and/or progression of CAD in native vessels**.** Nevertheless, recurrence of symptoms or ischaemia due to disease progression or restenosis deserve attention.

Strategies for follow-up and management in patients after myocardial revascularisation

Recommendations	**Class[a]**	**Level[b]**
After CABG or PCI for acute myocardial infarction participation in a cardiac rehabilitation programme is recommended to improve patient outcomes.[781]	I	A
It is recommended to start and reinforce secondary prevention measures including medical therapy and lifestyle changes after myocardial revascularisation[688, 782-789]	I	A
It is recommended to re-evaluate patients after myocardial revascularisation (e.g. at 3 months and thereafter at least on an annual basis) in order to reassess symptoms and adherence with secondary prevention measures and reinforce medical therapy and lifestyle changes when appropriate	I	C
Symptomatic patients		
Coronary angiography is recommended in patients	I	C

with intermediate- to high-risk findings[d] at stress testing.		
An imaging stress test should be considered in patients with prior revascularisation over stress ECG. [790]	IIa	B
Asymptomatic patients		
Surveillance by non-invasive imaging based stress testing may be considered in high-risk patient subsets 6 months after revascularisation.	IIb	C
After high-risk PCI (e.g. unprotected LM stenosis) late (3–12 months) surveillance angiography may be considered, irrespective of symptoms.	IIb	C
Routine non-invasive imaging based stress testing may be considered 1 year after PCI and > 5 years after CABG.	IIb	C

CABG = coronary artery bypass grafting; LM = left main; PCI = percutaneous coronary intervention.

[a]Class of recommendation.

[b]Level of evidence.

[c]Absence of intermediate- and high-risk findings[d].

[d]Intermediate- and high-risk findings at stress imaging are ischaemia at low workload with exercise stress testing, early onset ischaemia with pharmacological stress testing, inducible wall motion abnormality or reversible perfusion defect in ≥10% of LV myocardium

19.1 Gaps in evidence

In all studies on the optimal follow-up after PCI, the gain from discovering patients with restenosis is obscured by the high rate of false positive exercise ECG tests indicating ischaemia. Therefore, simple exercise ECG testing is not recommended for follow-up and a non-invasive imaging approach is preferred. Specific studies to clarify which subset of patients benefits more from a specific follow-up approach are missing. More studies are needed to assess the role of CT angiography in patient surveillance after myocardial revascularisation.

20. Key messages

1. Myocardial revascularisation is performed for relief of symptoms of myocardial ischaemia and improvement of prognosis. In SCAD, the prognostic benefit is dependent on the extent of myocardium subject to ischaemia.
2. The prognostic and symptomatic benefit of myocardial revascularisation critically depends on the completeness of revascularisation. Therefore, the ability to achieve complete revascularisation is a key issue when choosing the appropriate treatment strategy.
3. Apart from issues of individual operative risk and technical feasibility, diabetes mellitus and anatomical complexity of CAD determine the relative benefits of PCI and CABG.
4. The SYNTAX score is the recommended tool to gauge the anatomical complexity of coronary disease.
5. In some instances, both PCI and CABG are equally reasonable or sometimes even equally problematic options. This calls for the Heart Team to be consulted to develop individualised treatment concepts with respect for the preferences of the patient informed about early and late outcomes.
6. Timely PCI of the culprit lesion remains the mainstay of treatment of ACS.
7. After PCI of the culprit lesion in ACS, choice of further revascularisation modality should follow the criteria applied to patients with SCAD.
8. Radial access is preferred for any PCI irrespective of clinical presentation, unless there are overriding procedural considerations.
9. DES are recommended for any PCI irrespective of clinical presentation, lesion type, anticipated duration of DAPT or concomitant anticoagulant therapy.
10. Even though 6 months DAPT is generally recommended after PCI in SCAD and 12 months of DAPT after ACS, the type and duration of DAPT should be individualised according to the ischaemic risk and the bleeding risk and appropriately adapted during follow-up. Based on this judgement, treatment durations for DAPT after DES as short as 1 month or as long as life-long may be reasonable.
11. Off-pump surgery with no touch aorta for high risk patients should be considered when expertise exists.

12. Multiple arterial grafting should be considered using the radial artery for high-grade stenosis and/or bilateral internal mammary artery grafting for patients who do not have an increased risk of sternal wound infection.

21. Evidence-based "To do a and not to do" messages

Risk models to assess short- and long-term outcomes after myocardial revascularisation		
	Class[a]	**Level**[b]
When evidence of ischaemia is not available, FFR or iFR are recommended to assess the haemodynamic relevance of intermediate-grade stenosis	I	A
It is recommended to calculate the STS score to assess in-hospital or 30-day mortality, and in-hospital morbidity after CABG.	I	B
In patients with LM or multivessel disease it is recommended to calculate the SYNTAX score to assess the anatomical complexity of CAD and the long-term risk of mortality and morbidity after PCI.	I	B

Indications for revascularisation in patients with stable angina or silent ischaemia			
For prognosis	LM disease with stenosis > 50%[c]	I	A
	Any proximal LAD stenosis > 50%[c]	I	A
	Two-vessel or three-vessel disease with stenosis > 50%[c] with impaired LV function (LVEF ≤ 35%)[c]	I	A
	Large area of ischaemia detected by functional testing (> 10% LV) or abnormal invasive FFR[d]	I	B
For symptoms	Any haemodynamically significant coronary stenosis in the presence of limiting angina or angina equivalent, , with insufficient response to optimized medical therapy	I	A

Type of revascularisation (CABG or PCI) in patients with SCAD in the absence of diabetes with suitable coronary anatomy for both procedures and low predicted surgical mortality				
Recommendations according to extent of CAD	**CABG**		**PCI**	
	Class[a]	**Level**[b]	**Class**[a]	**Level**[b]
One vessel CAD				
with proximal LAD stenosis	I	A	I	A
Two-vessel CAD				
with proximal LAD stenosis	I	B		
Left main CAD				
Left main with low SYNTAX score 0−22	I	A	I	A

Left main with intermediate SYNTAX score > 22 ≤32	I	A		
Left main with high SYNTAX score >32	I	A	III	B
Invasive evaluation and revascularisation in NSTE-ACS				
Urgent coronary angiography (< 2 hours) is recommended in patients at very high ischaemic risk (Figure 3).			I	B
An **early** invasive strategy (< 24 hours) is recommended in patients with at least one high-risk criterion (Figure 3).			I	A
An invasive strategy (< 72 hours after first presentation) is indicated in patients with at least one intermediate-risk criterion (Figure 3) or recurrent symptoms.			I	A
It is recommended to base the revascularisation strategy (*ad hoc* culprit-lesion PCI/multivessel PCI/CABG) on the **clinical status** and comorbidities as well as the **disease severity**, i.e. distribution and angiographic lesion characteristics (e.g. SYNTAX score), according to the principles for SCAD.			I	B
In cardiogenic shock, routine revascularisation of non-IRA lesions is not recommended during primary PCI.			III	B
Primary PCI for myocardial reperfusion in STEMI				
Indication				
Reperfusion therapy is indicated in all patients with time from symptom onset < 12 hours duration and persistent ST-segment elevation.			I	A
A primary PCI strategy is recommended over fibrinolysis within indicated timeframes.			I	A
Logistics				
It is recommended that the prehospital management of STEMI patients be based on regional networks designed to deliver reperfusion therapy timely and effectively, and to offer primary PCI to as many patients as possible.			I	B
It is recommended that primary PCI-capable centres deliver a 24-hour/7-day service and ensure for primary PCI to be performed as fast as possible.			I	B
Patients transferred to a PCI-capable centre for primary PCI should bypass the emergency department and be transferred directly to the catheterization laboratory			I	B

Strategy/Technique			
In cardiogenic shock, routine revascularisation of non-IRA lesions is not recommended during primary PCI.		III	B
Routine use of thrombus aspiration is not recommended.		III	A
Recommendations on revascularisations in patients with chronic heart failure and systolic LV dysfunction (ejection fraction ≤ 35%)			
In patients with severe LV systolic dysfunction and coronary artery disease suitable for intervention, myocardial revascularisation is recommended.		I	B
CABG is recommended as first revascularisation strategy choice in patients with multivessel disease and acceptable surgical risk.		I	B
Revascularisations in patients with cardiogenic shock			
Emergency invasive evaluation is indicated in patients with acute heart failure or cardiogenic shock complicating ACS.		I	B
Emergency PCI is indicated for patients with cardiogenic shock due to STEMI or NSTE-ACS independent of time delay of symptom onset.if coronary anatomy is amenable.		I	B
Emergency CABG is recommended for patients with cardiogenic shock if the coronary anatomy is not amenable to PCI.		I	B
Routine use of IABP in patients with cardiogenic shock due to ACS is not recommended.		III	B
Recommendations for revascularisation in patients with diabetes			
In patients with stable multivessel CAD and an acceptable surgical risk, CABG is recommended over PCI.		I	A
Prevention of contrast-induced nephropathy			
Recommendations	**Dose**		
Patients with moderate-to-severe CKD			
Use of low-osmolar or iso-osmolar contrast media is recommended.		I	A
It is recommended to minimize volume of contrast media.	total contrast volume/GFR < 3.7[c].	I	B
Severe CKD			
Haemodialysis therapy is not		III	B

recommended as a preventive measure.			
Preoperative strategies to reduce the incidence of stroke in patients undergoing CABG			
In patients undergoing CABG, carotid DUS is recommended in patients with recent (< 6 months) history of stroke/TIA.		I	B
Disease progression and late graft failure			
Repeat revascularisation is indicated in patients with extensive ischaemia or severe symptoms despite medical therapy.		I	B
IMA is the conduit of choice for redo CABG in patients in whom the IMA was not used previously..		I	B
DES are recommended for the treatment of in-stent restenosis within BMS or DES.		I	A
Drug-coated balloons are recommended for the treatment of in-stent restenosis within BMS or DES.		I	A
Prevention of ventricular arrhythmias by revascularisation			
A primary PCI strategy is recommended in patients with resuscitated cardiac arrest and an SCG consistent with STEMI.		I	B
Peri-operative oral beta-blocker therapy is recommended for the prevention of postoperative AF after CABG surgery.		I	B
Procedural aspects of CABG			
Arterial grafting with IMA to the LAD system is recommended.		I	B
Use of the radial artery is recommended over saphenous vein in patients with high-degree stenosis		I	A
Skeletonized IMA dissection is recommended in patients with high risk of sternal wound infection.		I	B
Minimization of aortic manipulation is recommended.		I	B
Off-pump CABG should be considered for subgroups of high-risk patients by experienced off-pump teams.		I	B
Procedural aspects of PCI			
DES are recommended over BMS for any PCI irrespective of: clinical presentation lesion type planned non-cardiac surgery		I	A

anticipated duration of DAPT concomitant anticoagulant therapy.		
Radial access is recommended as the standard approach, unless there are overriding procedural considerations.	I	A
Stent implantation in the main vessel only, followed by provisional balloon angioplasty with or without stenting of the side branch, is recommended for PCI of bifurcation lesions.	I	A
Antithrombotic treatment in SCAD patients undergoing PCI		
Treatment with 600 mg clopidogrel is recommended in elective PCI patients once anatomy is known and decision to proceed with PCI.	I	A
Aspirin is indicated before elective stenting.	I	A
Clopidogrel (600 mg loading dose, 75 mg daily maintenance dose) is recommended for elective stenting.	I	A
UFH is indicated as a standard anticoagulant (70–100 U/kg).	I	B
Life-long single antiplatelet therapy, usually aspirin, is recommended.	I	A
In patients with SCAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended for 6 months, irrespective of the stent type.	I	A
Antithrombotic treatment in NSTE-ACS patients undergoing PCI		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor is recommended in addition to aspirin, and maintained over 12 months unless there are contraindications such as excessive risk of bleeding. Options are:	I	A
• Prasugrel in $P2Y_{12}$-naïve patients who proceed to PCI (60 mg loading dose, 10 mg daily dose)	I	B
• Ticagrelor irrespective of the pretreatment and revascularisation strategy (180 mg loading dose, 90 mg twice daily)	I	B
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B
Pretreatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended.	III	A

It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	III	B
Peri-interventional anticoagulation is recommended for all patients in addition to antiplatelet therapy.	I	A
In patients on fondaparinux (2.5 mg daily s.c.), a single bolus UFH (85 IU/kg, or 60 IU in the case of concomitant use of GP IIb/IIIa receptor inhibitors) is indicated.	I	B
Crossover of UFH and LMWH is not recommended.	III	B
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥ 25).	I	A
Antithrombotic treatment in STEMI patients undergoing PCI		
Aspirin is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 75–250 mg i.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A potent P2Y12 inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contraindicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
Strategies for follow-up and management		
After CABG or PCI for acute myocardial infarction participation in a cardiac rehabilitation programme is recommended to improve patient outcomes.	I	A
It is recommended to start and reinforce secondary prevention measures including medical therapy and lifestyle changes after myocardial revascularisation.	I	A

14.

ACS = acute coronary syndrome; BMS = bare metal stent; BRS = bioresorbable scaffolds; CABG = coronary artery bypass grafting; CKD = chronic kidney disease; DAPT = dual antiplatelet therapy; DES = drug eluting stents; DUS = duplex ultrasound; ECG = electrocardiogram; FFR = fractional flow reserve; GFR = glomerular filtration rate; GP = glycoprotein; IABP = intra-aortic balloon pump; iFR = instantaneous wave-free radio; IMA = internal mammary artery; i.v. = intravenous; LAD = left anterior descending; LBBB = left bundle branch block; LM = left main; LMWH = low-molecular-weight heparin; LV = left

ventricular; LVEF = left ventricular ejection fraction; MACCE = major adverse cardiac and cerebrovascular event; NSTE-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; s.c. = subcutaneous; SCAD = stable coronary artery disease; STEMI = ST-elevation myocardial infarction; STS = Society of Thoracic Surgeons; SVG = saphenous vein graft; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; TIA = transient ischaemic attack; UFH = unfractionated heparin.

[a]Class of recommendation.

[b]Level of evidence.

[c]With documented ischaemia or FFR ≤ 0.80, iFR ≤ 0.89 or diameter stenosis ≥ 90%.

[d]Based on clinical judgment and FFR < 0.75

[e]These recommendations refer to stents which are supported by large-scale randomised trials with clinical endpoint evaluation leading to unconditional CE mark (53).

22. References

Please note that in the final version, the references in the main document will be moved en bloc to the supplementary appendix with only references from 2015 on retained (as in the last version). After this round, the medical writer stage is planned. In order to facilitate edits arising from the medical writer, this version contains active citation tags and the full reference list. It is planned to eliminate the tags and finalize the reference list at this stage. We hope this is acceptable.

1. Task Force M, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabate M, Senior R, Taggart DP, van der Wall EE, Vrints CJ, Guidelines ESCCfP, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Document R, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Ryden L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J 2013;**34**(38):2949-3003.
2. Min JK, Leipsic J, Pencina MJ, Berman DS, Koo BK, van Mieghem C, Erglis A, Lin FY, Dunning AM, Apruzzese P, Budoff MJ, Cole JH, Jaffer FA, Leon MB, Malpeso J, Mancini GB, Park SJ, Schwartz RS, Shaw LJ, Mauri L. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. JAMA 2012;**308**(12):1237-45.
3. Norgaard BL, Leipsic J, Gaur S, Seneviratne S, Ko BS, Ito H, Jensen JM, Mauri L, De Bruyne B, Bezerra H, Osawa K, Marwan M, Naber C, Erglis A, Park SJ, Christiansen EH, Kaltoft A, Lassen JF, Botker HE, Achenbach S, Group NXTTS. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;**63**(12):1145-1155.
4. Douglas PS, Pontone G, Hlatky MA, Patel MR, Norgaard BL, Byrne RA, Curzen N, Purcell I, Gutberlet M, Rioufol G, Hink U, Schuchlenz HW, Feuchtner G, Gilard M, Andreini D, Jensen JM, Hadamitzky M, Chiswell K, Cyr D, Wilk A, Wang F, Rogers C, De Bruyne B, Bartorelli A, Andreini D, Pepi M, Bertella E, Mushtaq S, Beltrama V, Baggiano A, Gaur S, Romby L, Broderson JR, Hjelm L, Byrne R, Guerra E, Husser O, Koppara T, Nadjiri J, Hadamitzky M, Winogradow J, Repp J, Weigand S, Wimbaur F, Lohaus R, Rumpf PM, Lorenz E, Schoemig G, Hosl K, Ruf J, Curzen N, Shambrook J, Corbett S, Simpson I, Calver A, Wilkinson J, Nicholas Z, Radmore JA, Tyrell B, Elridge C, Lacoste R, Purcell I, Das R, Haq I, Zaman AG, Spyridopoulos I, Bagnall A, Ahmed J, Narytnyk A, Adams-Hall J, Bremner L, Hetherington S, Lamb S, Phillipson A, Wilson R, Procter K, Jones S, Richardson VA, Quinn L, Wealleans V, Rowling S, Price C, Gutberlet M, Lehmkuhl L, Woinke M, Schuler G, Urban D, Lücke C, Juhrich F, Luderer K, Fohlisch J, Dohnert C, Rioufol G, Finet G, Douek P, Varillon Y, Laval D, Mansuy A, Renaudin P, Rageade M, Hink U, Kreitner K, Jabs A, Yang Y, Gori T, Kaesberger B, Schuchlenz H, Botegal D, Genger M, Zechner P, Weihs W, Kullnig P, Kau W, Weikl S, Feuchtner G, Friedrich G, Plank F, Gilard M, Boschat J, Castellant P, Didier R, Martin F, Douglas PS, De Bruyne B, Hlatky M, Norgaard BL, Patel M, Pontone G, Rogers C, Patel M, Patel M, Jones WS, Shah R, Dunn G, Lowe A, Martinez B, Debus A, Jaeger J, Wang F, Wilk A. Clinical outcomes of fractional flow reserve by computed tomographic angiography-guided diagnostic strategies vs. usual care in patients with suspected coronary artery disease: the prospective longitudinal trial of FFRct: outcome and resource impacts stu…. Eur Heart J 2015.
5. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, Gonzalez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP,

Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, Authors/Task Force M. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;**37**(27):2129-200.
6. Beanlands RS, Nichol G, Huszti E, Humen D, Racine N, Freeman M, Gulenchyn KY, Garrard L, deKemp R, Guo A, Ruddy TD, Benard F, Lamy A, Iwanochko RM, Investigators P-. F-18-fluorodeoxyglucose positron emission tomography imaging-assisted management of patients with severe left ventricular dysfunction and suspected coronary disease: a randomized, controlled trial (PARR-2). J Am Coll Cardiol 2007;**50**(20):2002-12.
7. Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, Danziger-Isakov L, Kirklin JK, Kirk R, Kushwaha SS, Lund LH, Potena L, Ross HJ, Taylor DO, Verschuuren EA, Zuckermann A, International Society for Heart Lung Transplantation Infectious Diseases C, International Society for Heart Lung Transplantation Pediatric Transplantation C, International Society for Heart Lung Transplantation Heart F, Transplantation C. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. J Heart Lung Transplant 2016;**35**(1):1-23.
8. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J, International Society for H, Lung T. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. J Heart Lung Transplant 2013;**32**(2):157-87.
9. Bonow RO, Maurer G, Lee KL, Holly TA, Binkley PF, Desvigne-Nickens P, Drozdz J, Farsky PS, Feldman AM, Doenst T, Michler RE, Berman DS, Nicolau JC, Pellikka PA, Wrobel K, Alotti N, Asch FM, Favaloro LE, She L, Velazquez EJ, Jones RH, Panza JA, Investigators ST. Myocardial viability and survival in ischemic left ventricular dysfunction. N Engl J Med 2011;**364**(17):1617-25.
10. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol 2002;**39**(7):1151-8.
11. Ling LF, Marwick TH, Flores DR, Jaber WA, Brunken RC, Cerqueira MD, Hachamovitch R. Identification of therapeutic benefit from revascularization in patients with left ventricular systolic dysfunction: inducible ischemia versus hibernating myocardium. Circ Cardiovasc Imaging 2013;**6**(3):363-72.
12. Ahn JM, Park DW, Shin ES, Koo BK, Nam CW, Doh JH, Kim JH, Chae IH, Yoon JH, Her SH, Seung KB, Chung WY, Yoo SY, Lee JB, Choi SW, Park K, Hong TJ, Lee SY, Han M, Lee PH, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, Park SJ, Investigatorsdagger I-F. Fractional Flow Reserve and Cardiac Events in Coronary Artery Disease: Data From a Prospective IRIS-FFR Registry (Interventional Cardiology Research Incooperation Society Fractional Flow Reserve). Circulation 2017;**135**(23):2241-2251.
13. Bech GJ, De Bruyne B, Bonnier HJ, Bartunek J, Wijns W, Peels K, Heyndrickx GR, Koolen JJ, Pijls NH. Long-term follow-up after deferral of percutaneous transluminal coronary angioplasty of intermediate stenosis on the basis of coronary pressure measurement. J Am Coll Cardiol 1998;**31**(4):841-7.
14. Bech GJ, De Bruyne B, Pijls NH, de Muinck ED, Hoorntje JC, Escaned J, Stella PR, Boersma E, Bartunek J, Koolen JJ, Wijns W. Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary stenosis: a randomized trial. Circulation 2001;**103**(24):2928-34.
15. Pijls NH, van Schaardenburgh P, Manoharan G, Boersma E, Bech JW, van't Veer M, Bar F, Hoorntje J, Koolen J, Wijns W, de Bruyne B. Percutaneous coronary intervention of functionally nonsignificant stenosis: 5-year follow-up of the DEFER Study. J Am Coll Cardiol 2007;**49**(21):2105-11.
16. Adjedj J, De Bruyne B, Flore V, Di Gioia G, Ferrara A, Pellicano M, Toth GG, Bartunek J, Vanderheyden M, Heyndrickx GR, Wijns W, Barbato E. Significance of Intermediate Values of Fractional Flow Reserve in Patients With Coronary Artery Disease. Circulation 2016;**133**(5):502-8.

17. Davies JE, Sen S, Dehbi HM, Al-Lamee R, Petraco R, Nijjer SS, Bhindi R, Lehman SJ, Walters D, Sapontis J, Janssens L, Vrints CJ, Khashaba A, Laine M, Van Belle E, Krackhardt F, Bojara W, Going O, Harle T, Indolfi C, Niccoli G, Ribichini F, Tanaka N, Yokoi H, Takashima H, Kikuta Y, Erglis A, Vinhas H, Canas Silva P, Baptista SB, Alghamdi A, Hellig F, Koo BK, Nam CW, Shin ES, Doh JH, Brugaletta S, Alegria-Barrero E, Meuwissen M, Piek JJ, van Royen N, Sezer M, Di Mario C, Gerber RT, Malik IS, Sharp ASP, Talwar S, Tang K, Samady H, Altman J, Seto AH, Singh J, Jeremias A, Matsuo H, Kharbanda RK, Patel MR, Serruys P, Escaned J. Use of the Instantaneous Wave-free Ratio or Fractional Flow Reserve in PCI. N Engl J Med 2017;**376**(19):1824-1834.
18. Gotberg M, Christiansen EH, Gudmundsdottir IJ, Sandhall L, Danielewicz M, Jakobsen L, Olsson SE, Ohagen P, Olsson H, Omerovic E, Calais F, Lindroos P, Maeng M, Todt T, Venetsanos D, James SK, Karegren A, Nilsson M, Carlsson J, Hauer D, Jensen J, Karlsson AC, Panayi G, Erlinge D, Frobert O, i FRSI. Instantaneous Wave-free Ratio versus Fractional Flow Reserve to Guide PCI. N Engl J Med 2017;**376**(19):1813-1823.
19. Van Belle E, Rioufol G, Pouillot C, Cuisset T, Bougrini K, Teiger E, Champagne S, Belle L, Barreau D, Hanssen M, Besnard C, Dauphin R, Dallongeville J, El Hahi Y, Sideris G, Bretelle C, Lhoest N, Barnay P, Leborgne L, Dupouy P, Investigators of the Registre Francais de la F-RF. Outcome impact of coronary revascularization strategy reclassification with fractional flow reserve at time of diagnostic angiography: insights from a large French multicenter fractional flow reserve registry. Circulation 2014;**129**(2):173-85.
20. Curzen N, Rana O, Nicholas Z, Golledge P, Zaman A, Oldroyd K, Hanratty C, Banning A, Wheatcroft S, Hobson A, Chitkara K, Hildick-Smith D, McKenzie D, Calver A, Dimitrov BD, Corbett S. Does routine pressure wire assessment influence management strategy at coronary angiography for diagnosis of chest pain?: the RIPCORD study. Circ Cardiovasc Interv 2014;**7**(2):248-55.
21. Baptista SB, Raposo L, Santos L, Ramos R, Cale R, Jorge E, Machado C, Costa M, Infante de Oliveira E, Costa J, Pipa J, Fonseca N, Guardado J, Silva B, Sousa MJ, Silva JC, Rodrigues A, Seca L, Fernandes R. Impact of Routine Fractional Flow Reserve Evaluation During Coronary Angiography on Management Strategy and Clinical Outcome: One-Year Results of the POST-IT. Circ Cardiovasc Interv 2016;**9**(7).
22. Van Belle E, Baptista SB, Raposo L, Henderson J, Rioufol G, Santos L, Pouillot C, Ramos R, Cuisset T, Cale R, Teiger E, Jorge E, Belle L, Machado C, Barreau D, Costa M, Hanssen M, Oliveira E, Besnard C, Costa J, Dallongeville J, Pipa J, Sideris G, Fonseca N, Bretelle C, Guardado J, Lhoest N, Silva B, Barnay P, Sousa MJ, Leborgne L, Silva JC, Vincent F, Rodrigues A, Seca L, Fernandes R, Dupouy P, Group P-FS. Impact of Routine Fractional Flow Reserve on Management Decision and 1-Year Clinical Outcome of Patients With Acute Coronary Syndromes: PRIME-FFR (Insights From the POST-IT [Portuguese Study on the Evaluation of FFR-Guided Treatment of Coronary Disease] and R3F [French FFR Registry] Integrated Multicenter Registries - Implementation of FFR [Fractional Flow Reserve] in Routine Practice). Circ Cardiovasc Interv 2017;**10**(6).
23. Van Belle E, Dupouy P, Rioufol G. Routine Fractional Flow Reserve Combined to Diagnostic Coronary Angiography as a One-Stop Procedure: Episode 3. Circ Cardiovasc Interv 2016;**9**(7).
24. Johnson NP, Toth GG, Lai D, Zhu H, Acar G, Agostoni P, Appelman Y, Arslan F, Barbato E, Chen SL, Di Serafino L, Dominguez-Franco AJ, Dupouy P, Esen AM, Esen OB, Hamilos M, Iwasaki K, Jensen LO, Jimenez-Navarro MF, Katritsis DG, Kocaman SA, Koo BK, Lopez-Palop R, Lorin JD, Miller LH, Muller O, Nam CW, Oud N, Puymirat E, Rieber J, Rioufol G, Rodes-Cabau J, Sedlis SP, Takeishi Y, Tonino PA, Van Belle E, Verna E, Werner GS, Fearon WF, Pijls NH, De Bruyne B, Gould KL. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. J Am Coll Cardiol 2014;**64**(16):1641-54.
25. Mallidi J, Atreya AR, Cook J, Garb J, Jeremias A, Klein LW, Lotfi A. Long-term outcomes following fractional flow reserve-guided treatment of angiographically ambiguous left main coronary artery disease: A meta-analysis of prospective cohort studies. Catheter Cardiovasc Interv 2015;**86**(1):12-8.
26. Hamilos M, Muller O, Cuisset T, Ntalianis A, Chlouverakis G, Sarno G, Nelis O, Bartunek J, Vanderheyden M, Wyffels E, Barbato E, Heyndrickx GR, Wijns W, De Bruyne B. Long-term clinical

outcome after fractional flow reserve-guided treatment in patients with angiographically equivocal left main coronary artery stenosis. Circulation 2009;**120**(15):1505-12.
27. Yong AS, Daniels D, De Bruyne B, Kim HS, Ikeno F, Lyons J, Pijls NH, Fearon WF. Fractional flow reserve assessment of left main stenosis in the presence of downstream coronary stenoses. Circ Cardiovasc Interv 2013;**6**(2):161-5.
28. Toth G, De Bruyne B, Casselman F, De Vroey F, Pyxaras S, Di Serafino L, Van Praet F, Van Mieghem C, Stockman B, Wijns W, Degrieck I, Barbato E. Fractional flow reserve-guided versus angiography-guided coronary artery bypass graft surgery. Circulation 2013;**128**(13):1405-11.
29. Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, Klauss V, Manoharan G, Engstrom T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon WF, Investigators FS. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med 2009;**360**(3):213-24.
30. Pijls NH, Fearon WF, Tonino PA, Siebert U, Ikeno F, Bornschein B, van't Veer M, Klauss V, Manoharan G, Engstrom T, Oldroyd KG, Ver Lee PN, MacCarthy PA, De Bruyne B, Investigators FS. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention in patients with multivessel coronary artery disease: 2-year follow-up of the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) study. J Am Coll Cardiol 2010;**56**(3):177-84.
31. van Nunen LX, Zimmermann FM, Tonino PA, Barbato E, Baumbach A, Engstrom T, Klauss V, MacCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M, Fearon WF, De Bruyne B, Pijls NH, Investigators FS. Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. Lancet 2015.
32. De Bruyne B, Pijls NH, Kalesan B, Barbato E, Tonino PA, Piroth Z, Jagic N, Mobius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engstrom T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Juni P, Fearon WF, Investigators FT. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. N Engl J Med 2012;**367**(11):991-1001.
33. Fearon WF, Nishi T, De Bruyne B, Boothroyd DB, Barbato E, Tonino P, Juni P, Pijls NHJ, Hlatky MA, Investigators FT. Clinical Outcomes and Cost-Effectiveness of Fractional Flow Reserve-Guided Percutaneous Coronary Intervention in Patients With Stable Coronary Artery Disease: Three-Year Follow-Up of the FAME 2 Trial (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation). Circulation 2018;**137**(5):480-487.
34. Escaned J, Collet C, Ryan N, De Maria GL, Walsh S, Sabate M, Davies J, Lesiak M, Moreno R, Cruz-Gonzalez I, Hoole SP, Ej West N, Piek JJ, Zaman A, Fath-Ordoubadi F, Stables RH, Appleby C, van Mieghem N, van Geuns RJ, Uren N, Zueco J, Buszman P, Iniguez A, Goicolea J, Hildick-Smith D, Ochala A, Dudek D, Hanratty C, Cavalcante R, Kappetein AP, Taggart DP, van Es GA, Morel MA, de Vries T, Onuma Y, Farooq V, Serruys PW, Banning AP. Clinical outcomes of state-of-the-art percutaneous coronary revascularization in patients with de novo three vessel disease: 1-year results of the SYNTAX II study. Eur Heart J 2017;**38**(42):3124-3134.
35. Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW, Investigators M-C. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. Circ Cardiovasc Interv 2009;**2**(3):167-77.
36. Fassa AA, Wagatsuma K, Higano ST, Mathew V, Barsness GW, Lennon RJ, Holmes DR, Jr., Lerman A. Intravascular ultrasound-guided treatment for angiographically indeterminate left main coronary artery disease: a long-term follow-up study. J Am Coll Cardiol 2005;**45**(2):204-11.
37. de la Torre Hernandez JM, Hernandez Hernandez F, Alfonso F, Rumoroso JR, Lopez-Palop R, Sadaba M, Carrillo P, Rondan J, Lozano I, Ruiz Nodar JM, Baz JA, Fernandez Nofrerias E, Pajin F, Garcia Camarero T, Gutierrez H, Group LS. Prospective application of pre-defined intravascular ultrasound criteria for assessment of intermediate left main coronary artery lesions results from the multicenter LITRO study. J Am Coll Cardiol 2011;**58**(4):351-8.
38. Park SJ, Ahn JM, Kang SJ, Yoon SH, Koo BK, Lee JY, Kim WJ, Park DW, Lee SW, Kim YH, Lee CW, Park SW. Intravascular ultrasound-derived minimal lumen area criteria for functionally significant left main coronary artery stenosis. JACC Cardiovasc Interv 2014;**7**(8):868-74.

39. Pijls NH, De Bruyne B, Peels K, Van Der Voort PH, Bonnier HJ, Bartunek JKJJ, Koolen JJ. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N Engl J Med 1996;**334**(26):1703-8.
40. Ayton DR, Barker AL, Peeters G, Berkovic DE, Lefkovits J, Brennan A, Evans S, Zalcberg J, Reid C, Stoelwinder JJ, McNeil J. Exploring patient-reported outcomes following percutaneous coronary intervention: A qualitative study. Health Expect 2017.
41. Myles PS. Meaningful outcome measures in cardiac surgery. J Extra Corpor Technol 2014;**46**(1):23-7.
42. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney M-T, Corrà U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FDR, Løchen M-L, Löllgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WMM, Binno S, De Backer G, Roffi M, Aboyans V, Bachl N, Bueno H, Carerj S, Cho L, Cox J, De Sutter J, Egidi G, Fisher M, Fitzsimons D, Franco OH, Guenoun M, Jennings C, Jug B, Kirchhof P, Kotseva K, Lip GYH, Mach F, Mancia G, Bermudo FM, Mezzani A, Niessner A, Ponikowski P, Rauch B, Rydén L, Stauder A, Turc G, Wiklund O, Windecker S, Zamorano JL, Zamorano JL, Aboyans V, Achenbach S, Agewall S, Badimon L, Barón-Esquivias G, Baumgartner H, Bax JJ, Bueno H, Carerj S, Dean V, Erol Ç, Fitzsimons D, Gaemperli O, Kirchhof P, Kolh P, Lancellotti P, Lip GYH, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Roffi M, Torbicki A, Carneiro AV, Windecker S, Metzler B, Najafov R, Stelmashok V, De Maeyer C, Dilić M, Gruev I, Miličić D, Vaverkova H, Gustafsson I, Attia I, Duishvili D, Ferrières J, Kostova N, Klimiashvili Z, Hambrecht R, Tsioufis K, Szabados E, Andersen K, Vaughan C, Zafrir B, Novo S, Davletov K, Jashari F, Kerimkulova A, Mintale I, Saade G, Petrulioniene Z, Delagardelle C, Magri CJ, Rudi V, Oukerraj L, Çölkesen BE, Schirmer H, dos Reis RP, Gherasim D, Nedogoda S, Zavatta M, Giga V, Filipova S, Padial LR, Kiessling A, Mach F, Mahdhaoui A, Ural D, Nesukay E, Gale C. 2016 European Guidelines on cardiovascular disease prevention in clinical practiceThe Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016;**37**(29):2315-2381.
43. Head SJ, Kaul S, Mack MJ, Serruys PW, Taggart DP, Holmes DR, Jr., Leon MB, Marco J, Bogers AJ, Kappetein AP. The rationale for Heart Team decision-making for patients with stable, complex coronary artery disease. Eur Heart J 2013;**34**(32):2510-8.
44. Filardo G, Maggioni AP, Mura G, Valagussa F, Valagussa L, Schweiger C, Ballard DJ, Liberati A. The consequences of under-use of coronary revascularization; results of a cohort study in Northern Italy. Eur Heart J 2001;**22**(8):654-62.
45. Yates MT, Soppa GK, Valencia O, Jones S, Firoozi S, Jahangiri M. Impact of European Society of Cardiology and European Association for Cardiothoracic Surgery Guidelines on Myocardial Revascularization on the activity of percutaneous coronary intervention and coronary artery bypass graft surgery for stable coronary artery disease. J Thorac Cardiovasc Surg 2014;**147**(2):606-10.
46. OECD. *Health at a Glance*; 2015.
47. Bradley SM, Bohn CM, Malenka DJ, Graham MM, Bryson CL, McCabe JM, Curtis JP, Lambert-Kerzner A, Maynard C. Temporal Trends in Percutaneous Coronary Intervention AppropriatenessCLINICAL PERSPECTIVE. Insights From the Clinical Outcomes Assessment Program 2015;**132**(1):20-26.
48. Hannan EL, Samadashvili Z, Cozzens K, Gesten F, Osinaga A, Fish DG, Donahue CL, Bass RJ, Walford G, Jacobs AK, Venditti FJ, Stamato NJ, Berger PB, Sharma S, King Iii SB. Changes in Percutaneous Coronary Interventions Deemed “Inappropriate” by Appropriate Use Criteria. J Am Coll Cardiol 2017;**69**(10):1234-1242.
49. Denvir MA, Pell JP, Lee AJ, Rysdale J, Prescott RJ, Eteiba H, Walker A, Mankad P, Starkey IR. Variations in clinical decision-making between cardiologists and cardiac surgeons; a case for management by multidisciplinary teams? J Cardiothorac Surg 2006;**1**:2.

50. Pavlidis AN, Perera D, Karamasis GV, Bapat V, Young C, Clapp BR, Blauth C, Roxburgh J, Thomas MR, Redwood SR. Implementation and consistency of Heart Team decision-making in complex coronary revascularisation. Int J Cardiol 2016;**206**:37-41.
51. Sanchez CE, Dota A, Badhwar V, Kliner D, Smith AJ, Chu D, Toma C, Wei L, Marroquin OC, Schindler J, Lee JS, Mulukutla SR. Revascularization heart team recommendations as an adjunct to appropriate use criteria for coronary revascularization in patients with complex coronary artery disease. Catheter Cardiovasc Interv 2016;**88**(4):E103-E112.
52. Sobolev BG, Fradet G, Kuramoto L, Rogula B. The occurrence of adverse events in relation to time after registration for coronary artery bypass surgery: a population-based observational study. J Cardiothorac Surg 2013;**8**:74.
53. Head SJ, da Costa BR, Beumer B, Stefanini GG, Alfonso F, Clemmensen PM, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Kappetein AP, Kastrati A, Knuuti J, Kolh P, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A, Windecker S, Juni P, Sousa-Uva M. Adverse events while awaiting myocardial revascularization: a systematic review and meta-analysis. Eur J Cardiothorac Surg 2017.
54. Graham MM, Knudtson ML, O'Neill BJ, Ross DB, Canadian Cardiovascular Society Access to Care Working G. Treating the right patient at the right time: Access to cardiac catheterization, percutaneous coronary intervention and cardiac surgery. Can J Cardiol 2006;**22**(8):679-83.
55. Truffa MA, Alves GM, Bernardi F, Esteves Filho A, Ribeiro E, Galon MZ, Spadaro A, Kajita LJ, Arrieta R, Lemos PA. Does Ad Hoc Coronary Intervention Reduce Radiation Exposure? - Analysis of 568 Patients. Arq Bras Cardiol 2015;**105**(5):487-92.
56. Hannan EL, Samadashvili Z, Walford G, Holmes DR, Jacobs A, Sharma S, Katz S, King SB, 3rd. Predictors and outcomes of ad hoc versus non-ad hoc percutaneous coronary interventions. JACC Cardiovasc Interv 2009;**2**(4):350-6.
57. participants R-t. Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. . Lancet 1997;**350**(9076):461-8.
58. Investigators T. Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary-artery disease (TIME): a randomised trial. Lancet 2001;**358**(9286):951-7.
59. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, Booth DC, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS, Group CTR. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med 2007;**356**(15):1503-16.
60. Erne P, Schoenenberger AW, Burckhardt D, Zuber M, Kiowski W, Buser PT, Dubach P, Resink TJ, Pfisterer M. Effects of percutaneous coronary interventions in silent ischemia after myocardial infarction: the SWISSI II randomized controlled trial. JAMA 2007;**297**(18):1985-91.
61. Group BDS, Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, MacGregor JM, Orchard TJ, Chaitman BR, Genuth SM, Goldberg SH, Hlatky MA, Jones TL, Molitch ME, Nesto RW, Sako EY, Sobel BE. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med 2009;**360**(24):2503-15.
62. Hueb W, Lopes N, Gersh BJ, Soares PR, Ribeiro EE, Pereira AC, Favarato D, Rocha AS, Hueb AC, Ramires JA. Ten-year follow-up survival of the Medicine, Angioplasty, or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation 2010;**122**(10):949-57.
63. Al-Lamee R, Thompson D, Dehbi HM, Sen S, Tang K, Davies J, Keeble T, Mielewczik M, Kaprielian R, Malik IS, Nijjer SS, Petraco R, Cook C, Ahmad Y, Howard J, Baker C, Sharp A, Gerber R, Talwar S, Assomull R, Mayet J, Wensel R, Collier D, Shun-Shin M, Thom SA, Davies JE, Francis DP, investigators O. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. Lancet 2018;**391**(10115):31-40.
64. Chaitman BR, Mori Brooks M, Fox K, Luscher TF. ORBITA revisited: what it really means and what it does not? Eur Heart J 2018.
65. Baron SJ, Chinnakondepalli K, Magnuson EA, Kandzari DE, Puskas JD, Ben-Yehuda O, van Es GA, Taggart DP, Morice MC, Lembo NJ, Brown WM, 3rd, Banning A, Simonton CA, Kappetein AP, Sabik JF, Serruys PW, Stone GW, Cohen DJ, Investigators E. Quality-of-Life After Everolimus-Eluting

Stents or Bypass Surgery for Left-Main Disease: Results From the EXCEL Trial. J Am Coll Cardiol 2017;**70**(25):3113-3122.
66. Abdallah MS, Wang K, Magnuson EA, Osnabrugge RL, Kappetein AP, Morice MC, Mohr FA, Serruys PW, Cohen DJ, Investigators ST. Quality of Life After Surgery or DES in Patients With 3-Vessel or Left Main Disease. J Am Coll Cardiol 2017;**69**(16):2039-2050.
67. Abdallah MS, Wang K, Magnuson EA, Spertus JA, Farkouh ME, Fuster V, Cohen DJ, Investigators FT. Quality of life after PCI vs CABG among patients with diabetes and multivessel coronary artery disease: a randomized clinical trial. JAMA 2013;**310**(15):1581-90.
68. Yusuf S, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, Davis K, Killip T, Passamani E, Norris R, et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. Lancet 1994;**344**(8922):563-70.
69. Bittl JA, He Y, Jacobs AK, Yancy CW, Normand SL, American College of Cardiology Foundation/American Heart Association Task Force on Practice G. Bayesian methods affirm the use of percutaneous coronary intervention to improve survival in patients with unprotected left main coronary artery disease. Circulation 2013;**127**(22):2177-85.
70. Dzavik V, Ghali WA, Norris C, Mitchell LB, Koshal A, Saunders LD, Galbraith PD, Hui W, Faris P, Knudtson ML, Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease I. Long-term survival in 11,661 patients with multivessel coronary artery disease in the era of stenting: a report from the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease (APPROACH) Investigators. Am Heart J 2001;**142**(1):119-26.
71. Lee PH, Ahn JM, Chang M, Baek S, Yoon SH, Kang SJ, Lee SW, Kim YH, Lee CW, Park SW, Park DW, Park SJ. Left Main Coronary Artery Disease: Secular Trends in Patient Characteristics, Treatments, and Outcomes. J Am Coll Cardiol 2016;**68**(11):1233-46.
72. Smith PK, Califf RM, Tuttle RH, Shaw LK, Lee KL, Delong ER, Lilly RE, Sketch MH, Jr., Peterson ED, Jones RH. Selection of surgical or percutaneous coronary intervention provides differential longevity benefit. Ann Thorac Surg 2006;**82**(4):1420-8; discussion 1428-9.
73. Hannan EL, Wu C, Walford G, Culliford AT, Gold JP, Smith CR, Higgins RS, Carlson RE, Jones RH. Drug-eluting stents vs. coronary-artery bypass grafting in multivessel coronary disease. N Engl J Med 2008;**358**(4):331-41.
74. Hannan EL, Samadashvili Z, Cozzens K, Walford G, Jacobs AK, Holmes DR, Jr., Stamato NJ, Gold JP, Sharma S, Venditti FJ, Powell T, King SB, 3rd. Comparative outcomes for patients who do and do not undergo percutaneous coronary intervention for stable coronary artery disease in New York. Circulation 2012;**125**(15):1870-9.
75. Caracciolo EA, Davis KB, Sopko G, Kaiser GC, Corley SD, Schaff H, Taylor HA, Chaitman BR. Comparison of surgical and medical group survival in patients with left main equivalent coronary artery disease. Long-term CASS experience. Circulation 1995;**91**(9):2335-44.
76. Chaitman BR, Hardison RM, Adler D, Gebhart S, Grogan M, Ocampo S, Sopko G, Ramires JA, Schneider D, Frye RL, Bypass Angioplasty Revascularization Investigation 2 Diabetes Study G. The Bypass Angioplasty Revascularization Investigation 2 Diabetes randomized trial of different treatment strategies in type 2 diabetes mellitus with stable ischemic heart disease: impact of treatment strategy on cardiac mortality and myocardial infarction. Circulation 2009;**120**(25):2529-40.
77. Passamani E, Davis KB, Gillespie MJ, Killip T. A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. N Engl J Med 1985;**312**(26):1665-71.
78. Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A, Ali IS, Pohost G, Gradinac S, Abraham WT, Yii M, Prabhakaran D, Szwed H, Ferrazzi P, Petrie MC, O'Connor CM, Panchavinnin P, She L, Bonow RO, Rankin GR, Jones RH, Rouleau JL, Investigators S. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;**364**(17):1607-16.
79. Jones RH, Kesler K, Phillips HR, 3rd, Mark DB, Smith PK, Nelson CL, Newman MF, Reves JG, Anderson RW, Califf RM. Long-term survival benefits of coronary artery bypass grafting and percutaneous transluminal angioplasty in patients with coronary artery disease. J Thorac Cardiovasc Surg 1996;**111**(5):1013-25.

80. Baker DW, Jones R, Hodges J, Massie BM, Konstam MA, Rose EA. Management of heart failure. III. The role of revascularization in the treatment of patients with moderate or severe left ventricular systolic dysfunction. JAMA 1994;**272**(19):1528-34.
81. Velazquez EJ, Lee KL, Jones RH, Al-Khalidi HR, Hill JA, Panza JA, Michler RE, Bonow RO, Doenst T, Petrie MC, Oh JK, She L, Moore VL, Desvigne-Nickens P, Sopko G, Rouleau JL, Investigators S. Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy. N Engl J Med 2016;**374**(16):1511-20.
82. Panza JA, Velazquez EJ, She L, Smith PK, Nicolau JC, Favaloro RR, Gradinac S, Chrzanowski L, Prabhakaran D, Howlett JG, Jasinski M, Hill JA, Szwed H, Larbalestier R, Desvigne-Nickens P, Jones RH, Lee KL, Rouleau JL. Extent of coronary and myocardial disease and benefit from surgical revascularization in ischemic LV dysfunction [Corrected]. J Am Coll Cardiol 2014;**64**(6):553-61.
83. Petrie MC, Jhund PS, She L, Adlbrecht C, Doenst T, Panza JA, Hill JA, Lee KL, Rouleau JL, Prior DL, Ali IS, Maddury J, Golba KS, White HD, Carson P, Chrzanowski L, Romanov A, Miller AB, Velazquez EJ, Investigators ST. Ten-Year Outcomes After Coronary Artery Bypass Grafting According to Age in Patients With Heart Failure and Left Ventricular Systolic Dysfunction: An Analysis of the Extended Follow-Up of the STICH Trial (Surgical Treatment for Ischemic Heart Failure). Circulation 2016;**134**(18):1314-1324.
84. Hachamovitch R, Rozanski A, Shaw LJ, Stone GW, Thomson LE, Friedman JD, Hayes SW, Cohen I, Germano G, Berman DS. Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy. Eur Heart J 2011;**32**(8):1012-24.
85. Davies RF, Goldberg AD, Forman S, Pepine CJ, Knatterud GL, Geller N, Sopko G, Pratt C, Deanfield J, Conti CR. Asymptomatic Cardiac Ischemia Pilot (ACIP) study two-year follow-up: outcomes of patients randomized to initial strategies of medical therapy versus revascularization. Circulation 1997;**95**(8):2037-43.
86. Shaw LJ, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, Weintraub WS, O'Rourke RA, Dada M, Spertus JA, Chaitman BR, Friedman J, Slomka P, Heller GV, Germano G, Gosselin G, Berger P, Kostuk WJ, Schwartz RG, Knudtson M, Veledar E, Bates ER, McCallister B, Teo KK, Boden WE, Investigators C. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. Circulation 2008;**117**(10):1283-91.
87. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;**107**(23):2900-7.
88. Gada H, Kirtane AJ, Kereiakes DJ, Bangalore S, Moses JW, Genereux P, Mehran R, Dangas GD, Leon MB, Stone GW. Meta-analysis of trials on mortality after percutaneous coronary intervention compared with medical therapy in patients with stable coronary heart disease and objective evidence of myocardial ischemia. Am J Cardiol 2015;**115**(9):1194-9.
89. Stergiopoulos K, Boden WE, Hartigan P, Mobius-Winkler S, Hambrecht R, Hueb W, Hardison RM, Abbott JD, Brown DL. Percutaneous coronary intervention outcomes in patients with stable obstructive coronary artery disease and myocardial ischemia: a collaborative meta-analysis of contemporary randomized clinical trials. JAMA Intern Med 2014;**174**(2):232-40.
90. Nishigaki K, Yamazaki T, Kitabatake A, Yamaguchi T, Kanmatsuse K, Kodama I, Takekoshi N, Tomoike H, Hori M, Matsuzaki M, Takeshita A, Shimbo T, Fujiwara H, Japanese Stable Angina Pectoris Study I. Percutaneous coronary intervention plus medical therapy reduces the incidence of acute coronary syndrome more effectively than initial medical therapy only among patients with low-risk coronary artery disease a randomized, comparative, multicenter study. JACC Cardiovasc Interv 2008;**1**(5):469-79.
91. Katritsis DG, Ioannidis JP. Percutaneous coronary intervention versus conservative therapy in nonacute coronary artery disease: a meta-analysis. Circulation 2005;**111**(22):2906-12.

92. Schomig A, Mehilli J, de Waha A, Seyfarth M, Pache J, Kastrati A. A meta-analysis of 17 randomized trials of a percutaneous coronary intervention-based strategy in patients with stable coronary artery disease. J Am Coll Cardiol 2008;**52**(11):894-904.
93. Trikalinos TA, Alsheikh-Ali AA, Tatsioni A, Nallamothu BK, Kent DM. Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis. Lancet 2009;**373**(9667):911-8.
94. Bangalore S, Pursnani S, Kumar S, Bagos PG. Percutaneous coronary intervention versus optimal medical therapy for prevention of spontaneous myocardial infarction in subjects with stable ischemic heart disease. Circulation 2013;**127**(7):769-81.
95. Pursnani S, Korley F, Gopaul R, Kanade P, Chandra N, Shaw RE, Bangalore S. Percutaneous coronary intervention versus optimal medical therapy in stable coronary artery disease: a systematic review and meta-analysis of randomized clinical trials. Circ Cardiovasc Interv 2012;**5**(4):476-90.
96. Thomas S, Gokhale R, Boden WE, Devereaux PJ. A meta-analysis of randomized controlled trials comparing percutaneous coronary intervention with medical therapy in stable angina pectoris. Can J Cardiol 2013;**29**(4):472-82.
97. De Bruyne B, Fearon WF, Pijls NH, Barbato E, Tonino P, Piroth Z, Jagic N, Mobius-Winckler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engstrom T, Oldroyd K, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Limacher A, Nuesch E, Juni P, Investigators FT. Fractional flow reserve-guided PCI for stable coronary artery disease. N Engl J Med 2014;**371**(13):1208-17.
98. Bucher HC, Hengstler P, Schindler C, Guyatt GH. Percutaneous transluminal coronary angioplasty versus medical treatment for non-acute coronary heart disease: meta-analysis of randomised controlled trials. BMJ 2000;**321**(7253):73-7.
99. Stergiopoulos K, Brown DL. Initial coronary stent implantation with medical therapy vs medical therapy alone for stable coronary artery disease: meta-analysis of randomized controlled trials. Arch Intern Med 2012;**172**(4):312-9.
100. Windecker S, Stortecky S, Stefanini GG, da Costa BR, Rutjes AW, Di Nisio M, Silletta MG, Maione A, Alfonso F, Clemmensen PM, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head S, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter D, Schauerte P, Sousa Uva M, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A, Kolh P, Juni P. Revascularisation versus medical treatment in patients with stable coronary artery disease: network meta-analysis. BMJ 2014;**348**:g3859.
101. Jeremias A, Kaul S, Rosengart TK, Gruberg L, Brown DL. The impact of revascularization on mortality in patients with nonacute coronary artery disease. Am J Med 2009;**122**(2):152-61.
102. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. Eur J Cardiothorac Surg 2012;**41**(4):734-44; discussion 744-5.
103. Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, Normand SL, DeLong ER, Shewan CM, Dokholyan RS, Peterson ED, Edwards FH, Anderson RP, Society of Thoracic Surgeons Quality Measurement Task F. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1--coronary artery bypass grafting surgery. Ann Thorac Surg 2009;**88**(1 Suppl):S2-22.
104. Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, Normand SL, DeLong ER, Shewan CM, Dokholyan RS, Peterson ED, Edwards FH, Anderson RP, Society of Thoracic Surgeons Quality Measurement Task F. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 3--valve plus coronary artery bypass grafting surgery. Ann Thorac Surg 2009;**88**(1 Suppl):S43-62.
105. Biancari F, Vasques F, Mikkola R, Martin M, Lahtinen J, Heikkinen J. Validation of EuroSCORE II in patients undergoing coronary artery bypass surgery. Ann Thorac Surg 2012;**93**(6):1930-5.
106. Osnabrugge RL, Speir AM, Head SJ, Fonner CE, Fonner E, Kappetein AP, Rich JB. Performance of EuroSCORE II in a large US database: implications for transcatheter aortic valve implantation. Eur J Cardiothorac Surg 2014;**46**(3):400-8; discussion 408.
107. Sullivan PG, Wallach JD, Ioannidis JP. Meta-Analysis Comparing Established Risk Prediction Models (EuroSCORE II, STS Score, and ACEF Score) for Perioperative Mortality During Cardiac Surgery. Am J Cardiol 2016;**118**(10):1574-1582.
108. Kirmani BH, Mazhar K, Fabri BM, Pullan DM. Comparison of the EuroSCORE II and Society of Thoracic Surgeons 2008 risk tools. Eur J Cardiothorac Surg 2013;**44**(6):999-1005; discussion 1005.

109. Velicki L, Cemerlic-Adjic N, Pavlovic K, Mihajlovic BB, Bankovic D, Mihajlovic B, Fabri M. Clinical performance of the EuroSCORE II compared with the previous EuroSCORE iterations. Thorac Cardiovasc Surg 2014;**62**(4):288-97.
110. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, van den Brand M, Van Dyck N, Russell ME, Mohr FW, Serruys PW. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005;**1**(2):219-27.
111. Wykrzykowska JJ, Garg S, Girasis C, de Vries T, Morel MA, van Es GA, Buszman P, Linke A, Ischinger T, Klauss V, Corti R, Eberli F, Wijns W, Morice MC, di Mario C, van Geuns RJ, Juni P, Windecker S, Serruys PW. Value of the SYNTAX score for risk assessment in the all-comers population of the randomized multicenter LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) trial. J Am Coll Cardiol 2010;**56**(4):272-7.
112. Garg S, Serruys PW, Silber S, Wykrzykowska J, van Geuns RJ, Richardt G, Buszman PE, Kelbaek H, van Boven AJ, Hofma SH, Linke A, Klauss V, Wijns W, Macaya C, Garot P, DiMario C, Manoharan G, Kornowski R, Ischinger T, Bartorelli A, Van Remortel E, Ronden J, Windecker S. The prognostic utility of the SYNTAX score on 1-year outcomes after revascularization with zotarolimus- and everolimus-eluting stents: a substudy of the RESOLUTE All Comers Trial. JACC Cardiovasc Interv 2011;**4**(4):432-41.
113. Zhao M, Stampf S, Valina C, Kienzle RP, Ferenc M, Gick M, Essang E, Nuhrenberg T, Buttner HJ, Schumacher M, Neumann FJ. Role of euroSCORE II in predicting long-term outcome after percutaneous catheter intervention for coronary triple vessel disease or left main stenosis. Int J Cardiol 2013;**168**(4):3273-9.
114. Cavalcante R, Sotomi Y, Mancone M, Whan Lee C, Ahn JM, Onuma Y, Lemos PA, van Geuns RJ, Park SJ, Serruys PW. Impact of the SYNTAX scores I and II in patients with diabetes and multivessel coronary disease: a pooled analysis of patient level data from the SYNTAX, PRECOMBAT, and BEST trials. Eur Heart J 2017;**38**(25):1969-1977.
115. Medina A, Suarez de Lezo J, Pan M. [A new classification of coronary bifurcation lesions]. Rev Esp Cardiol 2006;**59**(2):183.
116. Mohr FW, Morice MC, Kappetein AP, Feldman TE, Stahle E, Colombo A, Mack MJ, Holmes DR, Jr., Morel MA, Van Dyck N, Houle VM, Dawkins KD, Serruys PW. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013;**381**(9867):629-38.
117. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Stahle E, Colombo A, Mack MJ, Holmes DR, Choi JW, Ruzyllo W, Religa G, Huang J, Roy K, Dawkins KD, Mohr F. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. Circulation 2014;**129**(23):2388-94.
118. Head SJ, Davierwala PM, Serruys PW, Redwood SR, Colombo A, Mack MJ, Morice MC, Holmes DR, Jr., Feldman TE, Stahle E, Underwood P, Dawkins KD, Kappetein AP, Mohr FW. Coronary artery bypass grafting vs. percutaneous coronary intervention for patients with three-vessel disease: final five-year follow-up of the SYNTAX trial. Eur Heart J 2014;**35**(40):2821-30.
119. Park SJ, Ahn JM, Kim YH, Park DW, Yun SC, Lee JY, Kang SJ, Lee SW, Lee CW, Park SW, Choo SJ, Chung CH, Lee JW, Cohen DJ, Yeung AC, Hur SH, Seung KB, Ahn TH, Kwon HM, Lim DS, Rha SW, Jeong MH, Lee BK, Tresukosol D, Fu GS, Ong TK, Investigators BT. Trial of everolimus-eluting stents or bypass surgery for coronary disease. N Engl J Med 2015;**372**(13):1204-12.
120. Makikallio T, Holm NR, Lindsay M, Spence MS, Erglis A, Menown IB, Trovik T, Eskola M, Romppanen H, Kellerth T, Ravkilde J, Jensen LO, Kalinauskas G, Linder RB, Pentikainen M, Hervold A, Banning A, Zaman A, Cotton J, Eriksen E, Margus S, Sorensen HT, Nielsen PH, Niemela M, Kervinen K, Lassen JF, Maeng M, Oldroyd K, Berg G, Walsh SJ, Hanratty CG, Kumsars I, Stradins P, Steigen TK, Frobert O, Graham AN, Endresen PC, Corbascio M, Kajander O, Trivedi U, Hartikainen J, Anttila V, Hildick-Smith D, Thuesen L, Christiansen EH, investigators Ns. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. Lancet 2016.

121. Stone GW, Sabik JF, Serruys PW, Simonton CA, Genereux P, Puskas J, Kandzari DE, Morice MC, Lembo N, Brown WM, 3rd, Taggart DP, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogats G, Mansour S, Noiseux N, Sabate M, Pomar J, Hickey M, Gershlick A, Buszman P, Bochenek A, Schampaert E, Page P, Dressler O, Kosmidou I, Mehran R, Pocock SJ, Kappetein AP, Investigators ET. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. N Engl J Med 2016.
122. Head SJ, Milojevic M, Daemen J, Ahn JM, Boersma E, Christiansen EH, Domanski MJ, Farkouh ME, Flather M, Fuster V, Hlatky MA, Holm NR, Hueb WA, Kamalesh M, Kim YH, Makikallio T, Mohr FW, Papageorgiou G, Park SJ, Rodriguez AE, Sabik JF, 3rd, Stables RH, Stone GW, Serruys PW, Kappetein AP. Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. Lancet 2018;**391**(10124):939-948.
123. Zhang YJ, Iqbal J, Campos CM, Klaveren DV, Bourantas CV, Dawkins KD, Banning AP, Escaned J, de Vries T, Morel MA, Farooq V, Onuma Y, Garcia-Garcia HM, Stone GW, Steyerberg EW, Mohr FW, Serruys PW. Prognostic value of site SYNTAX score and rationale for combining anatomic and clinical factors in decision making: insights from the SYNTAX trial. J Am Coll Cardiol 2014;**64**(5):423-32.
124. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR, Jr., Mack M, Feldman T, Morice MC, Stahle E, Onuma Y, Morel MA, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. Lancet 2013;**381**(9867):639-50.
125. Campos CM, Garcia-Garcia HM, van Klaveren D, Ishibashi Y, Cho YK, Valgimigli M, Raber L, Jonker H, Onuma Y, Farooq V, Garg S, Windecker S, Morel MA, Steyerberg EW, Serruys PW. Validity of SYNTAX score II for risk stratification of percutaneous coronary interventions: A patient-level pooled analysis of 5,433 patients enrolled in contemporary coronary stent trials. Int J Cardiol 2015;**187**:111-5.
126. Sotomi Y, Cavalcante R, van Klaveren D, Ahn JM, Lee CW, de Winter RJ, Wykrzykowska JJ, Onuma Y, Steyerberg EW, Park SJ, Serruys PW. Individual Long-Term Mortality Prediction Following Either Coronary Stenting or Bypass Surgery in Patients With Multivessel and/or Unprotected Left Main Disease: An External Validation of the SYNTAX Score II Model in the 1,480 Patients of the BEST and PRECOMBAT Randomized Controlled Trials. JACC Cardiovasc Interv 2016;**9**(15):1564-72.
127. Campos CM, van Klaveren D, Farooq V, Simonton CA, Kappetein AP, Sabik JF, 3rd, Steyerberg EW, Stone GW, Serruys PW, Investigators ET. Long-term forecasting and comparison of mortality in the Evaluation of the Xience Everolimus Eluting Stent vs. Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial: prospective validation of the SYNTAX Score II. Eur Heart J 2015;**36**(20):1231-41.
128. Farooq V, Serruys PW, Garcia-Garcia HM, Zhang Y, Bourantas CV, Holmes DR, Mack M, Feldman T, Morice MC, Stahle E, James S, Colombo A, Diletti R, Papafaklis MI, de Vries T, Morel MA, van Es GA, Mohr FW, Dawkins KD, Kappetein AP, Sianos G, Boersma E. The negative impact of incomplete angiographic revascularization on clinical outcomes and its association with total occlusions: the SYNTAX (Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial. J Am Coll Cardiol 2013;**61**(3):282-94.
129. Garcia S, Sandoval Y, Roukoz H, Adabag S, Canoniero M, Yannopoulos D, Brilakis ES. Outcomes after complete versus incomplete revascularization of patients with multivessel coronary artery disease: a meta-analysis of 89,883 patients enrolled in randomized clinical trials and observational studies. J Am Coll Cardiol 2013;**62**(16):1421-31.
130. Farooq V, Serruys PW, Bourantas CV, Zhang Y, Muramatsu T, Feldman T, Holmes DR, Mack M, Morice MC, Stahle E, Colombo A, de Vries T, Morel MA, Dawkins KD, Kappetein AP, Mohr FW. Quantification of incomplete revascularization and its association with five-year mortality in the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) trial validation of the residual SYNTAX score. Circulation 2013;**128**(2):141-51.

131. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Everolimus-eluting stents or bypass surgery for multivessel coronary disease. N Engl J Med 2015;**372**(13):1213-22.
132. Ahn JM, Park DW, Lee CW, Chang M, Cavalcante R, Sotomi Y, Onuma Y, Tenekecioglu E, Han M, Lee PH, Kang SJ, Lee SW, Kim YH, Park SW, Serruys PW, Park SJ. Comparison of Stenting Versus Bypass Surgery According to the Completeness of Revascularization in Severe Coronary Artery Disease: Patient-Level Pooled Analysis of the SYNTAX, PRECOMBAT, and BEST Trials. JACC Cardiovasc Interv 2017;**10**(14):1415-1424.
133. van Nunen LX, Zimmermann FM, Tonino PA, Barbato E, Baumbach A, Engstrom T, Klauss V, MacCarthy PA, Manoharan G, Oldroyd KG, Ver Lee PN, Van't Veer M, Fearon WF, De Bruyne B, Pijls NH, Investigators FS. Fractional flow reserve versus angiography for guidance of PCI in patients with multivessel coronary artery disease (FAME): 5-year follow-up of a randomised controlled trial. Lancet 2015;**386**(10006):1853-60.
134. Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, Junejo S, Ahmed N, Lee MM, Shaukat A, O'Donnell A, Nam J, Briggs A, Henderson R, McConnachie A, Berry C, investigators F-N. Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS-NSTEMI randomized trial. Eur Heart J 2015;**36**(2):100-11.
135. Ad N, Holmes SD, Patel J, Pritchard G, Shuman DJ, Halpin L. Comparison of EuroSCORE II, Original EuroSCORE, and The Society of Thoracic Surgeons Risk Score in Cardiac Surgery Patients. Ann Thorac Surg 2016;**102**(2):573-9.
136. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, Stahle E, Feldman TE, van den Brand M, Bass EJ, Van Dyck N, Leadley K, Dawkins KD, Mohr FW, Investigators S. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;**360**(10):961-72.
137. Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, Reichart B, Mudra H, Beier F, Gansera B, Neumann FJ, Gick M, Zietak T, Desch S, Schuler G, Mohr FW. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. J Am Coll Cardiol 2011;**57**(5):538-45.
138. Park SJ, Kim YH, Park DW, Yun SC, Ahn JM, Song HG, Lee JY, Kim WJ, Kang SJ, Lee SW, Lee CW, Park SW, Chung CH, Lee JW, Lim DS, Rha SW, Lee SG, Gwon HC, Kim HS, Chae IH, Jang Y, Jeong MH, Tahk SJ, Seung KB. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med 2011;**364**(18):1718-27.
139. Aziz O, Rao C, Panesar SS, Jones C, Morris S, Darzi A, Athanasiou T. Meta-analysis of minimally invasive internal thoracic artery bypass versus percutaneous revascularisation for isolated lesions of the left anterior descending artery. BMJ 2007;**334**(7594):617.
140. Kapoor JR, Gienger AL, Ardehali R, Varghese R, Perez MV, Sundaram V, McDonald KM, Owens DK, Hlatky MA, Bravata DM. Isolated disease of the proximal left anterior descending artery comparing the effectiveness of percutaneous coronary interventions and coronary artery bypass surgery. JACC Cardiovasc Interv 2008;**1**(5):483-91.
141. Blazek S, Holzhey D, Jungert C, Borger MA, Fuernau G, Desch S, Eitel I, de Waha S, Lurz P, Schuler G, Mohr FW, Thiele H. Comparison of bare-metal stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery: 10-year follow-up of a randomized trial. JACC Cardiovasc Interv 2013;**6**(1):20-6.
142. Hannan EL, Zhong Y, Walford G, Holmes DR, Jr., Venditti FJ, Berger PB, Jacobs AK, Stamato NJ, Curtis JP, Sharma S, King SB, 3rd. Coronary artery bypass graft surgery versus drug-eluting stents for patients with isolated proximal left anterior descending disease. J Am Coll Cardiol 2014;**64**(25):2717-26.
143. Blazek S, Rossbach C, Borger MA, Fuernau G, Desch S, Eitel I, Stiermaier T, Lurz P, Holzhey D, Schuler G, Mohr FW, Thiele H. Comparison of sirolimus-eluting stenting with minimally invasive bypass surgery for stenosis of the left anterior descending coronary artery: 7-year follow-up of a randomized trial. JACC Cardiovasc Interv 2015;**8**(1 Pt A):30-8.
144. Thiele H, Neumann-Schniedewind P, Jacobs S, Boudriot E, Walther T, Mohr FW, Schuler G, Falk V. Randomized comparison of minimally invasive direct coronary artery bypass surgery versus

sirolimus-eluting stenting in isolated proximal left anterior descending coronary artery stenosis. J Am Coll Cardiol 2009;**53**(25):2324-31.
145. Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. J Am Coll Cardiol 2011;**58**(14):1426-32.
146. Ahn JM, Roh JH, Kim YH, Park DW, Yun SC, Lee PH, Chang M, Park HW, Lee SW, Lee CW, Park SW, Choo SJ, Chung C, Lee J, Lim DS, Rha SW, Lee SG, Gwon HC, Kim HS, Chae IH, Jang Y, Jeong MH, Tahk SJ, Seung KB, Park SJ. Randomized Trial of Stents Versus Bypass Surgery for Left Main Coronary Artery Disease: 5-Year Outcomes of the PRECOMBAT Study. J Am Coll Cardiol 2015;**65**(20):2198-206.
147. Cavalcante R, Sotomi Y, Lee CW, Ahn JM, Farooq V, Tateishi H, Tenekecioglu E, Zeng Y, Suwannasom P, Collet C, Albuquerque FN, Onuma Y, Park SJ, Serruys PW. Outcomes After Percutaneous Coronary Intervention or Bypass Surgery in Patients With Unprotected Left Main Disease. J Am Coll Cardiol 2016;**68**(10):999-1009.
148. Giacoppo D, Colleran R, Cassese S, Frangieh AH, Wiebe J, Joner M, Schunkert H, Kastrati A, Byrne RA. Percutaneous Coronary Intervention vs Coronary Artery Bypass Grafting in Patients With Left Main Coronary Artery Stenosis: A Systematic Review and Meta-analysis. JAMA Cardiol 2017.
149. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, Yang M, Cohen DJ, Rosenberg Y, Solomon SD, Desai AS, Gersh BJ, Magnuson EA, Lansky A, Boineau R, Weinberger J, Ramanathan K, Sousa JE, Rankin J, Bhargava B, Buse J, Hueb W, Smith CR, Muratov V, Bansilal S, King S, 3rd, Bertrand M, Fuster V, Investigators FT. Strategies for multivessel revascularization in patients with diabetes. N Engl J Med 2012;**367**(25):2375-84.
150. Chang M, Ahn JM, Lee CW, Cavalcante R, Sotomi Y, Onuma Y, Tenekecioglu E, Han M, Park DW, Kang SJ, Lee SW, Kim YH, Park SW, Serruys PW, Park SJ. Long-Term Mortality After Coronary Revascularization in Nondiabetic Patients With Multivessel Disease. J Am Coll Cardiol 2016;**68**(1):29-36.
151. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S, Baumgartner H, Gaemperli O, Achenbach S, Agewall S, Badimon L, Baigent C, Bueno H, Bugiardini R, Carerj S, Casselman F, Cuisset T, Erol C, Fitzsimons D, Halle M, Hamm C, Hildick-Smith D, Huber K, Iliodromitis E, James S, Lewis BS, Lip GY, Piepoli MF, Richter D, Rosemann T, Sechtem U, Steg PG, Vrints C, Luis Zamorano J, Management of Acute Coronary Syndromes in Patients Presenting without Persistent STSEotESoC. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;**37**(3):267-315.
152. Goldstein JA, Demetriou D, Grines CL, Pica M, Shoukfeh M, O'Neill WW. Multiple complex coronary plaques in patients with acute myocardial infarction. N Engl J Med 2000;**343**(13):915-22.
153. Shishehbor MH, Venkatachalam S, Sun Z, Rajeswaran J, Kapadia SR, Bajzer C, Gornik HL, Gray BH, Bartholomew JR, Clair DG, Sabik JF, 3rd, Blackstone EH. A direct comparison of early and late outcomes with three approaches to carotid revascularization and open heart surgery. J Am Coll Cardiol 2013;**62**(21):1948-56.
154. Cheruvu PK, Finn AV, Gardner C, Caplan J, Goldstein J, Stone GW, Virmani R, Muller JE. Frequency and distribution of thin-cap fibroatheroma and ruptured plaques in human coronary arteries: a pathologic study. J Am Coll Cardiol 2007;**50**(10):940-9.
155. Kerensky RA, Wade M, Deedwania P, Boden WE, Pepine CJ, Veterans Affairs Non QWISi-HTI. Revisiting the culprit lesion in non-Q-wave myocardial infarction. Results from the VANQWISH trial angiographic core laboratory. J Am Coll Cardiol 2002;**39**(9):1456-63.
156. Kastrati A, Neumann FJ, Schulz S, Massberg S, Byrne RA, Ferenc M, Laugwitz KL, Pache J, Ott I, Hausleiter J, Seyfarth M, Gick M, Antoniucci D, Schomig A, Berger PB, Mehilli J, Investigators I-RT. Abciximab and heparin versus bivalirudin for non-ST-elevation myocardial infarction. N Engl J Med 2011;**365**(21):1980-9.
157. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, Afzal R, Chrolavicius S, Jolly SS, Widimsky P, Avezum A, Rupprecht HJ, Zhu J, Col J, Natarajan MK, Horsman C, Fox KA, Yusuf S,

Investigators T. Early versus delayed invasive intervention in acute coronary syndromes. N Engl J Med 2009;**360**(21):2165-75.
158. Montalescot G, Bolognese L, Dudek D, Goldstein P, Hamm C, Tanguay JF, ten Berg JM, Miller DL, Costigan TM, Goedicke J, Silvain J, Angioli P, Legutko J, Niethammer M, Motovska Z, Jakubowski JA, Cayla G, Visconti LO, Vicaut E, Widimsky P, Investigators A. Pretreatment with prasugrel in non-ST-segment elevation acute coronary syndromes. N Engl J Med 2013;**369**(11):999-1010.
159. Thiele H, Rach J, Klein N, Pfeiffer D, Hartmann A, Hambrecht R, Sick P, Eitel I, Desch S, Schuler G, Group L-NT. Optimal timing of invasive angiography in stable non-ST-elevation myocardial infarction: the Leipzig Immediate versus early and late PercutaneouS coronary Intervention triAl in NSTEMI (LIPSIA-NSTEMI Trial). Eur Heart J 2012;**33**(16):2035-43.
160. Tanaka A, Shimada K, Tearney GJ, Kitabata H, Taguchi H, Fukuda S, Kashiwagi M, Kubo T, Takarada S, Hirata K, Mizukoshi M, Yoshikawa J, Bouma BE, Akasaka T. Conformational change in coronary artery structure assessed by optical coherence tomography in patients with vasospastic angina. J Am Coll Cardiol 2011;**58**(15):1608-13.
161. Kato M, Dote K, Sasaki S, Kagawa E, Nakano Y, Watanabe Y, Higashi A, Itakura K, Ochiumi Y, Takiguchi Y. Presentations of acute coronary syndrome related to coronary lesion morphologies as assessed by intravascular ultrasound and optical coherence tomography. Int J Cardiol 2013;**165**(3):506-11.
162. Motreff P, Malcles G, Combaret N, Barber-Chamoux N, Bouajila S, Pereira B, Amonchot A, Citron B, Lusson JR, Eschalier R, Souteyrand G. How and when to suspect spontaneous coronary artery dissection: novel insights from a single-centre series on prevalence and angiographic appearance. EuroIntervention 2017;**12**(18):e2236-e2243.
163. Bavry AA, Kumbhani DJ, Rassi AN, Bhatt DL, Askari AT. Benefit of early invasive therapy in acute coronary syndromes: a meta-analysis of contemporary randomized clinical trials. J Am Coll Cardiol 2006;**48**(7):1319-25.
164. Fox KA, Clayton TC, Damman P, Pocock SJ, de Winter RJ, Tijssen JG, Lagerqvist B, Wallentin L, Collaboration FIR. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome a meta-analysis of individual patient data. J Am Coll Cardiol 2010;**55**(22):2435-45.
165. Valgimigli M, Gagnor A, Calabro P, Frigoli E, Leonardi S, Zaro T, Rubartelli P, Briguori C, Ando G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S, Nazzaro M, Zingarelli A, de Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbuhler M, Vranckx P, Juni P, Investigators M. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015;**385**(9986):2465-76.
166. Urban P, Meredith IT, Abizaid A, Pocock SJ, Carrie D, Naber C, Lipiecki J, Richardt G, Iniguez A, Brunel P, Valdes-Chavarri M, Garot P, Talwar S, Berland J, Abdellaoui M, Eberli F, Oldroyd K, Zambahari R, Gregson J, Greene S, Stoll HP, Morice MC, Investigators LF. Polymer-free Drug-Coated Coronary Stents in Patients at High Bleeding Risk. N Engl J Med 2015;**373**(21):2038-2047.
167. Katritsis DG, Siontis GC, Kastrati A, van't Hof AW, Neumann FJ, Siontis KC, Ioannidis JP. Optimal timing of coronary angiography and potential intervention in non-ST-elevation acute coronary syndromes. Eur Heart J 2011;**32**(1):32-40.
168. Navarese EP, Gurbel PA, Andreotti F, Tantry U, Jeong YH, Kozinski M, Engstrom T, Di Pasquale G, Kochman W, Ardissino D, Kedhi E, Stone GW, Kubica J. Optimal timing of coronary invasive strategy in non-ST-segment elevation acute coronary syndromes: a systematic review and meta-analysis. Ann Intern Med 2013;**158**(4):261-70.
169. Jobs A, Mehta SR, Montalescot G, Vicaut E, Van't Hof AWJ, Badings EA, Neumann FJ, Kastrati A, Sciahbasi A, Reuter PG, Lapostolle F, Milosevic A, Stankovic G, Milasinovic D, Vonthein R, Desch S, Thiele H. Optimal timing of an invasive strategy in patients with non-ST-elevation acute coronary syndrome: a meta-analysis of randomised trials. Lancet 2017;**390**(10096):737-746.
170. Raber L, Kelbaek H, Ostojic M, Baumbach A, Heg D, Tuller D, von Birgelen C, Roffi M, Moschovitis A, Khattab AA, Wenaweser P, Bonvini R, Pedrazzini G, Kornowski R, Weber K, Trelle S, Luscher TF, Taniwaki M, Matter CM, Meier B, Juni P, Windecker S, Investigators CAT. Effect of

biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the COMFORTABLE AMI randomized trial. JAMA 2012;**308**(8):777-87.
171. Sabate M, Raber L, Heg D, Brugaletta S, Kelbaek H, Cequier A, Ostojic M, Iniguez A, Tuller D, Serra A, Baumbach A, von Birgelen C, Hernandez-Antolin R, Roffi M, Mainar V, Valgimigli M, Serruys PW, Juni P, Windecker S. Comparison of newer-generation drug-eluting with bare-metal stents in patients with acute ST-segment elevation myocardial infarction: a pooled analysis of the EXAMINATION (clinical Evaluation of the Xience-V stent in Acute Myocardial INfArcTION) and COMFORTABLE-AMI (Comparison of Biolimus Eluted From an Erodible Stent Coating With Bare Metal Stents in Acute ST-Elevation Myocardial Infarction) trials. JACC Cardiovasc Interv 2014;**7**(1):55-63.
172. Valgimigli M, Tebaldi M, Borghesi M, Vranckx P, Campo G, Tumscitz C, Cangiano E, Minarelli M, Scalone A, Cavazza C, Marchesini J, Parrinello G, Investigators P. Two-year outcomes after first- or second-generation drug-eluting or bare-metal stent implantation in all-comer patients undergoing percutaneous coronary intervention: a pre-specified analysis from the PRODIGY study (PROlonging Dual Antiplatelet Treatment After Grading stent-induced Intimal hyperplasia studY). JACC Cardiovasc Interv 2014;**7**(1):20-8.
173. Thiele H, de Waha S, Zeymer U, Desch S, Scheller B, Lauer B, Geisler T, Gawaz M, Gunkel O, Bruch L, Klein N, Pfeiffer D, Schuler G, Eitel I. Effect of aspiration thrombectomy on microvascular obstruction in NSTEMI patients: the TATORT-NSTEMI trial. J Am Coll Cardiol 2014;**64**(11):1117-24.
174. Hakeem A, Edupuganti MM, Almomani A, Pothineni NV, Payne J, Abualsuod AM, Bhatti S, Ahmed Z, Uretsky BF. Long-Term Prognosis of Deferred Acute Coronary Syndrome Lesions Based on Nonischemic Fractional Flow Reserve. J Am Coll Cardiol 2016;**68**(11):1181-1191.
175. Wallentin L, Lagerqvist B, Husted S, Kontny F, Stahle E, Swahn E. Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. FRISC II Investigators. Fast Revascularisation during Instability in Coronary artery disease. Lancet 2000;**356**(9223):9-16.
176. Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, DiBattiste PM, Gibson CM, Braunwald E, Investigators TTiMI. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;**344**(25):1879-87.
177. Genereux P, Palmerini T, Caixeta A, Cristea E, Mehran R, Sanchez R, Lazar D, Jankovic I, Corral MD, Dressler O, Fahy MP, Parise H, Lansky AJ, Stone GW. SYNTAX score reproducibility and variability between interventional cardiologists, core laboratory technicians, and quantitative coronary measurements. Circ Cardiovasc Interv 2011;**4**(6):553-61.
178. Sardella G, Lucisano L, Garbo R, Pennacchi M, Cavallo E, Stio RE, Calcagno S, Ugo F, Boccuzzi G, Fedele F, Mancone M. Single-Staged Compared With Multi-Staged PCI in Multivessel NSTEMI Patients: The SMILE Trial. J Am Coll Cardiol 2016;**67**(3):264-72.
179. Tricoci P, Huang Z, Held C, Moliterno DJ, Armstrong PW, Van de Werf F, White HD, Aylward PE, Wallentin L, Chen E, Lokhnygina Y, Pei J, Leonardi S, Rorick TL, Kilian AM, Jennings LH, Ambrosio G, Bode C, Cequier A, Cornel JH, Diaz R, Erkan A, Huber K, Hudson MP, Jiang L, Jukema JW, Lewis BS, Lincoff AM, Montalescot G, Nicolau JC, Ogawa H, Pfisterer M, Prieto JC, Ruzyllo W, Sinnaeve PR, Storey RF, Valgimigli M, Whellan DJ, Widimsky P, Strony J, Harrington RA, Mahaffey KW, Investigators T. Thrombin-receptor antagonist vorapaxar in acute coronary syndromes. N Engl J Med 2012;**366**(1):20-33.
180. Lindholm D, Varenhorst C, Cannon CP, Harrington RA, Himmelmann A, Maya J, Husted S, Steg PG, Cornel JH, Storey RF, Stevens SR, Wallentin L, James SK. Ticagrelor vs. clopidogrel in patients with non-ST-elevation acute coronary syndrome with or without revascularization: results from the PLATO trial. Eur Heart J 2014;**35**(31):2083-93.
181. Curtis JP, Schreiner G, Wang Y, Chen J, Spertus JA, Rumsfeld JS, Brindis RG, Krumholz HM. All-cause readmission and repeat revascularization after percutaneous coronary intervention in a cohort of medicare patients. J Am Coll Cardiol 2009;**54**(10):903-7.

182. Meadows ES, Bae JP, Zagar A, Sugihara T, Ramaswamy K, McCracken R, Heiselman D. Rehospitalization following percutaneous coronary intervention for commercially insured patients with acute coronary syndrome: a retrospective analysis. BMC Res Notes 2012;**5**:342.
183. Thiele H, Akin I, Sandri M, Fuernau G, de Waha S, Meyer-Saraei R, Nordbeck P, Geisler T, Landmesser U, Skurk C, Fach A, Lapp H, Piek JJ, Noc M, Goslar T, Felix SB, Maier LS, Stepinska J, Oldroyd K, Serpytis P, Montalescot G, Barthelemy O, Huber K, Windecker S, Savonitto S, Torremante P, Vrints C, Schneider S, Desch S, Zeymer U, Investigators C-S. PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock. N Engl J Med 2017.
184. Ranasinghe I, Alprandi-Costa B, Chow V, Elliott JM, Waites J, Counsell JT, Lopez-Sendon J, Avezum A, Goodman SG, Granger CB, Brieger D. Risk stratification in the setting of non-ST elevation acute coronary syndromes 1999-2007. Am J Cardiol 2011;**108**(5):617-24.
185. Fukui T, Tabata M, Morita S, Takanashi S. Early and long-term outcomes of coronary artery bypass grafting in patients with acute coronary syndrome versus stable angina pectoris. J Thorac Cardiovasc Surg 2013;**145**(6):1577-83, 1583 e1.
186. Malm CJ, Hansson EC, Akesson J, Andersson M, Hesse C, Shams Hakimi C, Jeppsson A. Preoperative platelet function predicts perioperative bleeding complications in ticagrelor-treated cardiac surgery patients: a prospective observational study. Br J Anaesth 2016;**117**(3):309-15.
187. Chang M, Lee CW, Ahn JM, Cavalcante R, Sotomi Y, Onuma Y, Han M, Park DW, Kang SJ, Lee SW, Kim YH, Park SW, Serruys PW, Park SJ. Comparison of Outcome of Coronary Artery Bypass Grafting Versus Drug-Eluting Stent Implantation for Non-ST-Elevation Acute Coronary Syndrome. Am J Cardiol 2017;**120**(3):380-386.
188. Palmerini T, Genereux P, Caixeta A, Cristea E, Lansky A, Mehran R, Dangas G, Lazar D, Sanchez R, Fahy M, Xu K, Stone GW. Prognostic value of the SYNTAX score in patients with acute coronary syndromes undergoing percutaneous coronary intervention: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) trial. J Am Coll Cardiol 2011;**57**(24):2389-97.
189. Ramanathan K, Abel JG, Park JE, Fung A, Mathew V, Taylor CM, Mancini GBJ, Gao M, Ding L, Verma S, Humphries KH, Farkouh ME. Surgical Versus Percutaneous Coronary Revascularization in Patients With Diabetes and Acute Coronary Syndromes. J Am Coll Cardiol 2017;**70**(24):2995-3006.
190. Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, Jain D, Cooper HA, Frishman WH, Menon V, Bhatt DL, Abbott JD, Fonarow GC, Panza JA. Trends in Coronary Angiography, Revascularization, and Outcomes of Cardiogenic Shock Complicating Non-ST-Elevation Myocardial Infarction. Am J Cardiol 2016;**117**(1):1-9.
191. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimsky P. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2017.
192. Scholz KH, Maier SKG, Maier LS, Lengenfelder B, Jacobshagen C, Jung J, Fleischmann C, Werner GS, Olbrich HG, Ott R, Mudra H, Seidl K, Schulze PC, Weiss C, Haimerl J, Friede T, Meyer T. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. Eur Heart J 2018.
193. Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. Lancet 2006;**367**(9510):579-88.
194. Boersma E, Primary Coronary Angioplasty vs. Thrombolysis G. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J 2006;**27**(7):779-88.
195. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. JAMA 2000;**283**(20):2686-92.
196. Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY, Cattan S, Boullenger E, Machecourt J, Lacroute JM, Cassagnes J, Dissait F, Touboul P, Comparison of A,

Prehospital Thromboysis in Acute Myocardial Infarction study g. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet 2002;**360**(9336):825-9.
197. Bonnefoy E, Steg PG, Boutitie F, Dubien PY, Lapostolle F, Roncalli J, Dissait F, Vanzetto G, Leizorowicz A, Kirkorian G, Investigators C, Mercier C, McFadden EP, Touboul P. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. Eur Heart J 2009;**30**(13):1598-606.
198. Pinto DS, Frederick PD, Chakrabarti AK, Kirtane AJ, Ullman E, Dejam A, Miller DP, Henry TD, Gibson CM, National Registry of Myocardial Infarction I. Benefit of transferring ST-segment-elevation myocardial infarction patients for percutaneous coronary intervention compared with administration of onsite fibrinolytic declines as delays increase. Circulation 2011;**124**(23):2512-21.
199. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC, Nanas J, Arntz HR, Halvorsen S, Huber K, Grajek S, Fresco C, Bluhmki E, Regelin A, Vandenberghe K, Bogaerts K, Van de Werf F, Team SI. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. N Engl J Med 2013;**368**(15):1379-87.
200. Park DW, Clare RM, Schulte PJ, Pieper KS, Shaw LK, Califf RM, Ohman EM, Van de Werf F, Hirji S, Harrington RA, Armstrong PW, Granger CB, Jeong MH, Patel MR. Extent, location, and clinical significance of non-infarct-related coronary artery disease among patients with ST-elevation myocardial infarction. JAMA 2014;**312**(19):2019-27.
201. Kornowski R, Mehran R, Dangas G, Nikolsky E, Assali A, Claessen BE, Gersh BJ, Wong SC, Witzenbichler B, Guagliumi G, Dudek D, Fahy M, Lansky AJ, Stone GW, Investigators H-AT. Prognostic impact of staged versus "one-time" multivessel percutaneous intervention in acute myocardial infarction: analysis from the HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trial. J Am Coll Cardiol 2011;**58**(7):704-11.
202. Politi L, Sgura F, Rossi R, Monopoli D, Guerri E, Leuzzi C, Bursi F, Sangiorgi GM, Modena MG. A randomised trial of target-vessel versus multi-vessel revascularisation in ST-elevation myocardial infarction: major adverse cardiac events during long-term follow-up. Heart 2010;**96**(9):662-7.
203. Di Mario C, Mara S, Flavio A, Imad S, Antonio M, Anna P, Emanuela P, Stefano DS, Angelo R, Stefania C, Anna F, Carmelo C, Antonio C, Monzini N, Bonardi MA. Single vs multivessel treatment during primary angioplasty: results of the multicentre randomised HEpacoat for cuLPrit or multivessel stenting for Acute Myocardial Infarction (HELP AMI) Study. Int J Cardiovasc Intervent 2004;**6**(3-4):128-33.
204. Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, Berry C, Oldroyd KG, Investigators P. Randomized trial of preventive angioplasty in myocardial infarction. N Engl J Med 2013;**369**(12):1115-23.
205. Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, Blackman DJ, Dalby M, Fairbrother KL, Banya W, Wang D, Flather M, Hetherington SL, Kelion AD, Talwar S, Gunning M, Hall R, Swanton H, McCann GP. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. J Am Coll Cardiol 2015;**65**(10):963-72.
206. Engstrom T, Kelbaek H, Helqvist S, Hofsten DE, Klovgaard L, Holmvang L, Jorgensen E, Pedersen F, Saunamaki K, Clemmensen P, De Backer O, Ravkilde J, Tilsted HH, Villadsen AB, Aaroe J, Jensen SE, Raungaard B, Kober L, Investigators D-P. Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3-PRIMULTI): an open-label, randomised controlled trial. Lancet 2015;**386**(9994):665-71.
207. Smits PC, Abdel-Wahab M, Neumann FJ, Boxma-de Klerk BM, Lunde K, Schotborgh CE, Piroth Z, Horak D, Wlodarczak A, Ong PJ, Hambrecht R, Angeras O, Richardt G, Omerovic E, Compare-Acute I. Fractional Flow Reserve-Guided Multivessel Angioplasty in Myocardial Infarction. N Engl J Med 2017;**376**(13):1234-1244.
208. Elgendy IY, Mahmoud AN, Kumbhani DJ, Bhatt DL, Bavry AA. Complete or Culprit-Only Revascularization for Patients With Multivessel Coronary Artery Disease Undergoing Percutaneous

Coronary Intervention: A Pairwise and Network Meta-Analysis of Randomized Trials. JACC Cardiovasc Interv 2017;**10**(4):315-324.
209. Kastrati A, Dibra A, Spaulding C, Laarman GJ, Menichelli M, Valgimigli M, Di Lorenzo E, Kaiser C, Tierala I, Mehilli J, Seyfarth M, Varenne O, Dirksen MT, Percoco G, Varricchio A, Pittl U, Syvanne M, Suttorp MJ, Violini R, Schomig A. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. Eur Heart J 2007;**28**(22):2706-13.
210. Sabate M, Cequier A, Iniguez A, Serra A, Hernandez-Antolin R, Mainar V, Valgimigli M, Tespili M, den Heijer P, Bethencourt A, Vazquez N, Gomez-Hospital JA, Baz JA, Martin-Yuste V, van Geuns RJ, Alfonso F, Bordes P, Tebaldi M, Masotti M, Silvestro A, Backx B, Brugaletta S, van Es GA, Serruys PW. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (EXAMINATION): 1 year results of a randomised controlled trial. Lancet 2012;**380**(9852):1482-90.
211. Sabate M, Brugaletta S, Cequier A, Iniguez A, Serra A, Jimenez-Quevedo P, Mainar V, Campo G, Tespili M, den Heijer P, Bethencourt A, Vazquez N, van Es GA, Backx B, Valgimigli M, Serruys PW. Clinical outcomes in patients with ST-segment elevation myocardial infarction treated with everolimus-eluting stents versus bare-metal stents (EXAMINATION): 5-year results of a randomised trial. Lancet 2016;**387**(10016):357-66.
212. Belle L, Motreff P, Mangin L, Range G, Marcaggi X, Marie A, Ferrier N, Dubreuil O, Zemour G, Souteyrand G, Caussin C, Amabile N, Isaaz K, Dauphin R, Koning R, Robin C, Faurie B, Bonello L, Champin S, Delhaye C, Cuilleret F, Mewton N, Genty C, Viallon M, Bosson JL, Croisille P, Investigators* M. Comparison of Immediate With Delayed Stenting Using the Minimalist Immediate Mechanical Intervention Approach in Acute ST-Segment-Elevation Myocardial Infarction: The MIMI Study. Circ Cardiovasc Interv 2016;**9**(3):e003388.
213. Carrick D, Oldroyd KG, McEntegart M, Haig C, Petrie MC, Eteiba H, Hood S, Owens C, Watkins S, Layland J, Lindsay M, Peat E, Rae A, Behan M, Sood A, Hillis WS, Mordi I, Mahrous A, Ahmed N, Wilson R, Lasalle L, Genereux P, Ford I, Berry C. A randomized trial of deferred stenting versus immediate stenting to prevent no- or slow-reflow in acute ST-segment elevation myocardial infarction (DEFER-STEMI). J Am Coll Cardiol 2014;**63**(20):2088-98.
214. Kelbaek H, Hofsten DE, Kober L, Helqvist S, Klovgaard L, Holmvang L, Jorgensen E, Pedersen F, Saunamaki K, De Backer O, Bang LE, Kofoed KF, Lonborg J, Ahtarovski K, Vejlstrup N, Botker HE, Terkelsen CJ, Christiansen EH, Ravkilde J, Tilsted HH, Villadsen AB, Aaroe J, Jensen SE, Raungaard B, Jensen LO, Clemmensen P, Grande P, Madsen JK, Torp-Pedersen C, Engstrom T. Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomised controlled trial. Lancet 2016;**387**(10034):2199-206.
215. De Luca G, Navarese EP, Suryapranata H. A meta-analytic overview of thrombectomy during primary angioplasty. Int J Cardiol 2013;**166**(3):606-12.
216. Frobert O, Lagerqvist B, Olivecrona GK, Omerovic E, Gudnason T, Maeng M, Aasa M, Angeras O, Calais F, Danielewicz M, Erlinge D, Hellsten L, Jensen U, Johansson AC, Karegren A, Nilsson J, Robertson L, Sandhall L, Sjogren I, Ostlund O, Harnek J, James SK, Trial T. Thrombus aspiration during ST-segment elevation myocardial infarction. N Engl J Med 2013;**369**(17):1587-97.
217. Lagerqvist B, Frobert O, Olivecrona GK, Gudnason T, Maeng M, Alstrom P, Andersson J, Calais F, Carlsson J, Collste O, Gotberg M, Hardhammar P, Ioanes D, Kallryd A, Linder R, Lundin A, Odenstedt J, Omerovic E, Puskar V, Todt T, Zelleroth E, Ostlund O, James SK. Outcomes 1 year after thrombus aspiration for myocardial infarction. N Engl J Med 2014;**371**(12):1111-20.
218. Jolly SS, Cairns JA, Yusuf S, Meeks B, Pogue J, Rokoss MJ, Kedev S, Thabane L, Stankovic G, Moreno R, Gershlick A, Chowdhary S, Lavi S, Niemela K, Steg PG, Bernat I, Xu Y, Cantor WJ, Overgaard CB, Naber CK, Cheema AN, Welsh RC, Bertrand OF, Avezum A, Bhindi R, Pancholy S, Rao SV, Natarajan MK, ten Berg JM, Shestakovska O, Gao P, Widimsky P, Dzavik V, Investigators T. Randomized trial of primary PCI with or without routine manual thrombectomy. N Engl J Med 2015;**372**(15):1389-98.
219. Jolly SS, Cairns JA, Yusuf S, Rokoss MJ, Gao P, Meeks B, Kedev S, Stankovic G, Moreno R, Gershlick A, Chowdhary S, Lavi S, Niemela K, Bernat I, Cantor WJ, Cheema AN, Steg PG, Welsh RC, Sheth T, Bertrand OF, Avezum A, Bhindi R, Natarajan MK, Horak D, Leung RC, Kassam S, Rao SV, El-Omar M, Mehta SR, Velianou JL, Pancholy S, Dzavik V, Investigators T. Outcomes after thrombus

aspiration for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. Lancet 2016;**387**(10014):127-35.
220. Jolly SS, Cairns JA, Yusuf S, Meeks B, Gao P, Hart RG, Kedev S, Stankovic G, Moreno R, Horak D, Kassam S, Rokoss MJ, Leung RC, El-Omar M, Romppanen HO, Alazzoni A, Alak A, Fung A, Alexopoulos D, Schwalm JD, Valettas N, Dzavik V, Investigators T. Stroke in the TOTAL trial: a randomized trial of routine thrombectomy vs. percutaneous coronary intervention alone in ST elevation myocardial infarction. Eur Heart J 2015;**36**(35):2364-72.
221. Jolly SS, James S, Dzavik V, Cairns JA, Mahmoud KD, Zijlstra F, Yusuf S, Olivecrona GK, Renlund H, Gao P, Lagerqvist B, Alazzoni A, Kedev S, Stankovic G, Meeks B, Frobert O. Thrombus Aspiration in ST-Segment-Elevation Myocardial Infarction: An Individual Patient Meta-Analysis: Thrombectomy Trialists Collaboration. Circulation 2017;**135**(2):143-152.
222. Bohmer E, Hoffmann P, Abdelnoor M, Arnesen H, Halvorsen S. Efficacy and safety of immediate angioplasty versus ischemia-guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances results of the NORDISTEMI (NORwegian study on DIstrict treatment of ST-elevation myocardial infarction). J Am Coll Cardiol 2010;**55**(2):102-10.
223. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, Morrison LJ, Langer A, Dzavik V, Mehta SR, Lazzam C, Schwartz B, Casanova A, Goodman SG, Investigators T-AT. Routine early angioplasty after fibrinolysis for acute myocardial infarction. N Engl J Med 2009;**360**(26):2705-18.
224. Di Mario C, Dudek D, Piscione F, Mielecki W, Savonitto S, Murena E, Dimopoulos K, Manari A, Gaspardone A, Ochala A, Zmudka K, Bolognese L, Steg PG, Flather M, Investigators CA-i-A. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. Lancet 2008;**371**(9612):559-68.
225. Gershlick AH, Stephens-Lloyd A, Hughes S, Abrams KR, Stevens SE, Uren NG, de Belder A, Davis J, Pitt M, Banning A, Baumbach A, Shiu MF, Schofield P, Dawkins KD, Henderson RA, Oldroyd KG, Wilcox R, Investigators RT. Rescue angioplasty after failed thrombolytic therapy for acute myocardial infarction. N Engl J Med 2005;**353**(26):2758-68.
226. Schomig A, Mehilli J, Antoniucci D, Ndrepepa G, Markwardt C, Di Pede F, Nekolla SG, Schlotterbeck K, Schuhlen H, Pache J, Seyfarth M, Martinoff S, Benzer W, Schmitt C, Dirschinger J, Schwaiger M, Kastrati A, Beyond 12 hours Reperfusion AlternatiVe Evaluation Trial I. Mechanical reperfusion in patients with acute myocardial infarction presenting more than 12 hours from symptom onset: a randomized controlled trial. JAMA 2005;**293**(23):2865-72.
227. Busk M, Kaltoft A, Nielsen SS, Bottcher M, Rehling M, Thuesen L, Botker HE, Lassen JF, Christiansen EH, Krusell LR, Andersen HR, Nielsen TT, Kristensen SD. Infarct size and myocardial salvage after primary angioplasty in patients presenting with symptoms for <12 h vs. 12-72 h. Eur Heart J 2009;**30**(11):1322-30.
228. Hochman JS, Lamas GA, Buller CE, Dzavik V, Reynolds HR, Abramsky SJ, Forman S, Ruzyllo W, Maggioni AP, White H, Sadowski Z, Carvalho AC, Rankin JM, Renkin JP, Steg PG, Mascette AM, Sopko G, Pfisterer ME, Leor J, Fridrich V, Mark DB, Knatterud GL, Occluded Artery Trial I. Coronary intervention for persistent occlusion after myocardial infarction. N Engl J Med 2006;**355**(23):2395-407.
229. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet 1996;**348**(9030):771-5.
230. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, Abildgaard U, Pedersen F, Madsen JK, Grande P, Villadsen AB, Krusell LR, Haghfelt T, Lomholt P, Husted SE, Vigholt E, Kjaergard HK, Mortensen LS. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003;**349**(8):733-42.
231. Dalby M, Bouzamondo A, Lechat P, Montalescot G. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. Circulation 2003;**108**(15):1809-14.
232. Mehilli J, Kastrati A, Schulz S, Frungel S, Nekolla SG, Moshage W, Dotzer F, Huber K, Pache J, Dirschinger J, Seyfarth M, Martinoff S, Schwaiger M, Schomig A. Abciximab in patients with acute ST-

segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention after clopidogrel loading: a randomized double-blind trial. Circulation 2009;**119**(14):1933-40.
233. Kalla K, Christ G, Karnik R, Malzer R, Norman G, Prachar H, Schreiber W, Unger G, Glogar HD, Kaff A, Laggner AN, Maurer G, Mlczoch J, Slany J, Weber HS, Huber K. Implementation of guidelines improves the standard of care: the Viennese registry on reperfusion strategies in ST-elevation myocardial infarction (Vienna STEMI registry). Circulation 2006;**113**(20):2398-405.
234. Henry TD, Sharkey SW, Burke MN, Chavez IJ, Graham KJ, Henry CR, Lips DL, Madison JD, Menssen KM, Mooney MR, Newell MC, Pedersen WR, Poulose AK, Traverse JH, Unger BT, Wang YL, Larson DM. A regional system to provide timely access to percutaneous coronary intervention for ST-elevation myocardial infarction. Circulation 2007;**116**(7):721-8.
235. Nallamothu BK, Krumholz HM, Ko DT, LaBresh KA, Rathore S, Roe MT, Schwamm L. Development of systems of care for ST-elevation myocardial infarction patients: gaps, barriers, and implications. Circulation 2007;**116**(2):e68-72.
236. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, Andrikopoulos G, Baz JA, Betriu A, Claeys M, Danchin N, Djambazov S, Erne P, Hartikainen J, Huber K, Kala P, Klinceva M, Kristensen SD, Ludman P, Ferre JM, Merkely B, Milicic D, Morais J, Noc M, Opolski G, Ostojic M, Radovanovic D, De Servi S, Stenestrand U, Studencan M, Tubaro M, Vasiljevic Z, Weidinger F, Witkowski A, Zeymer U. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. Eur Heart J 2010;**31**(8):943-57.
237. Knot J, Widimsky P, Wijns W, Stenestrand U, Kristensen SD, Van THA, Weidinger F, Janzon M, Norgaard BL, Soerensen JT, van de Wetering H, Thygesen K, Bergsten PA, Digerfeldt C, Potgieter A, Tomer N, Fajadet J. How to set up an effective national primary angioplasty network: lessons learned from five European countries. EuroIntervention 2009;**5**(3):299, 301-309.
238. Bradley EH, Herrin J, Wang Y, Barton BA, Webster TR, Mattera JA, Roumanis SA, Curtis JP, Nallamothu BK, Magid DJ, McNamara RL, Parkosewich J, Loeb JM, Krumholz HM. Strategies for reducing the door-to-balloon time in acute myocardial infarction. N Engl J Med 2006;**355**(22):2308-20.
239. Pinto DS, Kirtane AJ, Nallamothu BK, Murphy SA, Cohen DJ, Laham RJ, Cutlip DE, Bates ER, Frederick PD, Miller DP, Carrozza JP, Jr., Antman EM, Cannon CP, Gibson CM. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. Circulation 2006;**114**(19):2019-25.
240. Steg PG, Cambou JP, Goldstein P, Durand E, Sauval P, Kadri Z, Blanchard D, Lablanche JM, Gueret P, Cottin Y, Juliard JM, Hanania G, Vaur L, Danchin N. Bypassing the emergency room reduces delays and mortality in ST elevation myocardial infarction: the USIC 2000 registry. Heart 2006;**92**(10):1378-83.
241. Wolff G, Dimitroulis D, Andreotti F, Kolodziejczak M, Jung C, Scicchitano P, Devito F, Zito A, Occhipinti M, Castiglioni B, Calveri G, Maisano F, Ciccone MM, De Servi S, Navarese EP. Survival Benefits of Invasive Versus Conservative Strategies in Heart Failure in Patients With Reduced Ejection Fraction and Coronary Artery Disease: A Meta-Analysis. Circ Heart Fail 2017;**10**(1).
242. Wrobel K, Stevens SR, Jones RH, Selzman CH, Lamy A, Beaver TM, Djokovic LT, Wang N, Velazquez EJ, Sopko G, Kron IL, DiMaio JM, Michler RE, Lee KL, Yii M, Leng CY, Zembala M, Rouleau JL, Daly RC, Al-Khalidi HR. Influence of Baseline Characteristics, Operative Conduct, and Postoperative Course on 30-Day Outcomes of Coronary Artery Bypass Grafting Among Patients With Left Ventricular Dysfunction: Results From the Surgical Treatment for Ischemic Heart Failure (STICH) Trial. Circulation 2015;**132**(8):720-30.
243. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Hannan EL. Revascularization in Patients With Multivessel Coronary Artery Disease and Severe Left Ventricular Systolic Dysfunction: Everolimus-Eluting Stents Versus Coronary Artery Bypass Graft Surgery. Circulation 2016;**133**(22):2132-40.
244. Nagendran J, Bozso SJ, Norris CM, McAlister FA, Appoo JJ, Moon MC, Freed DH, Nagendran J. Coronary Artery Bypass Surgery Improves Outcomes in Patients With Diabetes and Left Ventricular Dysfunction. J Am Coll Cardiol 2018;**71**(8):819-827.

245. Jones RH, Velazquez EJ, Michler RE, Sopko G, Oh JK, O'Connor CM, Hill JA, Menicanti L, Sadowski Z, Desvigne-Nickens P, Rouleau JL, Lee KL, Investigators SH. Coronary bypass surgery with or without surgical ventricular reconstruction. N Engl J Med 2009;**360**(17):1705-17.
246. Oh JK, Velazquez EJ, Menicanti L, Pohost GM, Bonow RO, Lin G, Hellkamp AS, Ferrazzi P, Wos S, Rao V, Berman D, Bochenek A, Cherniavsky A, Rogowski J, Rouleau JL, Lee KL, Investigators S. Influence of baseline left ventricular function on the clinical outcome of surgical ventricular reconstruction in patients with ischaemic cardiomyopathy. Eur Heart J 2013;**34**(1):39-47.
247. Dor V, Civaia F, Alexandrescu C, Sabatier M, Montiglio F. Favorable effects of left ventricular reconstruction in patients excluded from the Surgical Treatments for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg 2011;**141**(4):905-16, 916 e1-4.
248. Killip T, Passamani E, Davis K. Coronary artery surgery study (CASS): a randomized trial of coronary bypass surgery. Eight years follow-up and survival in patients with reduced ejection fraction. Circulation 1985;**72**(6 Pt 2):V102-9.
249. Di Donato M, Castelvecchio S, Menicanti L. End-systolic volume following surgical ventricular reconstruction impacts survival in patients with ischaemic dilated cardiomyopathy. Eur J Heart Fail 2010;**12**(4):375-81.
250. Michler RE, Rouleau JL, Al-Khalidi HR, Bonow RO, Pellikka PA, Pohost GM, Holly TA, Oh JK, Dagenais F, Milano C, Wrobel K, Pirk J, Ali IS, Jones RH, Velazquez EJ, Lee KL, Di Donato M, Investigators ST. Insights from the STICH trial: change in left ventricular size after coronary artery bypass grafting with and without surgical ventricular reconstruction. J Thorac Cardiovasc Surg 2013;**146**(5):1139-1145 e6.
251. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, McKinlay SM, LeJemtel TH. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med 1999;**341**(9):625-34.
252. White HD, Assmann SF, Sanborn TA, Jacobs AK, Webb JG, Sleeper LA, Wong CK, Stewart JT, Aylward PE, Wong SC, Hochman JS. Comparison of percutaneous coronary intervention and coronary artery bypass grafting after acute myocardial infarction complicated by cardiogenic shock: results from the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial. Circulation 2005;**112**(13):1992-2001.
253. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, de Waha A, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Lauer B, Bohm M, Ebelt H, Schneider S, Werdan K, Schuler G, Intraaortic Balloon Pump in cardiogenic shock IIti. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. Lancet 2013;**382**(9905):1638-45.
254. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Bohm M, Ebelt H, Schneider S, Schuler G, Werdan K, Investigators I-SIT. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012;**367**(14):1287-96.
255. Unverzagt S, Buerke M, de Waha A, Haerting J, Pietzner D, Seyfarth M, Thiele H, Werdan K, Zeymer U, Prondzinsky R. Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. Cochrane Database Syst Rev 2015(3):CD007398.
256. Ouweneel DM, Schotborgh JV, Limpens J, Sjauw KD, Engstrom AE, Lagrand WK, Cherpanath TGV, Driessen AHG, de Mol B, Henriques JPS. Extracorporeal life support during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis. Intensive Care Med 2016;**42**(12):1922-1934.
257. Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW, TandemHeart Investigators G. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. Am Heart J 2006;**152**(3):469 e1-8.
258. Seyfarth M, Sibbing D, Bauer I, Frohlich G, Bott-Flugel L, Byrne R, Dirschinger J, Kastrati A, Schomig A. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left

ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol 2008;**52**(19):1584-8.
259. Thiele H, Jobs A, Ouweneel DM, Henriques JPS, Seyfarth M, Desch S, Eitel I, Poss J, Fuernau G, de Waha S. Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials. Eur Heart J 2017.
260. O'Neill WW, Kleiman NS, Moses J, Henriques JP, Dixon S, Massaro J, Palacios I, Maini B, Mulukutla S, Dzavik V, Popma J, Douglas PS, Ohman M. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation 2012;**126**(14):1717-27.
261. Acharya D, Loyaga-Rendon RY, Pamboukian SV, Tallaj JA, Holman WL, Cantor RS, Naftel DC, Kirklin JK. Ventricular Assist Device in Acute Myocardial Infarction. J Am Coll Cardiol 2016;**67**(16):1871-80.
262. Hochman JS, Sleeper LA, Webb JG, Dzavik V, Buller CE, Aylward P, Col J, White HD, Investigators S. Early revascularization and long-term survival in cardiogenic shock complicating acute myocardial infarction. JAMA 2006;**295**(21):2511-5.
263. Hammoud T, Tanguay JF, Bourassa MG. Management of coronary artery disease: therapeutic options in patients with diabetes. J Am Coll Cardiol 2000;**36**:355-365.
264. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in non-diabetic subjects with and without prior myocardial infarction. . N Engl J Med 1998;**339**:229-234.
265. Luscher TF, Creager MA, Beckman JA, Cosentino F. Diabetes and vascular disease: pathophysiology, clinical consequences, and medical therapy: Part II. Circulation 2003;**108**:1655-1661.
266. Ledru F, Ducimetière P, Battaglia S, Courbon D, Beverelli F, Guize L, Guermonprez JL, Diébold B. New diagnostic criteria for diabetes and coronary artery disease: insights from an angiographic study. J Am Coll Cardiol 2001 **37**:1543-1550.
267. Moreno PR, Murcia AM, Palacios IF, Leon MN, Bernardi VH, Fuster V, Fallon JT. Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. Circulation 2000 **102**:2180-2184.
268. Marso SP, Mercado N, Maehara A, Weisz G, Mintz GS, McPherson J, Schiele F, Dudek D, Fahy M, Xu K, Lansky A, Templin B, Zhang Z, de Bruyne B, Serruys PW, Stone GW. Plaque composition and clinical outcomes in acute coronary syndrome patients with metabolic syndrome or diabetes. JACC Cardiovasc Imaging 2012;**5(3 Suppl)**:S42-52.
269. Silva JA, Escobar A, Collins TJ, Ramee SR, White CJ. Unstable angina. A comparison of angioscopic findings between diabetic and nondiabetic patients. Circulation 199 **92**.
270. O'Donoghue ML, Vaidya A, Afsal R, Alfredsson J, Boden WE, Braunwald E, Cannon CP, Clayton TC, de Winter RJ, Fox KA, Lagerqvist B, McCullough PA, Murphy SA, Spacek R, Swahn E, Windhausen F, Sabatine MS. An invasive or conservative strategy in patients with diabetes mellitus and non-ST-segment elevation acute coronary syndromes: a collaborative meta-analysis of randomized trials. J Am Coll Cardiol 2012;**60**(2):106-11.
271. Schwartz L, Bertolet M, Feit F, Fuentes F, Sako EY, Toosi MS, Davidson CJ, Ikeno F, King SB, 3rd. Impact of completeness of revascularization on long-term cardiovascular outcomes in patients with type 2 diabetes mellitus: results from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D). Circ Cardiovasc Interv 2012;**5**(2):166-73.
272. Dangas GD, Farkouh ME, Sleeper LA, Yang M, Schoos MM, Macaya C, Abizaid A, Buller CE, Devlin G, Rodriguez AE, Lansky AJ, Siami FS, Domanski M, Fuster V, Investigators F. Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial. J Am Coll Cardiol 2014;**64**(12):1189-97.
273. Kamalesh M, Sharp TG, Tang XC, Shunk K, Ward HB, Walsh J, King Srd, Colling C, Moritz T, Stroupe K, Reda D. Percutaneous coronary intervention versus coronary bypass surgery in United States veterans with diabetes. J Am Coll Cardiol 2013;**61**:808-816.
274. Kapur A, Hall RJ, Malik IS, Qureshi AC, Butts J, de Belder M, Baumbach A, Angelini G, de Belder A, Oldroyd KG, Flather M, Roughton M, Nihoyannopoulos P, Bagger JP, Morgan K, Beatt KJ.

Randomized comparison of percutaneous coronary intervention with coronary artery bypass grafting in diabetic patients. 1-year results of the CARDia (Coronary Artery Revascularization in Diabetes) trial. J Am Coll Cardiol 2010 **55**:432-440.
275. Kappetein AP, Head SJ, Morice MC, Banning AP, Serruys PW, Mohr FW, Dawkins KD, Mack MJ. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. Eur J Cardiothorac Surg 2013;**43**:1006-1013.
276. Koskinas KC, Siontis GC, Piccolo R, Franzone A, Haynes A, Rat-Wirtzler J, Silber S, Serruys PW, Pilgrim T, Räber L, Heg D, Jüni P, Windecker S. Impact of Diabetic Status on Outcomes After Revascularization With Drug-Eluting Stents in Relation to Coronary Artery Disease Complexity: Patient-Level Pooled Analysis of 6081 Patients. Circ Cardiovasc Interv 2016 **9**:e003255.
277. Hakeem A, Garg N, Bhatti S, Rajpurohit N, Ahmed Z, Uretsky BF. Effectiveness of percutaneous coronary intervention with drug-eluting stents compared with bypass surgery in diabetics with multivessel coronary disease: comprehensive systematic review and meta-analysis of randomized clinical data. J Am Heart Assoc 2013 **2**:e000354.
278. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Xu J, Hannan EL. Everolimus Eluting Stents Versus Coronary Artery Bypass Graft Surgery for Patients With Diabetes Mellitus and Multivessel Disease. Circ Cardiovasc Interv 2015;**8**(7):e002626.
279. Herbison P, Wong CK. Has the difference in mortality between percutaneous coronary intervention and coronary artery bypass grafting in people with heart disease and diabetes changed over the years? A systematic review and meta-regression. BMJ Open 2015;**5**(12):e010055.
280. Goergen SK, Rumbold G, Compton G, Harris C. Systematic review of current guidelines, and their evidence base, on risk of lactic acidosis after administration of contrast medium for patients receiving metformin. Radiology 2010;**254**(1):261-9.
281. Milojevic M, Head SJ, Mack MJ, Mohr FW, Morice MC, Dawkins KD, Holmes DR, Jr., Serruys PW, Kappetein AP. The impact of chronic kidney disease on outcomes following percutaneous coronary interventions versus coronary artery bypass grafting in patients with complex coronary artery disease: 5-year follow-up of the SYNTAX trial. EuroIntervention 2017.
282. Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB, Dangas G. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;**44**(7):1393-9.
283. Ohno Y, Maekawa Y, Miyata H, Inoue S, Ishikawa S, Sueyoshi K, Noma S, Kawamura A, Kohsaka S, Fukuda K. Impact of periprocedural bleeding on incidence of contrast-induced acute kidney injury in patients treated with percutaneous coronary intervention. J Am Coll Cardiol 2013;**62**(14):1260-6.
284. Aspelin P, Aubry P, Fransson SG, Strasser R, Willenbrock R, Berg KJ. Nephrotoxic effects in high-risk patients undergoing angiography. N Engl J Med 2003;**348**(6):491-9.
285. Jo SH, Youn TJ, Koo BK, Park JS, Kang HJ, Cho YS, Chung WY, Joo GW, Chae IH, Choi DJ, Oh BH, Lee MM, Park YB, Kim HS. Renal toxicity evaluation and comparison between visipaque (iodixanol) and hexabrix (ioxaglate) in patients with renal insufficiency undergoing coronary angiography: the RECOVER study: a randomized controlled trial. J Am Coll Cardiol 2006;**48**(5):924-30.
286. Solomon RJ, Natarajan MK, Doucet S, Sharma SK, Staniloae CS, Katholi RE, Gelormini JL, Labinaz M, Moreyra AE. Cardiac Angiography in Renally Impaired Patients (CARE) study: a randomized double-blind trial of contrast-induced nephropathy in patients with chronic kidney disease. Circulation 2007;**115**(25):3189-96.
287. Marenzi G, Assanelli E, Campodonico J, Lauri G, Marana I, De Metrio M, Moltrasio M, Grazi M, Rubino M, Veglia F, Fabbiocchi F, Bartorelli AL. Contrast volume during primary percutaneous coronary intervention and subsequent contrast-induced nephropathy and mortality. Ann Intern Med 2009;**150**(3):170-7.
288. Laskey WK, Jenkins C, Selzer F, Marroquin OC, Wilensky RL, Glaser R, Cohen HA, Holmes DR, Jr. Volume-to-creatinine clearance ratio: a pharmacokinetically based risk factor for prediction of

early creatinine increase after percutaneous coronary intervention. J Am Coll Cardiol 2007;**50**(7):584-90.
289. Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, Marsch S, Roskamm H. Prevention of contrast media-associated nephropathy: randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. Arch Intern Med 2002;**162**(3):329-36.
290. Merten GJ, Burgess WP, Gray LV, Holleman JH, Roush TS, Kowalchuk GJ, Bersin RM, Van Moore A, Simonton CA, 3rd, Rittase RA, Norton HJ, Kennedy TP. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. JAMA 2004;**291**(19):2328-34.
291. Brar SS, Shen AY, Jorgensen MB, Kotlewski A, Aharonian VJ, Desai N, Ree M, Shah AI, Burchette RJ. Sodium bicarbonate vs sodium chloride for the prevention of contrast medium-induced nephropathy in patients undergoing coronary angiography: a randomized trial. JAMA 2008;**300**(9):1038-46.
292. Nijssen EC, Rennenberg RJ, Nelemans PJ, Essers BA, Janssen MM, Vermeeren MA, Ommen VV, Wildberger JE. Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial. Lancet 2017;**389**(10076):1312-1322.
293. Giacoppo D, Gargiulo G, Buccheri S, Aruta P, Byrne RA, Cassese S, Dangas G, Kastrati A, Mehran R, Tamburino C, Capodanno D. Preventive Strategies for Contrast-Induced Acute Kidney Injury in Patients Undergoing Percutaneous Coronary Procedures: Evidence From a Hierarchical Bayesian Network Meta-Analysis of 124 Trials and 28 240 Patients. Circ Cardiovasc Interv 2017;**10**(5).
294. Weisbord SD, Gallagher M, Jneid H, Garcia S, Cass A, Thwin SS, Conner TA, Chertow GM, Bhatt DL, Shunk K, Parikh CR, McFalls EO, Brophy M, Ferguson R, Wu H, Androsenko M, Myles J, Kaufman J, Palevsky PM, Group PT. Outcomes after Angiography with Sodium Bicarbonate and Acetylcysteine. N Engl J Med 2017.
295. Qian G, Fu Z, Guo J, Cao F, Chen Y. Prevention of Contrast-Induced Nephropathy by Central Venous Pressure-Guided Fluid Administration in Chronic Kidney Disease and Congestive Heart Failure Patients. JACC Cardiovasc Interv 2016;**9**(1):89-96.
296. Briguori C, Visconti G, Focaccio A, Airoldi F, Valgimigli M, Sangiorgi GM, Golia B, Ricciardelli B, Condorelli G. Renal Insufficiency After Contrast Media Administration Trial II (REMEDIAL II): RenalGuard System in high-risk patients for contrast-induced acute kidney injury. Circulation 2011;**124**(11):1260-9.
297. Putzu A, Boscolo Berto M, Belletti A, Pasotti E, Cassina T, Moccetti T, Pedrazzini G. Prevention of Contrast-Induced Acute Kidney Injury by Furosemide With Matched Hydration in Patients Undergoing Interventional Procedures: A Systematic Review and Meta-Analysis of Randomized Trials. JACC Cardiovasc Interv 2017;**10**(4):355-363.
298. Marenzi G, Marana I, Lauri G, Assanelli E, Grazi M, Campodonico J, Trabattoni D, Fabbiocchi F, Montorsi P, Bartorelli AL. The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. N Engl J Med 2003;**349**(14):1333-40.
299. Marenzi G, Lauri G, Campodonico J, Marana I, Assanelli E, De Metrio M, Grazi M, Veglia F, Fabbiocchi F, Montorsi P, Bartorelli AL. Comparison of two hemofiltration protocols for prevention of contrast-induced nephropathy in high-risk patients. Am J Med 2006;**119**(2):155-62.
300. Cruz DN, Goh CY, Marenzi G, Corradi V, Ronco C, Perazella MA. Renal replacement therapies for prevention of radiocontrast-induced nephropathy: a systematic review. Am J Med 2012;**125**(1):66-78 e3.
301. Vogt B, Ferrari P, Schonholzer C, Marti HP, Mohaupt M, Wiederkehr M, Cereghetti C, Serra A, Huynh-Do U, Uehlinger D, Frey FJ. Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. Am J Med 2001;**111**(9):692-8.
302. Scarsini R, Pesarini G, Zivelonghi C, Piccoli A, Ferrero V, Lunardi M, Barbierato M, Caprioglio F, Vassanelli C, Ribichini F. Coronary physiology in patients with severe aortic stenosis: Comparison between fractional flow reserve and instantaneous wave-free ratio. Int J Cardiol 2017;**243**:40-46.

303. Scarsini R, Pesarini G, Zivelonghi C, Piccoli A, Ferrero V, Lunardi M, Gottin L, Zanetti C, Faggian G, Ribichini F. Physiologic Evaluation of Coronary Lesions Using Instantaneous Wave-free Ratio (iFR) in Patients with Severe Aortic Stenosis Undergoing Trans-catheter Aortic Valve Implantation. EuroIntervention 2017.
304. Di Gioia G, Scarsini R, Strisciuglio T, De Biase C, Zivelonghi C, Franco D, De Bruyne B, Ribichini F, Barbato E. Correlation between Angiographic and Physiologic Evaluation of Coronary Artery Narrowings in Patients With Aortic Valve Stenosis. Am J Cardiol 2017;**120**(1):106-110.
305. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjogren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL, Group ESCSD. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017;**38**(36):2739-2791.
306. Yamashita K, Fujita T, Hata H, Shimahara Y, Kume Y, Matsumoto Y, Kobayashi J. Long-term outcome of isolated off-pump coronary artery bypass grafting in patients with coronary artery disease and mild to moderate aortic stenosis. J Cardiol 2017;**70**(1):48-54.
307. Goldstein D, Moskowitz AJ, Gelijns AC, Ailawadi G, Parides MK, Perrault LP, Hung JW, Voisine P, Dagenais F, Gillinov AM, Thourani V, Argenziano M, Gammie JS, Mack M, Demers P, Atluri P, Rose EA, O'Sullivan K, Williams DL, Bagiella E, Michler RE, Weisel RD, Miller MA, Geller NL, Taddei-Peters WC, Smith PK, Moquete E, Overbey JR, Kron IL, O'Gara PT, Acker MA, Ctsn. Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation. N Engl J Med 2016;**374**(4):344-53.
308. Smith PK, Puskas JD, Ascheim DD, Voisine P, Gelijns AC, Moskowitz AJ, Hung JW, Parides MK, Ailawadi G, Perrault LP, Acker MA, Argenziano M, Thourani V, Gammie JS, Miller MA, Page P, Overbey JR, Bagiella E, Dagenais F, Blackstone EH, Kron IL, Goldstein DJ, Rose EA, Moquete EG, Jeffries N, Gardner TJ, O'Gara PT, Alexander JH, Michler RE, Cardiothoracic Surgical Trials Network I. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014;**371**(23):2178-88.
309. Michler RE, Smith PK, Parides MK, Ailawadi G, Thourani V, Moskowitz AJ, Acker MA, Hung JW, Chang HL, Perrault LP, Gillinov AM, Argenziano M, Bagiella E, Overbey JR, Moquete EG, Gupta LN, Miller MA, Taddei-Peters WC, Jeffries N, Weisel RD, Rose EA, Gammie JS, DeRose JJ, Jr., Puskas JD, Dagenais F, Burks SG, El-Hamamsy I, Milano CA, Atluri P, Voisine P, O'Gara PT, Gelijns AC, Ctsn. Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation. N Engl J Med 2016;**374**(20):1932-41.
310. Chan KM, Punjabi PP, Flather M, Wage R, Symmonds K, Roussin I, Rahman-Haley S, Pennell DJ, Kilner PJ, Dreyfus GD, Pepper JR, Investigators R. Coronary artery bypass surgery with or without mitral valve annuloplasty in moderate functional ischemic mitral regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) trial. Circulation 2012;**126**(21):2502-10.
311. Lancellotti P, Tribouilloy C, Hagendorff A, Popescu BA, Edvardsen T, Pierard LA, Badano L, Zamorano JL, Scientific Document Committee of the European Association of Cardiovascular I. Recommendations for the echocardiographic assessment of native valvular regurgitation: an executive summary from the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2013;**14**(7):611-44.
312. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, Little SH, Shah DJ, Shernan S, Thavendiranathan P, Thomas JD, Weissman NJ. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2017;**30**(4):303-371.
313. Palmerini T, Biondi-Zoccai G, Reggiani LB, Sangiorgi D, Alessi L, De Servi S, Branzi A, Stone GW. Risk of stroke with coronary artery bypass graft surgery compared with percutaneous coronary intervention. J Am Coll Cardiol 2012;**60**(9):798-805.
314. Naylor AR, Bown MJ. Stroke after cardiac surgery and its association with asymptomatic carotid disease: an updated systematic review and meta-analysis. Eur J Vasc Endovasc Surg 2011;**41**(5):607-24.
315. Masabni K, Raza S, Blackstone EH, Gornik HL, Sabik JF, 3rd. Does preoperative carotid stenosis screening reduce perioperative stroke in patients undergoing coronary artery bypass grafting? J Thorac Cardiovasc Surg 2015;**149**(5):1253-60.

316. Naylor AR. Does the risk of post-CABG stroke merit staged or synchronous reconstruction in patients with symptomatic or asymptomatic carotid disease? J Cardiovasc Surg (Torino) 2009;**50**(1):71-81.
317. Aboyans V, Ricco JB, Bartelink MEL, Bjorck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzolai L, Naylor AR, Roffi M, Rother J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO)The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2017.
318. Lee R, Matsutani N, Polimenakos AC, Levers LC, Lee M, Johnson RG. Preoperative noncontrast chest computed tomography identifies potential aortic emboli. Ann Thorac Surg 2007;**84**(1):38-41; discussion 42.
319. Naylor AR, Cuffe RL, Rothwell PM, Bell PR. A systematic review of outcomes following staged and synchronous carotid endarterectomy and coronary artery bypass. Eur J Vasc Endovasc Surg 2003;**25**(5):380-9.
320. Paraskevas KI, Nduwayo S, Saratzis AN, Naylor AR. Carotid Stenting Prior to Coronary Bypass Surgery: An Updated Systematic Review and Meta-Analysis. Eur J Vasc Endovasc Surg 2017;**53**(3):309-319.
321. Lin JC, Kabbani LS, Peterson EL, Masabni K, Morgan JA, Brooks S, Wertella KP, Paone G. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. J Vasc Surg 2016;**63**(3):710-4.
322. Aboyans V, Lacroix P. Indications for carotid screening in patients with coronary artery disease. Presse Med 2009;**38**(6):977-86.
323. Zhao DX, Leacche M, Balaguer JM, Boudoulas KD, Damp JA, Greelish JP, Byrne JG, Writing Group of the Cardiac Surgery CA, Interventional Cardiology Groups at the Vanderbilt H, Vascular I, Ahmad RM, Ball SK, Cleator JH, Deegan RJ, Eagle SS, Fong PP, Fredi JL, Hoff SJ, Jennings HS, 3rd, McPherson JA, Piana RN, Pretorius M, Robbins MA, Slosky DA, Thompson A. Routine intraoperative completion angiography after coronary artery bypass grafting and 1-stop hybrid revascularization results from a fully integrated hybrid catheterization laboratory/operating room. J Am Coll Cardiol 2009;**53**(3):232-41.
324. Thielmann M, Massoudy P, Jaeger BR, Neuhauser M, Marggraf G, Sack S, Erbel R, Jakob H. Emergency re-revascularization with percutaneous coronary intervention, reoperation, or conservative treatment in patients with acute perioperative graft failure following coronary artery bypass surgery. Eur J Cardiothorac Surg 2006;**30**(1):117-25.
325. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Writing Group on the Joint ESCAAHAWHFTFftUDoMI, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, Guidelines ESCCfP. Third universal definition of myocardial infarction. Eur Heart J 2012;**33**(20):2551-67.
326. Davierwala PM, Verevkin A, Leontyev S, Misfeld M, Borger MA, Mohr FW. Impact of expeditious management of perioperative myocardial ischemia in patients undergoing isolated coronary artery bypass surgery. Circulation 2013;**128**(11 Suppl 1):S226-34.
327. Laflamme M, DeMey N, Bouchard D, Carrier M, Demers P, Pellerin M, Couture P, Perrault LP. Management of early postoperative coronary artery bypass graft failure. Interact Cardiovasc Thorac Surg 2012;**14**(4):452-6.

328. Gaudino M, Nesta M, Burzotta F, Trani C, Coluccia V, Crea F, Massetti M. Results of emergency postoperative re-angiography after cardiac surgery procedures. Ann Thorac Surg 2015;**99**(5):1576-82.
329. Thielmann M, Sharma V, Al-Attar N, Bulluck H, Bisleri G, Jh Bunge J, Czerny M, Ferdinandy P, Frey UH, Heusch G, Holfeld J, Kleinbongard P, Kunst G, Lang I, Lentini S, Madonna R, Meybohm P, Muneretto C, Obadia JF, Perrino C, Prunier F, Sluijter JPG, Van Laake LW, Sousa-Uva M, Hausenloy DJ. ESC Joint Working Groups on Cardiovascular Surgery and the Cellular Biology of the Heart Position Paper: Perioperative myocardial injury and infarction in patients undergoing coronary artery bypass graft surgery. Eur Heart J 2017;**38**(31):2392-2407.
330. Seshadri N, Whitlow PL, Acharya N, Houghtaling P, Blackstone EH, Ellis SG. Emergency coronary artery bypass surgery in the contemporary percutaneous coronary intervention era. Circulation 2002;**106**(18):2346-50.
331. Mattichak SJ, Dixon SR, Shannon F, Boura JA, Safian RD. Failed percutaneous coronary intervention: a decade of experience in 21,000 patients. Catheter Cardiovasc Interv 2008;**71**(2):131-7.
332. Davierwala PM, Leontyev S, Verevkin A, Rastan AJ, Mohr M, Bakhtiary F, Misfeld M, Mohr FW. Temporal Trends in Predictors of Early and Late Mortality After Emergency Coronary Artery Bypass Grafting for Cardiogenic Shock Complicating Acute Myocardial Infarction. Circulation 2016;**134**(17):1224-1237.
333. Axelsson TA, Mennander A, Malmberg M, Gunn J, Jeppsson A, Gudbjartsson T. Is emergency and salvage coronary artery bypass grafting justified? The Nordic Emergency/Salvage coronary artery bypass grafting study. Eur J Cardiothorac Surg 2016;**49**(5):1451-6.
334. Parasca CA, Head SJ, Milojevic M, Mack MJ, Serruys PW, Morice MC, Mohr FW, Feldman TE, Colombo A, Dawkins KD, Holmes DR, Jr., Kappetein PA, Investigators S. Incidence, Characteristics, Predictors, and Outcomes of Repeat Revascularization After Percutaneous Coronary Intervention and Coronary Artery Bypass Grafting: The SYNTAX Trial at 5 Years. JACC Cardiovasc Interv 2016;**9**(24):2493-2507.
335. Cassese S, Byrne RA, Tada T, Pinieck S, Joner M, Ibrahim T, King LA, Fusaro M, Laugwitz KL, Kastrati A. Incidence and predictors of restenosis after coronary stenting in 10 004 patients with surveillance angiography. Heart 2014;**100**(2):153-9.
336. Tada T, Byrne RA, Simunovic I, King LA, Cassese S, Joner M, Fusaro M, Schneider S, Schulz S, Ibrahim T, Ott I, Massberg S, Laugwitz KL, Kastrati A. Risk of stent thrombosis among bare-metal stents, first-generation drug-eluting stents, and second-generation drug-eluting stents: results from a registry of 18,334 patients. JACC Cardiovasc Interv 2013;**6**(12):1267-74.
337. Sabik JF, 3rd, Blackstone EH, Houghtaling PL, Walts PA, Lytle BW. Is reoperation still a risk factor in coronary artery bypass surgery? Ann Thorac Surg 2005;**80**(5):1719-27.
338. Yap CH, Sposato L, Akowuah E, Theodore S, Dinh DT, Shardey GC, Skillington PD, Tatoulis J, Yii M, Smith JA, Mohajeri M, Pick A, Seevanayagam S, Reid CM. Contemporary results show repeat coronary artery bypass grafting remains a risk factor for operative mortality. Ann Thorac Surg 2009;**87**(5):1386-91.
339. Fosbol EL, Zhao Y, Shahian DM, Grover FL, Edwards FH, Peterson ED. Repeat coronary revascularization after coronary artery bypass surgery in older adults: the Society of Thoracic Surgeons' national experience, 1991-2007. Circulation 2013;**127**(16):1656-63.
340. Brener SJ, Lytle BW, Casserly IP, Ellis SG, Topol EJ, Lauer MS. Predictors of revascularization method and long-term outcome of percutaneous coronary intervention or repeat coronary bypass surgery in patients with multivessel coronary disease and previous coronary bypass surgery. Eur Heart J 2006;**27**(4):413-8.
341. Morrison DA, Sethi G, Sacks J, Henderson WG, Grover F, Sedlis S, Esposito R, Investigators of the Department of Veterans Affairs Cooperative Study AWESOME. Percutaneous coronary intervention versus repeat bypass surgery for patients with medically refractory myocardial ischemia: AWESOME randomized trial and registry experience with post-CABG patients. J Am Coll Cardiol 2002;**40**(11):1951-4.

342. Morrison DA, Sethi G, Sacks J, Henderson W, Grover F, Sedlis S, Esposito R, Ramanathan K, Weiman D, Saucedo J, Antakli T, Paramesh V, Pett S, Vernon S, Birjiniuk V, Welt F, Krucoff M, Wolfe W, Lucke JC, Mediratta S, Booth D, Barbiere C, Lewis D, Angina With Extremely Serious Operative Mortality E. Percutaneous coronary intervention versus coronary artery bypass graft surgery for patients with medically refractory myocardial ischemia and risk factors for adverse outcomes with bypass: a multicenter, randomized trial. Investigators of the Department of Veterans Affairs Cooperative Study #385, the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME). J Am Coll Cardiol 2001;**38**(1):143-9.
343. Harskamp RE, Beijk MA, Damman P, Kuijt WJ, Woudstra P, Grundeken MJ, Kloek JJ, Tijssen JG, de Mol BA, de Winter RJ. Clinical outcome after surgical or percutaneous revascularization in coronary bypass graft failure. J Cardiovasc Med (Hagerstown) 2013;**14**(6):438-45.
344. Sabik JF, 3rd, Raza S, Blackstone EH, Houghtaling PL, Lytle BW. Value of internal thoracic artery grafting to the left anterior descending coronary artery at coronary reoperation. J Am Coll Cardiol 2013;**61**(3):302-10.
345. Nwaejike N, Tennyson C, Mosca R, Venkateswaran R. Reusing the patent internal mammary artery as a conduit in redo coronary artery bypass surgery. Interact Cardiovasc Thorac Surg 2016;**22**(3):346-50.
346. Coolong A, Baim DS, Kuntz RE, O'Malley AJ, Marulkar S, Cutlip DE, Popma JJ, Mauri L. Saphenous vein graft stenting and major adverse cardiac events: a predictive model derived from a pooled analysis of 3958 patients. Circulation 2008;**117**(6):790-7.
347. Baim DS, Wahr D, George B, Leon MB, Greenberg J, Cutlip DE, Kaya U, Popma JJ, Ho KK, Kuntz RE, Saphenous vein graft Angioplasty Free of Emboli Randomized Trial I. Randomized trial of a distal embolic protection device during percutaneous intervention of saphenous vein aorto-coronary bypass grafts. Circulation 2002;**105**(11):1285-90.
348. Paul TK, Bhatheja S, Panchal HB, Zheng S, Banerjee S, Rao SV, Guzman L, Beohar N, Zhao D, Mehran R, Mukherjee D. Outcomes of Saphenous Vein Graft Intervention With and Without Embolic Protection Device: A Comprehensive Review and Meta-Analysis. Circ Cardiovasc Interv 2017;**10**(12).
349. Brennan JM, Al-Hejily W, Dai D, Shaw RE, Trilesskaya M, Rao SV, Brilakis ES, Anstrom KJ, Messenger JC, Peterson ED, Douglas PS, Sketch MH, Jr. Three-year outcomes associated with embolic protection in saphenous vein graft intervention: results in 49 325 senior patients in the Medicare-linked National Cardiovascular Data Registry CathPCI Registry. Circ Cardiovasc Interv 2015;**8**(3):e001403.
350. Stone GW, Rogers C, Hermiller J, Feldman R, Hall P, Haber R, Masud A, Cambier P, Caputo RP, Turco M, Kovach R, Brodie B, Herrmann HC, Kuntz RE, Popma JJ, Ramee S, Cox DA, FilterWire EXREI. Randomized comparison of distal protection with a filter-based catheter and a balloon occlusion and aspiration system during percutaneous intervention of diseased saphenous vein aorto-coronary bypass grafts. Circulation 2003;**108**(5):548-53.
351. Mauri L, Cox D, Hermiller J, Massaro J, Wahr J, Tay SW, Jonas M, Popma JJ, Pavliska J, Wahr D, Rogers C. The PROXIMAL trial: proximal protection during saphenous vein graft intervention using the Proxis Embolic Protection System: a randomized, prospective, multicenter clinical trial. J Am Coll Cardiol 2007;**50**(15):1442-9.
352. Schachinger V, Hamm CW, Munzel T, Haude M, Baldus S, Grube E, Bonzel T, Konorza T, Koster R, Arnold R, Haase J, Probst P, vom Dahl J, Neumann FJ, Mudra H, Hennen B, Thiele L, Zeiher AM, Investigators S. A randomized trial of polytetrafluoroethylene-membrane-covered stents compared with conventional stents in aortocoronary saphenous vein grafts. J Am Coll Cardiol 2003;**42**(8):1360-9.
353. Stankovic G, Colombo A, Presbitero P, van den Branden F, Inglese L, Cernigliaro C, Niccoli L, Bartorelli AL, Rubartelli P, Reifart N, Heyndrickx GR, Saunamaki K, Morice MC, Sgura FA, Di Mario C, Randomized Evaluation of polytetrafluoroethylene CsiSvgi. Randomized evaluation of polytetrafluoroethylene-covered stent in saphenous vein grafts: the Randomized Evaluation of polytetrafluoroethylene COVERed stent in Saphenous vein grafts (RECOVERS) Trial. Circulation 2003;**108**(1):37-42.

354. Mehilli J, Pache J, Abdel-Wahab M, Schulz S, Byrne RA, Tiroch K, Hausleiter J, Seyfarth M, Ott I, Ibrahim T, Fusaro M, Laugwitz KL, Massberg S, Neumann FJ, Richardt G, Schomig A, Kastrati A, Is Drug-Eluting-Stenting Associated with Improved Results in Coronary Artery Bypass Grafts I. Drug-eluting versus bare-metal stents in saphenous vein graft lesions (ISAR-CABG): a randomised controlled superiority trial. Lancet 2011;**378**(9796):1071-8.
355. Brilakis ES, Lichtenwalter C, de Lemos JA, Roesle M, Obel O, Haagen D, Saeed B, Gadiparthi C, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger P, Banerjee S. A randomized controlled trial of a paclitaxel-eluting stent versus a similar bare-metal stent in saphenous vein graft lesions the SOS (Stenting of Saphenous Vein Grafts) trial. J Am Coll Cardiol 2009;**53**(11):919-28.
356. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Bruining N, Van den Branden F, Van Langenhove G. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC Trial. J Am Coll Cardiol 2006;**48**(12):2423-31.
357. Brilakis ES, Lichtenwalter C, Abdel-karim AR, de Lemos JA, Obel O, Addo T, Roesle M, Haagen D, Rangan BV, Saeed B, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger P, Banerjee S. Continued benefit from paclitaxel-eluting compared with bare-metal stent implantation in saphenous vein graft lesions during long-term follow-up of the SOS (Stenting of Saphenous Vein Grafts) trial. JACC Cardiovasc Interv 2011;**4**(2):176-82.
358. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Van den Branden F, Van Langenhove G, Investigators DR. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC Trial. J Am Coll Cardiol 2007;**50**(3):261-7.
359. Mehilli J, Byrne RA, Tiroch K, Pinieck S, Schulz S, Kufner S, Massberg S, Laugwitz KL, Schomig A, Kastrati A. Randomized trial of paclitaxel- versus sirolimus-eluting stents for treatment of coronary restenosis in sirolimus-eluting stents: the ISAR-DESIRE 2 (Intracoronary Stenting and Angiographic Results: Drug Eluting Stents for In-Stent Restenosis 2) study. J Am Coll Cardiol 2010;**55**(24):2710-6.
360. Kastrati A, Mehilli J, von Beckerath N, Dibra A, Hausleiter J, Pache J, Schuhlen H, Schmitt C, Dirschinger J, Schomig A. Sirolimus-eluting stent or paclitaxel-eluting stent vs balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. JAMA 2005;**293**(2):165-71.
361. Alfonso F, Perez-Vizcayno MJ, Hernandez R, Bethencourt A, Marti V, Lopez-Minguez JR, Angel J, Mantilla R, Moris C, Cequier A, Sabate M, Escaned J, Moreno R, Banuelos C, Suarez A, Macaya C. A randomized comparison of sirolimus-eluting stent with balloon angioplasty in patients with in-stent restenosis: results of the Restenosis Intrastent: Balloon Angioplasty Versus Elective Sirolimus-Eluting Stenting (RIBS-II) trial. J Am Coll Cardiol 2006;**47**(11):2152-60.
362. Alfonso F, Zueco J, Cequier A, Mantilla R, Bethencourt A, Lopez-Minguez JR, Angel J, Auge JM, Gomez-Recio M, Moris C, Seabra-Gomes R, Perez-Vizcayno MJ, Macaya C. A randomized comparison of repeat stenting with balloon angioplasty in patients with in-stent restenosis. J Am Coll Cardiol 2003;**42**(5):796-805.
363. Dibra A, Kastrati A, Alfonso F, Seyfarth M, Perez-Vizcayno MJ, Mehilli J, Schomig A. Effectiveness of drug-eluting stents in patients with bare-metal in-stent restenosis: meta-analysis of randomized trials. J Am Coll Cardiol 2007;**49**(5):616-23.
364. Scheller B, Clever YP, Kelsch B, Hehrlein C, Bocksch W, Rutsch W, Haghi D, Dietz U, Speck U, Bohm M, Cremers B. Long-term follow-up after treatment of coronary in-stent restenosis with a paclitaxel-coated balloon catheter. JACC Cardiovasc Interv 2012;**5**(3):323-30.
365. Scheller B, Hehrlein C, Bocksch W, Rutsch W, Haghi D, Dietz U, Bohm M, Speck U. Treatment of coronary in-stent restenosis with a paclitaxel-coated balloon catheter. N Engl J Med 2006;**355**(20):2113-24.
366. Habara S, Iwabuchi M, Inoue N, Nakamura S, Asano R, Nanto S, Hayashi Y, Shiode N, Saito S, Ikari Y, Kimura T, Hosokawa J, Nakamura M, Kotani J, Kozuma K, Mitsudo K. A multicenter randomized comparison of paclitaxel-coated balloon catheter with conventional balloon angioplasty

in patients with bare-metal stent restenosis and drug-eluting stent restenosis. Am Heart J 2013;**166**(3):527-533 e2.
367. Unverdorben M, Vallbracht C, Cremers B, Heuer H, Hengstenberg C, Maikowski C, Werner GS, Antoni D, Kleber FX, Bocksch W, Leschke M, Ackermann H, Boxberger M, Speck U, Degenhardt R, Scheller B. Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis. Circulation 2009;**119**(23):2986-94.
368. Rittger H, Brachmann J, Sinha AM, Waliszewski M, Ohlow M, Brugger A, Thiele H, Birkemeyer R, Kurowski V, Breithardt OA, Schmidt M, Zimmermann S, Lonke S, von Cranach M, Nguyen TV, Daniel WG, Wohrle J. A randomized, multicenter, single-blinded trial comparing paclitaxel-coated balloon angioplasty with plain balloon angioplasty in drug-eluting stent restenosis: the PEPCAD-DES study. J Am Coll Cardiol 2012;**59**(15):1377-82.
369. Habara S, Mitsudo K, Kadota K, Goto T, Fujii S, Yamamoto H, Katoh H, Oka N, Fuku Y, Hosogi S, Hirono A, Maruo T, Tanaka H, Shigemoto Y, Hasegawa D, Tasaka H, Kusunose M, Otsuru S, Okamoto Y, Saito N, Tsujimoto Y, Eguchi H, Miyake K, Yoshino M. Effectiveness of paclitaxel-eluting balloon catheter in patients with sirolimus-eluting stent restenosis. JACC Cardiovasc Interv 2011;**4**(2):149-54.
370. Byrne RA, Neumann FJ, Mehilli J, Pinieck S, Wolff B, Tiroch K, Schulz S, Fusaro M, Ott I, Ibrahim T, Hausleiter J, Valina C, Pache J, Laugwitz KL, Massberg S, Kastrati A, investigators I-D. Paclitaxel-eluting balloons, paclitaxel-eluting stents, and balloon angioplasty in patients with restenosis after implantation of a drug-eluting stent (ISAR-DESIRE 3): a randomised, open-label trial. Lancet 2013;**381**(9865):461-7.
371. Indermuehle A, Bahl R, Lansky AJ, Froehlich GM, Knapp G, Timmis A, Meier P. Drug-eluting balloon angioplasty for in-stent restenosis: a systematic review and meta-analysis of randomised controlled trials. Heart 2013;**99**(5):327-33.
372. Alfonso F, Perez-Vizcayno MJ, Cardenas A, Garcia Del Blanco B, Seidelberger B, Iniguez A, Gomez-Recio M, Masotti M, Velazquez MT, Sanchis J, Garcia-Touchard A, Zueco J, Bethencourt A, Melgares R, Cequier A, Dominguez A, Mainar V, Lopez-Minguez JR, Moreu J, Marti V, Moreno R, Jimenez-Quevedo P, Gonzalo N, Fernandez C, Macaya C, Ribs V Study Investigators utaotWGoICotSSoC. A randomized comparison of drug-eluting balloon versus everolimus-eluting stent in patients with bare-metal stent-in-stent restenosis: the RIBS V Clinical Trial (Restenosis Intra-stent of Bare Metal Stents: paclitaxel-eluting balloon vs. everolimus-eluting stent). J Am Coll Cardiol 2014;**63**(14):1378-86.
373. Pleva L, Kukla P, Kusnierova P, Zapletalova J, Hlinomaz O. Comparison of the Efficacy of Paclitaxel-Eluting Balloon Catheters and Everolimus-Eluting Stents in the Treatment of Coronary In-Stent Restenosis: The Treatment of In-Stent Restenosis Study. Circ Cardiovasc Interv 2016;**9**(4):e003316.
374. Alfonso F, Perez-Vizcayno MJ, Cardenas A, Garcia del Blanco B, Garcia-Touchard A, Lopez-Minguez JR, Benedicto A, Masotti M, Zueco J, Iniguez A, Velazquez M, Moreno R, Mainar V, Dominguez A, Pomar F, Melgares R, Rivero F, Jimenez-Quevedo P, Gonzalo N, Fernandez C, Macaya C, Investigators RIS. A Prospective Randomized Trial of Drug-Eluting Balloons Versus Everolimus-Eluting Stents in Patients With In-Stent Restenosis of Drug-Eluting Stents: The RIBS IV Randomized Clinical Trial. J Am Coll Cardiol 2015;**66**(1):23-33.
375. Baan J, Claessen BE, Dijk KB-v, Vendrik J, van der Schaaf RJ, Meuwissen M, van Royen N, Gosselink ATM, van Wely MH, Dirkali A, Arkenbout EK, de Winter RJ, Koch KT, Sjauw KD, Beijk MA, Vis MM, Wykrzykowska JJ, Piek JJ, Tijssen JGP, Henriques JPS. A Randomized Comparison of Paclitaxel-eluting Balloon Versus Everolimus-eluting Stent for the Treatment of Any In-stent Restenosis: The DARE Trial. JACC Cardiovasc Interv 2017.
376. Kufner S, Joner M, Schneider S, Tolg R, Zrenner B, Repp J, Starkmann A, Xhepa E, Ibrahim T, Cassese S, Fusaro M, Ott I, Hengstenberg C, Schunkert H, Abdel-Wahab M, Laugwitz KL, Kastrati A, Byrne RA, Investigators I-D. Neointimal Modification With Scoring Balloon and Efficacy of Drug-Coated Balloon Therapy in Patients With Restenosis in Drug-Eluting Coronary Stents: A Randomized Controlled Trial. JACC Cardiovasc Interv 2017;**10**(13):1332-1340.

377. Siontis GC, Stefanini GG, Mavridis D, Siontis KC, Alfonso F, Perez-Vizcayno MJ, Byrne RA, Kastrati A, Meier B, Salanti G, Juni P, Windecker S. Percutaneous coronary interventional strategies for treatment of in-stent restenosis: a network meta-analysis. Lancet 2015;**386**(9994):655-64.
378. Giacoppo D, Gargiulo G, Aruta P, Capranzano P, Tamburino C, Capodanno D. Treatment strategies for coronary in-stent restenosis: systematic review and hierarchical Bayesian network meta-analysis of 24 randomised trials and 4880 patients. BMJ 2015;**351**:h5392.
379. Kufner S, Cassese S, Valeskini M, Neumann FJ, Schulz-Schupke S, Hoppmann P, Fusaro M, Schunkert H, Laugwitz KL, Kastrati A, Byrne RA, Investigators I-D. Long-Term Efficacy and Safety of Paclitaxel-Eluting Balloon for the Treatment of Drug-Eluting Stent Restenosis: 3-Year Results of a Randomized Controlled Trial. JACC Cardiovasc Interv 2015;**8**(7):877-84.
380. Xu B, Qian J, Ge J, Wang J, Chen F, Chen J, Wei M, Chen Y, Yang Y, Gao R, investigators PCI. Two-year results and subgroup analyses of the PEPCAD China in-stent restenosis trial: A prospective, multicenter, randomized trial for the treatment of drug-eluting stent in-stent restenosis. Catheter Cardiovasc Interv 2016;**87 Suppl 1**:624-9.
381. Byrne RA, Cassese S, Windisch T, King LA, Joner M, Tada T, Mehilli J, Pache J, Kastrati A. Differential relative efficacy between drug-eluting stents in patients with bare metal and drug-eluting stent restenosis; evidence in support of drug resistance: insights from the ISAR-DESIRE and ISAR-DESIRE 2 trials. EuroIntervention 2013;**9**(7):797-802.
382. Zellweger MJ, Kaiser C, Jeger R, Brunner-La Rocca HP, Buser P, Bader F, Mueller-Brand J, Pfisterer M. Coronary artery disease progression late after successful stent implantation. J Am Coll Cardiol 2012;**59**(9):793-9.
383. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, Mehran R, McPherson J, Farhat N, Marso SP, Parise H, Templin B, White R, Zhang Z, Serruys PW, Investigators P. A prospective natural-history study of coronary atherosclerosis. N Engl J Med 2011;**364**(3):226-35.
384. Chechi T, Vecchio S, Vittori G, Giuliani G, Lilli A, Spaziani G, Consoli L, Baldereschi G, Biondi-Zoccai GG, Sheiban I, Margheri M. ST-segment elevation myocardial infarction due to early and late stent thrombosis a new group of high-risk patients. J Am Coll Cardiol 2008;**51**(25):2396-402.
385. Alfonso F, Dutary J, Paulo M, Gonzalo N, Perez-Vizcayno MJ, Jimenez-Quevedo P, Escaned J, Banuelos C, Hernandez R, Macaya C. Combined use of optical coherence tomography and intravascular ultrasound imaging in patients undergoing coronary interventions for stent thrombosis. Heart 2012;**98**(16):1213-20.
386. Adriaenssens T, Joner M, Godschalk TC, Malik N, Alfonso F, Xhepa E, De Cock D, Komukai K, Tada T, Cuesta J, Sirbu V, Feldman LJ, Neumann FJ, Goodall AH, Heestermans T, Buysschaert I, Hlinomaz O, Belmans A, Desmet W, Ten Berg JM, Gershlick AH, Massberg S, Kastrati A, Guagliumi G, Byrne RA, Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort I. Optical Coherence Tomography Findings in Patients With Coronary Stent Thrombosis: A Report of the PRESTIGE Consortium (Prevention of Late Stent Thrombosis by an Interdisciplinary Global European Effort). Circulation 2017;**136**(11):1007-1021.
387. Armstrong EJ, Feldman DN, Wang TY, Kaltenbach LA, Yeo KK, Wong SC, Spertus J, Shaw RE, Minutello RM, Moussa I, Ho KK, Rogers JH, Shunk KA. Clinical presentation, management, and outcomes of angiographically documented early, late, and very late stent thrombosis. JACC Cardiovasc Interv 2012;**5**(2):131-40.
388. Holmes DR, Jr., Davis KB, Mock MB, Fisher LD, Gersh BJ, Killip T, 3rd, Pettinger M. The effect of medical and surgical treatment on subsequent sudden cardiac death in patients with coronary artery disease: a report from the Coronary Artery Surgery Study. Circulation 1986;**73**(6):1254-63.
389. Long-term results of prospective randomised study of coronary artery bypass surgery in stable angina pectoris. European Coronary Surgery Study Group. Lancet 1982;**2**(8309):1173-80.
390. Veenhuyzen GD, Singh SN, McAreavey D, Shelton BJ, Exner DV. Prior coronary artery bypass surgery and risk of death among patients with ischemic left ventricular dysfunction. Circulation 2001;**104**(13):1489-93.
391. Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, Daubert JP, Higgins SL, Brown MW, Andrews ML, Multicenter Automatic Defibrillator Implantation Trial III. Prophylactic

implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;**346**(12):877-83.
392. Al-Khatib SM, Hellkamp AS, Lee KL, Anderson J, Poole JE, Mark DB, Bardy GH, scd-heft i. Implantable cardioverter defibrillator therapy in patients with prior coronary revascularization in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). J Cardiovasc Electrophysiol 2008;**19**(10):1059-65.
393. Sesselberg HW, Moss AJ, McNitt S, Zareba W, Daubert JP, Andrews ML, Hall WJ, McClinitic B, Huang DT, Group M-IR. Ventricular arrhythmia storms in postinfarction patients with implantable defibrillators for primary prevention indications: a MADIT-II substudy. Heart Rhythm 2007;**4**(11):1395-402.
394. Spaulding CM, Joly LM, Rosenberg A, Monchi M, Weber SN, Dhainaut JF, Carli P. Immediate coronary angiography in survivors of out-of-hospital cardiac arrest. N Engl J Med 1997;**336**(23):1629-33.
395. Kern KB. Optimal treatment of patients surviving out-of-hospital cardiac arrest. JACC Cardiovasc Interv 2012;**5**(6):597-605.
396. Garot P, Lefevre T, Eltchaninoff H, Morice MC, Tamion F, Abry B, Lesault PF, Le Tarnec JY, Pouges C, Margenet A, Monchi M, Laurent I, Dumas P, Garot J, Louvard Y. Six-month outcome of emergency percutaneous coronary intervention in resuscitated patients after cardiac arrest complicating ST-elevation myocardial infarction. Circulation 2007;**115**(11):1354-62.
397. Radsel P, Knafelj R, Kocjancic S, Noc M. Angiographic characteristics of coronary disease and postresuscitation electrocardiograms in patients with aborted cardiac arrest outside a hospital. Am J Cardiol 2011;**108**(5):634-8.
398. Anyfantakis ZA, Baron G, Aubry P, Himbert D, Feldman LJ, Juliard JM, Ricard-Hibon A, Burnod A, Cokkinos DV, Steg PG. Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest. Am Heart J 2009;**157**(2):312-8.
399. Dumas F, Cariou A, Manzo-Silberman S, Grimaldi D, Vivien B, Rosencher J, Empana JP, Carli P, Mira JP, Jouven X, Spaulding C. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Interv 2010;**3**(3):200-7.
400. Cronier P, Vignon P, Bouferrache K, Aegerter P, Charron C, Templier F, Castro S, El Mahmoud R, Lory C, Pichon N, Dubourg O, Vieillard-Baron A. Impact of routine percutaneous coronary intervention after out-of-hospital cardiac arrest due to ventricular fibrillation. Crit Care 2011;**15**(3):R122.
401. Geri G, Dumas F, Bougouin W, Varenne O, Daviaud F, Pene F, Lamhaut L, Chiche JD, Spaulding C, Mira JP, Empana JP, Cariou A. Immediate Percutaneous Coronary Intervention Is Associated With Improved Short- and Long-Term Survival After Out-of-Hospital Cardiac Arrest. Circ Cardiovasc Interv 2015;**8**(10).
402. Vyas A, Chan PS, Cram P, Nallamothu BK, McNally B, Girotra S. Early Coronary Angiography and Survival After Out-of-Hospital Cardiac Arrest. Circ Cardiovasc Interv 2015;**8**(10).
403. Noc M, Fajadet J, Lassen JF, Kala P, MacCarthy P, Olivecrona GK, Windecker S, Spaulding C. Invasive Coronary Treatment Strategies for Out-Of-Hospital Cardiac Arrest: A Consensus Statement from the European Association for Percutaneous Cardiovascular Interventions (EAPCI)/Stent for Life (SFL) groups. EuroIntervention 2014.
404. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G, Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;**37**(38):2893-2962.
405. Chan W, Ajani AE, Clark DJ, Stub D, Andrianopoulos N, Brennan AL, New G, Sebastian M, Johnston R, Walton A, Reid CM, Dart AM, Duffy SJ. Impact of periprocedural atrial fibrillation on

short-term clinical outcomes following percutaneous coronary intervention. Am J Cardiol 2012;**109**(4):471-7.
406. Lopes RD, Elliott LE, White HD, Hochman JS, Van de Werf F, Ardissino D, Nielsen TT, Weaver WD, Widimsky P, Armstrong PW, Granger CB. Antithrombotic therapy and outcomes of patients with atrial fibrillation following primary percutaneous coronary intervention: results from the APEX-AMI trial. Eur Heart J 2009;**30**(16):2019-28.
407. Mrdovic I, Savic L, Krljanac G, Perunicic J, Asanin M, Lasica R, Antonijevic N, Kocev N, Marinkovic J, Vasiljevic Z, Ostojic M. Incidence, predictors, and 30-day outcomes of new-onset atrial fibrillation after primary percutaneous coronary intervention: insight into the RISK-PCI trial. Coron Artery Dis 2012;**23**(1):1-8.
408. Pilgrim T, Kalesan B, Zanchin T, Pulver C, Jung S, Mattle H, Carrel T, Moschovitis A, Stortecky S, Wenaweser P, Stefanini GG, Raber L, Meier B, Juni P, Windecker S. Impact of atrial fibrillation on clinical outcomes among patients with coronary artery disease undergoing revascularisation with drug-eluting stents. EuroIntervention 2013;**8**(9):1061-71.
409. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, Juni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann FJ, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2017.
410. Ahlsson AJ, Bodin L, Lundblad OH, Englund AG. Postoperative atrial fibrillation is not correlated to C-reactive protein. Ann Thorac Surg 2007;**83**(4):1332-7.
411. Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, Whitlock RP. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. Cochrane Database Syst Rev 2013;**1**:Cd003611.
412. Mathew JP, Fontes ML, Tudor IC, Ramsay J, Duke P, Mazer CD, Barash PG, Hsu PH, Mangano DT. A multicenter risk index for atrial fibrillation after cardiac surgery. Jama 2004;**291**(14):1720-9.
413. Shen J, Lall S, Zheng V, Buckley P, Damiano RJ, Jr., Schuessler RB. The persistent problem of new-onset postoperative atrial fibrillation: a single-institution experience over two decades. J Thorac Cardiovasc Surg 2011;**141**(2):559-70.
414. LaPar DJ, Speir AM, Crosby IK, Fonner E, Jr., Brown M, Rich JB, Quader M, Kern JA, Kron IL, Ailawadi G. Postoperative atrial fibrillation significantly increases mortality, hospital readmission, and hospital costs. Ann Thorac Surg 2014;**98**(2):527-33; discussion 533.
415. Saxena A, Dinh DT, Smith JA, Shardey GC, Reid CM, Newcomb AE. Usefulness of postoperative atrial fibrillation as an independent predictor for worse early and late outcomes after isolated coronary artery bypass grafting (multicenter Australian study of 19,497 patients). Am J Cardiol 2012;**109**(2):219-25.
416. Steinberg BA, Zhao Y, He X, Hernandez AF, Fullerton DA, Thomas KL, Mills R, Klaskala W, Peterson ED, Piccini JP. Management of postoperative atrial fibrillation and subsequent outcomes in contemporary patients undergoing cardiac surgery: insights from the Society of Thoracic Surgeons CAPS-Care Atrial Fibrillation Registry. Clin Cardiol 2014;**37**(1):7-13.
417. Ahlsson A, Bodin L, Fengsrud E, Englund A. Patients with postoperative atrial fibrillation have a doubled cardiovascular mortality. Scandinavian Cardiovascular Journal 2009:1-7.
418. Ahlsson A, Fengsrud E, Bodin L, Englund A. Postoperative atrial fibrillation in patients undergoing aortocoronary bypass surgery carries an eightfold risk of future atrial fibrillation and a doubled cardiovascular mortality. European Journal of Cardio-Thoracic Surgery 2010;**37**(6):1353-9.
419. Gialdini G, Nearing K, Bhave PD, Bonuccelli U, Iadecola C, Healey JS, Kamel H. Perioperative atrial fibrillation and the long-term risk of ischemic stroke. Jama 2014;**312**(6):616-22.
420. Mariscalco G, Klersy C, Zanobini M, Banach M, Ferrarese S, Borsani P, Cantore C, Biglioli P, Sala A. Atrial fibrillation after isolated coronary surgery affects late survival. Circulation 2008;**118**(16):1612-8.

421. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, Lopez JA, Rasekh A, Wilson JM, Massumi A. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004;**43**(5):742-8.
422. Burgess DC, Kilborn MJ, Keech AC. Interventions for prevention of post-operative atrial fibrillation and its complications after cardiac surgery: a meta-analysis. Eur Heart J 2006;**27**(23):2846-57.
423. Connolly SJ, Cybulsky I, Lamy A, Roberts RS, O'Brien B, Carroll S, Crystal E, Thorpe KE, Gent M. Double-blind, placebo-controlled, randomized trial of prophylactic metoprolol for reduction of hospital length of stay after heart surgery: the beta-Blocker Length Of Stay (BLOS) study. Am Heart J 2003;**145**(2):226-32.
424. Crystal E, Connolly SJ, Sleik K, Ginger TJ, Yusuf S. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. Circulation 2002;**106**(1):75-80.
425. Dunning J, Treasure T, Versteegh M, Nashef SA. Guidelines on the prevention and management of de novo atrial fibrillation after cardiac and thoracic surgery. Eur J Cardiothorac Surg 2006;**30**(6):852-72.
426. Koniari I, Apostolakis E, Rogkakou C, Baikoussis NG, Dougenis D. Pharmacologic prophylaxis for atrial fibrillation following cardiac surgery: a systematic review. J Cardiothorac Surg 2010;**5**:121.
427. Lucio Ede A, Flores A, Blacher C, Leaes PE, Lucchese FA, Ribeiro JP. Effectiveness of metoprolol in preventing atrial fibrillation and flutter in the postoperative period of coronary artery bypass graft surgery. Arq Bras Cardiol 2004;**82**(1):42-46, 37-41.
428. Tsuboi J, Kawazoe K, Izumoto H, Okabayashi H. Postoperative treatment with carvedilol, a beta-adrenergic blocker, prevents paroxysmal atrial fibrillation after coronary artery bypass grafting. Circ J 2008;**72**(4):588-91.
429. Anderson E, Dyke C, Levy JH. Anticoagulation strategies for the management of postoperative atrial fibrillation. Clin Lab Med 2014;**34**(3):537-61.
430. El-Chami MF, Kilgo P, Thourani V, Lattouf OM, Delurgio DB, Guyton RA, Leon AR, Puskas JD. New-onset atrial fibrillation predicts long-term mortality after coronary artery bypass graft. J Am Coll Cardiol 2010;**55**(13):1370-6.
431. Melduni RM, Schaff HV, Lee HC, Gersh BJ, Noseworthy PA, Bailey KR, Ammash NM, Cha SS, Fatema K, Wysokinski WE, Seward JB, Packer DL, Rihal CS, Asirvatham SJ. Impact of Left Atrial Appendage Closure During Cardiac Surgery on the Occurrence of Early Postoperative Atrial Fibrillation, Stroke, and Mortality: A Propensity Score-Matched Analysis of 10 633 Patients. Circulation 2017;**135**(4):366-378.
432. Tsai YC, Phan K, Munkholm-Larsen S, Tian DH, La Meir M, Yan TD. Surgical left atrial appendage occlusion during cardiac surgery for patients with atrial fibrillation: a meta-analysis. Eur J Cardiothorac Surg 2015;**47**(5):847-54.
433. Friedman DJ, Piccini JP, Wang T, Zheng J, Malaisrie SC, Holmes DR, Suri RM, Mack MJ, Badhwar V, Jacobs JP, Gaca JG, Chow SC, Peterson ED, Brennan JM. Association Between Left Atrial Appendage Occlusion and Readmission for Thromboembolism Among Patients With Atrial Fibrillation Undergoing Concomitant Cardiac Surgery. JAMA 2018;**319**(4):365-374.
434. Whitlock R, Healey J, Vincent J, Brady K, Teoh K, Royse A, Shah P, Guo Y, Alings M, Folkeringa RJ, Paparella D, Colli A, Meyer SR, Legare JF, Lamontagne F, Reents W, Boning A, Connolly S. Rationale and design of the Left Atrial Appendage Occlusion Study (LAAOS) III. Ann Cardiothorac Surg 2014;**3**(1):45-54.
435. Kern KB, Rahman O. Emergent percutaneous coronary intervention for resuscitated victims of out-of-hospital cardiac arrest. Catheter Cardiovasc Interv 2010;**75**(4):616-24.
436. Garcia-Tejada J, Jurado-Roman A, Rodriguez J, Velazquez M, Hernandez F, Albarran A, Martin-Asenjo R, Granda-Nistal C, Coma R, Tascon J. Post-resuscitation electrocardiograms, acute coronary findings and in-hospital prognosis of survivors of out-of-hospital cardiac arrest. Resuscitation 2014;**85**(9):1245-50.

437. Khan MF, Wendel CS, Movahed MR. Prevention of post-coronary artery bypass grafting (CABG) atrial fibrillation: efficacy of prophylactic beta-blockers in the modern era: a meta-analysis of latest randomized controlled trials. Ann Noninvasive Electrocardiol 2013;**18**(1):58-68.
438. Chatterjee S, Sardar P, Mukherjee D, Lichstein E, Aikat S. Timing and route of amiodarone for prevention of postoperative atrial fibrillation after cardiac surgery: a network regression meta-analysis. Pacing Clin Electrophysiol 2013;**36**(8):1017-23.
439. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J 2012;**33**(12):1500-10.
440. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;**137**(2):263-72.
441. Gillinov AM, Bagiella E, Moskowitz AJ, Raiten JM, Groh MA, Bowdish ME, Ailawadi G, Kirkwood KA, Perrault LP, Parides MK, Smith RL, 2nd, Kern JA, Dussault G, Hackmann AE, Jeffries NO, Miller MA, Taddei-Peters WC, Rose EA, Weisel RD, Williams DL, Mangusan RF, Argenziano M, Moquete EG, O'Sullivan KL, Pellerin M, Shah KJ, Gammie JS, Mayer ML, Voisine P, Gelijns AC, O'Gara PT, Mack MJ. Rate Control versus Rhythm Control for Atrial Fibrillation after Cardiac Surgery. N Engl J Med 2016;**374**(20):1911-21.
442. Head SJ, Milojevic M, Taggart DP, Puskas JD. Current Practice of State-of-the-Art Surgical Coronary Revascularization. Circulation 2017;**136**(14):1331-1345.
443. Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic S, the European Association of Cardiothoracic A, Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, von Heymann C, Jeppsson A, Koster A, Osnabrugge RL, Ranucci M, Ravn HB, Vonk ABA, Wahba A, Pagano D, Wyler von Ballmoos MWV, Petricevic M, Kappetein AP, Sousa-Uva M, Trummer G, Rosseel PM, Sander M, Colson P, Bauer A. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth 2017.
444. Head SJ, Mack MJ, Holmes DR, Jr., Mohr FW, Morice MC, Serruys PW, Kappetein AP. Incidence, predictors and outcomes of incomplete revascularization after percutaneous coronary intervention and coronary artery bypass grafting: a subgroup analysis of 3-year SYNTAX data. Eur J Cardiothorac Surg 2012;**41**(3):535-41.
445. Kim YH, Park DW, Lee JY, Kim WJ, Yun SC, Ahn JM, Song HG, Oh JH, Park JS, Kang SJ, Lee SW, Lee CW, Park SW, Park SJ. Impact of angiographic complete revascularization after drug-eluting stent implantation or coronary artery bypass graft surgery for multivessel coronary artery disease. Circulation 2011;**123**(21):2373-81.
446. Mohammadi S, Kalavrouziotis D, Dagenais F, Voisine P, Charbonneau E. Completeness of revascularization and survival among octogenarians with triple-vessel disease. Ann Thorac Surg 2012;**93**(5):1432-7.
447. Rastan AJ, Walther T, Falk V, Kempfert J, Merk D, Lehmann S, Holzhey D, Mohr FW. Does reasonable incomplete surgical revascularization affect early or long-term survival in patients with multivessel coronary artery disease receiving left internal mammary artery bypass to left anterior descending artery? Circulation 2009;**120**(11 Suppl):S70-7.
448. Yi G, Youn YN, Joo HC, Hong S, Yoo KJ. Association of incomplete revascularization with long-term survival after off-pump coronary artery bypass grafting. J Surg Res 2013;**185**(1):166-73.
449. Scott R, Blackstone EH, McCarthy PM, Lytle BW, Loop FD, White JA, Cosgrove DM. Isolated bypass grafting of the left internal thoracic artery to the left anterior descending coronary artery: late consequences of incomplete revascularization. J Thorac Cardiovasc Surg 2000;**120**(1):173-84.
450. Melby SJ, Saint LL, Balsara K, Itoh A, Lawton JS, Maniar H, Pasque MK, Damiano RJ, Jr., Moon MR. Complete Coronary Revascularization Improves Survival in Octogenarians. Ann Thorac Surg 2016;**102**(2):505-11.
451. Botman CJ, Schonberger J, Koolen S, Penn O, Botman H, Dib N, Eeckhout E, Pijls N. Does stenosis severity of native vessels influence bypass graft patency? A prospective fractional flow reserve-guided study. Ann Thorac Surg 2007;**83**(6):2093-7.

452. Boylan MJ, Lytle BW, Loop FD, Taylor PC, Borsh JA, Goormastic M, Cosgrove DM. Surgical treatment of isolated left anterior descending coronary stenosis. Comparison of left internal mammary artery and venous autograft at 18 to 20 years of follow-up. J Thorac Cardiovasc Surg 1994;**107**(3):657-62.
453. Sabik JF, 3rd, Blackstone EH, Gillinov AM, Banbury MK, Smedira NG, Lytle BW. Influence of patient characteristics and arterial grafts on freedom from coronary reoperation. J Thorac Cardiovasc Surg 2006;**131**(1):90-8.
454. Schmitto JD, Rajab TK, Cohn LH. Prevalence and variability of internal mammary graft use in contemporary multivessel coronary artery bypass graft. Curr Opin Cardiol 2010;**25**(6):609-12.
455. Hess CN, Lopes RD, Gibson CM, Hager R, Wojdyla DM, Englum BR, Mack MJ, Califf RM, Kouchoukos NT, Peterson ED, Alexander JH. Saphenous vein graft failure after coronary artery bypass surgery: insights from PREVENT IV. Circulation 2014;**130**(17):1445-51.
456. Benedetto U, Raja SG, Albanese A, Amrani M, Biondi-Zoccai G, Frati G. Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trialsdagger. Eur J Cardiothorac Surg 2015;**47**(1):59-65; discussion 65.
457. Dorman MJ, Kurlansky PA, Traad EA, Galbut DL, Zucker M, Ebra G. Bilateral internal mammary artery grafting enhances survival in diabetic patients: a 30-year follow-up of propensity score-matched cohorts. Circulation 2012;**126**(25):2935-42.
458. Galbut DL, Kurlansky PA, Traad EA, Dorman MJ, Zucker M, Ebra G. Bilateral internal thoracic artery grafting improves long-term survival in patients with reduced ejection fraction: a propensity-matched study with 30-year follow-up. J Thorac Cardiovasc Surg 2012;**143**(4):844-853.e4.
459. Grau JB, Ferrari G, Mak AW, Shaw RE, Brizzio ME, Mindich BP, Strobeck J, Zapolanski A. Propensity matched analysis of bilateral internal mammary artery versus single left internal mammary artery grafting at 17-year follow-up: validation of a contemporary surgical experience. Eur J Cardiothorac Surg 2012;**41**(4):770-5; discussion 776.
460. Kurlansky PA, Traad EA, Dorman MJ, Galbut DL, Zucker M, Ebra G. Thirty-year follow-up defines survival benefit for second internal mammary artery in propensity-matched groups. Ann Thorac Surg 2010;**90**(1):101-8.
461. Lytle BW. Bilateral internal thoracic artery grafting. Ann Cardiothorac Surg 2013;**2**(4):485-92.
462. Ruttmann E, Fischler N, Sakic A, Chevtchik O, Alber H, Schistek R, Ulmer H, Grimm M. Second internal thoracic artery versus radial artery in coronary artery bypass grafting: a long-term, propensity score-matched follow-up study. Circulation 2011;**124**(12):1321-9.
463. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. Lancet 2001;**358**(9285):870-5.
464. Weiss AJ, Zhao S, Tian DH, Taggart DP, Yan TD. A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting. Ann Cardiothorac Surg 2013;**2**(4):390-400.
465. Gaudino M, Di Franco A, Rahouma M, Tam DY, Iannaccone M, Deb S, D'Ascenzo F, Abouarab AA, Girardi LN, Taggart DP, Fremes SE. Unmeasured Confounders in Observational Studies Comparing Bilateral Versus Single Internal Thoracic Artery for Coronary Artery Bypass Grafting: A Meta-Analysis. J Am Heart Assoc 2018;**7**(1).
466. Taggart DP, Altman DG, Gray AM, Lees B, Gerry S, Benedetto U, Flather M. Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2016.
467. Gaudino M, Tranbaugh R, Fremes S. Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2017;**376**(18):e37.
468. Raza S, Blackstone EH, Sabik JF, III. Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2017;**376**(18):e37.
469. Royse A, Eccleston D, Royse C, i GC. Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2017;**376**(18):e37.
470. Deo SV, Shah IK, Dunlay SM, Erwin PJ, Locker C, Altarabsheh SE, Boilson BA, Park SJ, Joyce LD. Bilateral internal thoracic artery harvest and deep sternal wound infection in diabetic patients. Ann Thorac Surg 2013;**95**(3):862-9.

471. Elmistekawy EM, Gawad N, Bourke M, Mesana T, Boodhwani M, Rubens FD. Is bilateral internal thoracic artery use safe in the elderly? J Card Surg 2012;**27**(1):1-5.
472. Hemo E, Mohr R, Uretzky G, Katz G, Popovits N, Pevni D, Medalion B. Long-term outcomes of patients with diabetes receiving bilateral internal thoracic artery grafts. J Thorac Cardiovasc Surg 2013;**146**(3):586-92.
473. Taggart DP, Lees B, Gray A, Altman DG, Flather M, Channon K. Protocol for the Arterial Revascularisation Trial (ART). A randomised trial to compare survival following bilateral versus single internal mammary grafting in coronary revascularisation [ISRCTN46552265]. Trials 2006;**7**:7.
474. Toumpoulis IK, Theakos N, Dunning J. Does bilateral internal thoracic artery harvest increase the risk of mediastinitis? Interact Cardiovasc Thorac Surg 2007;**6**(6):787-91.
475. Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R, Flather M, Taggart DP, Arterial Revascularization Trial i. Pedicled and skeletonized single and bilateral internal thoracic artery grafts and the incidence of sternal wound complications: Insights from the Arterial Revascularization Trial. J Thorac Cardiovasc Surg 2016;**152**(1):270-6.
476. Hayward PA, Gordon IR, Hare DL, Matalanis G, Horrigan ML, Rosalion A, Buxton BF. Comparable patencies of the radial artery and right internal thoracic artery or saphenous vein beyond 5 years: results from the Radial Artery Patency and Clinical Outcomes trial. J Thorac Cardiovasc Surg 2010;**139**(1):60-5; discussion 65-7.
477. Schwann TA, Engoren M, Bonnell M, Clancy C, Habib RH. Comparison of late coronary artery bypass graft survival effects of radial artery versus saphenous vein grafting in male and female patients. Ann Thorac Surg 2012;**94**(5):1485-91.
478. Tranbaugh RF, Dimitrova KR, Friedmann P, Geller CM, Harris LJ, Stelzer P, Cohen B, Hoffman DM. Radial artery conduits improve long-term survival after coronary artery bypass grafting. Ann Thorac Surg 2010;**90**(4):1165-72.
479. Tranbaugh RF, Dimitrova KR, Friedmann P, Geller CM, Harris LJ, Stelzer P, Cohen BM, Ko W, DeCastro H, Lucido D, Hoffman DM. Coronary artery bypass grafting using the radial artery: clinical outcomes, patency, and need for reintervention. Circulation 2012;**126**(11 Suppl 1):S170-5.
480. Cao C, Manganas C, Horton M, Bannon P, Munkholm-Larsen S, Ang SC, Yan TD. Angiographic outcomes of radial artery versus saphenous vein in coronary artery bypass graft surgery: a meta-analysis of randomized controlled trials. J Thorac Cardiovasc Surg 2013;**146**(2):255-61.
481. Gaudino M. Radial artery versus saphenous vein in coronary artery bypass surgery. N Engl J Med 2018.
482. Lytle BW. Skeletonized internal thoracic artery grafts and wound complications. J Thorac Cardiovasc Surg 2001;**121**(4):625-7.
483. Sa MP, Ferraz PE, Escobar RR, Vasconcelos FP, Ferraz AA, Braile DM, Lima RC. Skeletonized versus pedicled internal thoracic artery and risk of sternal wound infection after coronary bypass surgery: meta-analysis and meta-regression of 4817 patients. Interact Cardiovasc Thorac Surg 2013;**16**(6):849-57.
484. Sakic A, Chevtchik O, Kilo J, Schistek R, Mueller LC, Ulmer H, Grimm M, Ruttmann E. Simple adaptations of surgical technique to critically reduce the risk of postoperative sternal complications in patients receiving bilateral internal thoracic arteries. Interact Cardiovasc Thorac Surg 2013;**17**(2):378-82.
485. Wendler O, Hennen B, Markwirth T, Konig J, Tscholl D, Huang Q, Shahangi E, Schafers HJ. T grafts with the right internal thoracic artery to left internal thoracic artery versus the left internal thoracic artery and radial artery: flow dynamics in the internal thoracic artery main stem. J Thorac Cardiovasc Surg 1999;**118**(5):841-8.
486. Kajimoto K, Yamamoto T, Amano A. Coronary artery bypass revascularization using bilateral internal thoracic arteries in diabetic patients: a systematic review and meta-analysis. Ann Thorac Surg 2015;**99**(3):1097-104.
487. Sa MP, Cavalcanti PE, Santos HJ, Soares AF, Miranda RG, Araujo ML, Lima RC. Flow capacity of skeletonized versus pedicled internal thoracic artery in coronary artery bypass graft surgery: systematic review, meta-analysis and meta-regression. Eur J Cardiothorac Surg 2015;**48**(1):25-31.

488. Navia JL, Olivares G, Ehasz P, Gillinov AM, Svensson LG, Brozzi N, Lytle B. Endoscopic radial artery harvesting procedure for coronary artery bypass grafting. Ann Cardiothorac Surg 2013;**2**(4):557-64.
489. Cao C, Tian DH, Ang SC, Peeceeyen S, Allan J, Fu B, Yan TD. A meta-analysis of endoscopic versus conventional open radial artery harvesting for coronary artery bypass graft surgery. Innovations (Phila) 2014;**9**(4):269-75.
490. Gaudino M, Leone A, Lupascu A, Toesca A, Mazza A, Ponziani FR, Flore R, Tondi P, Massetti M. Morphological and functional consequences of transradial coronary angiography on the radial artery: implications for its use as a bypass conduit. Eur J Cardiothorac Surg 2015;**48**(3):370-4.
491. Ouzounian M, Hassan A, Buth KJ, MacPherson C, Ali IM, Hirsch GM, Ali IS. Impact of endoscopic versus open saphenous vein harvest techniques on outcomes after coronary artery bypass grafting. Ann Thorac Surg 2010;**89**(2):403-8.
492. Yun KL, Wu Y, Aharonian V, Mansukhani P, Pfeffer TA, Sintek CF, Kochamba GS, Grunkemeier G, Khonsari S. Randomized trial of endoscopic versus open vein harvest for coronary artery bypass grafting: six-month patency rates. J Thorac Cardiovasc Surg 2005;**129**(3):496-503.
493. Chernyavskiy A, Volkov A, Lavrenyuk O, Terekhov I, Kareva Y. Comparative results of endoscopic and open methods of vein harvesting for coronary artery bypass grafting: a prospective randomized parallel-group trial. J Cardiothorac Surg 2015;**10**:163.
494. Krishnamoorthy B, Critchley WR, Glover AT, Nair J, Jones MT, Waterworth PD, Fildes JE, Yonan N. A randomized study comparing three groups of vein harvesting methods for coronary artery bypass grafting: endoscopic harvest versus standard bridging and open techniques. Interact Cardiovasc Thorac Surg 2012;**15**(2):224-8.
495. Lopes RD, Hafley GE, Allen KB, Ferguson TB, Peterson ED, Harrington RA, Mehta RH, Gibson CM, Mack MJ, Kouchoukos NT, Califf RM, Alexander JH. Endoscopic versus open vein-graft harvesting in coronary-artery bypass surgery. N Engl J Med 2009;**361**(3):235-44.
496. Zenati MA, Shroyer AL, Collins JF, Hattler B, Ota T, Almassi GH, Amidi M, Novitzky D, Grover FL, Sonel AF. Impact of endoscopic versus open saphenous vein harvest technique on late coronary artery bypass grafting patient outcomes in the ROOBY (Randomized On/Off Bypass) Trial. J Thorac Cardiovasc Surg 2011;**141**(2):338-44.
497. Andreasen JJ, Vadmann H, Oddershede L, Tilsted HH, Frokjaer JB, Jensen SE. Decreased patency rates following endoscopic vein harvest in coronary artery bypass surgery. Scand Cardiovasc J 2015;**49**(5):286-92.
498. Deppe AC, Liakopoulos OJ, Choi YH, Slottosch I, Kuhn EW, Scherner M, Stange S, Wahlers T. Endoscopic vein harvesting for coronary artery bypass grafting: a systematic review with meta-analysis of 27,789 patients. J Surg Res 2013;**180**(1):114-24.
499. Williams JB, Peterson ED, Brennan JM, Sedrakyan A, Tavris D, Alexander JH, Lopes RD, Dokholyan RS, Zhao Y, O'Brien SM, Michler RE, Thourani VH, Edwards FH, Duggirala H, Gross T, Marinac-Dabic D, Smith PK. Association between endoscopic vs open vein-graft harvesting and mortality, wound complications, and cardiovascular events in patients undergoing CABG surgery. JAMA 2012;**308**(5):475-84.
500. Brown EN, Kon ZN, Tran R, Burris NS, Gu J, Laird P, Brazio PS, Kallam S, Schwartz K, Bechtel L, Joshi A, Zhang S, Poston RS. Strategies to reduce intraluminal clot formation in endoscopically harvested saphenous veins. J Thorac Cardiovasc Surg 2007;**134**(5):1259-65.
501. Khaleel MS, Dorheim TA, Duryee MJ, Durbin HE, Jr., Bussey WD, Garvin RP, Klassen LW, Thiele GM, Anderson DR. High-pressure distention of the saphenous vein during preparation results in increased markers of inflammation: a potential mechanism for graft failure. Ann Thorac Surg 2012;**93**(2):552-8.
502. Rousou LJ, Taylor KB, Lu XG, Healey N, Crittenden MD, Khuri SF, Thatte HS. Saphenous vein conduits harvested by endoscopic technique exhibit structural and functional damage. Ann Thorac Surg 2009;**87**(1):62-70.
503. Johansson BL, Souza DS, Bodin L, Filbey D, Loesch A, Geijer H, Bojo L. Slower progression of atherosclerosis in vein grafts harvested with 'no touch' technique compared with conventional

harvesting technique in coronary artery bypass grafting: an angiographic and intravascular ultrasound study. Eur J Cardiothorac Surg 2010;**38**(4):414-9.
504. Souza DS, Dashwood MR, Tsui JC, Filbey D, Bodin L, Johansson B, Borowiec J. Improved patency in vein grafts harvested with surrounding tissue: results of a randomized study using three harvesting techniques. Ann Thorac Surg 2002;**73**(4):1189-95.
505. Dreifaldt M, Mannion JD, Bodin L, Olsson H, Zagozdzon L, Souza D. The no-touch saphenous vein as the preferred second conduit for coronary artery bypass grafting. Ann Thorac Surg 2013;**96**(1):105-11.
506. Samano N, Geijer H, Liden M, Fremes S, Bodin L, Souza D. The no-touch saphenous vein for coronary artery bypass grafting maintains a patency, after 16 years, comparable to the left internal thoracic artery: A randomized trial. J Thorac Cardiovasc Surg 2015;**150**(4):880-8.
507. Emmert MY, Seifert B, Wilhelm M, Grunenfelder J, Falk V, Salzberg SP. Aortic no-touch technique makes the difference in off-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg 2011;**142**(6):1499-506.
508. Borgermann J, Hakim K, Renner A, Parsa A, Aboud A, Becker T, Masshoff M, Zittermann A, Gummert JF, Kuss O. Clampless off-pump versus conventional coronary artery revascularization: a propensity score analysis of 788 patients. Circulation 2012;**126**(11 Suppl 1):S176-82.
509. Misfeld M, Brereton RJ, Sweetman EA, Doig GS. Neurologic complications after off-pump coronary artery bypass grafting with and without aortic manipulation: meta-analysis of 11,398 cases from 8 studies. J Thorac Cardiovasc Surg 2011;**142**(2):e11-7.
510. Wolf LG, Abu-Omar Y, Choudhary BP, Pigott D, Taggart DP. Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: The effect of an aortic side-biting clamp and two clampless devices. Journal of Thoracic and Cardiovascular Surgery 2007;**133**(2):485-493.
511. El Zayat H, Puskas JD, Hwang S, Thourani VH, Lattouf OM, Kilgo P, Halkos ME. Avoiding the clamp during off-pump coronary artery bypass reduces cerebral embolic events: results of a prospective randomized trial. Interactive Cardiovascular and Thoracic Surgery 2012;**14**(1):12-16.
512. Kieser TM, Rose S, Kowalewski R, Belenkie I. Transit-time flow predicts outcomes in coronary artery bypass graft patients: a series of 1000 consecutive arterial grafts. Eur J Cardiothorac Surg 2010;**38**(2):155-62.
513. Mujanovic E, Kabil E, Bergsland J. Transit time flowmetry in coronary surgery--an important tool in graft verification. Bosn J Basic Med Sci 2007;**7**(3):275-8.
514. Jokinen JJ, Werkkala K, Vainikka T, Perakyla T, Simpanen J, Ihlberg L. Clinical value of intra-operative transit-time flow measurement for coronary artery bypass grafting: a prospective angiography-controlled study. Eur J Cardiothorac Surg 2011;**39**(6):918-23.
515. Lehnert P, Moller CH, Damgaard S, Gerds TA, Steinbruchel DA. Transit-time flow measurement as a predictor of coronary bypass graft failure at one year angiographic follow-up. J Card Surg 2015;**30**(1):47-52.
516. Niclauss L. Techniques and standards in intraoperative graft verification by transit time flow measurement after coronary artery bypass graft surgery: a critical review. Eur J Cardiothorac Surg 2016.
517. Diegeler A, Borgermann J, Kappert U, Breuer M, Boning A, Ursulescu A, Rastan A, Holzhey D, Treede H, Riess FC, Veeckmann P, Asfoor A, Reents W, Zacher M, Hilker M. Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. N Engl J Med 2013;**368**(13):1189-98.
518. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaijyanath P, Reddy S, Tao L, Olavegogeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Ng J, Chrolavicius S, Yusuf S. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med 2012;**366**(16):1489-97.
519. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaijyanath P, Reddy SK, Tao L, Olavegogeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Pogue J, Chrolavicius S, Yusuf S. Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year. N Engl J Med 2013;**368**(13):1179-88.

520. Hattler B, Messenger JC, Shroyer AL, Collins JF, Haugen SJ, Garcia JA, Baltz JH, Cleveland JC, Jr., Novitzky D, Grover FL. Off-Pump coronary artery bypass surgery is associated with worse arterial and saphenous vein graft patency and less effective revascularization: Results from the Veterans Affairs Randomized On/Off Bypass (ROOBY) trial. Circulation 2012;**125**(23):2827-35.
521. Houlind K, Kjeldsen BJ, Madsen SN, Rasmussen BS, Holme SJ, Nielsen PH, Mortensen PE. On-pump versus off-pump coronary artery bypass surgery in elderly patients: results from the Danish on-pump versus off-pump randomization study. Circulation 2012;**125**(20):2431-9.
522. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D. On-pump versus off-pump coronary-artery bypass surgery. N Engl J Med 2009;**361**(19):1827-37.
523. Keeling WB, Kilgo PD, Puskas JD, Halkos ME, Lattouf OM, Guyton RA, Thourani VH. Off-pump coronary artery bypass grafting attenuates morbidity and mortality for patients with low and high body mass index. J Thorac Cardiovasc Surg 2013;**146**(6):1442-8.
524. Puskas JD, Thourani VH, Kilgo P, Cooper W, Vassiliades T, Vega JD, Morris C, Chen E, Schmotzer BJ, Guyton RA, Lattouf OM. Off-pump coronary artery bypass disproportionately benefits high-risk patients. Ann Thorac Surg 2009;**88**(4):1142-7.
525. Puskas JD, Williams WH, O'Donnell R, Patterson RE, Sigman SR, Smith AS, Baio KT, Kilgo PD, Guyton RA. Off-pump and on-pump coronary artery bypass grafting are associated with similar graft patency, myocardial ischemia, and freedom from reintervention: long-term follow-up of a randomized trial. Ann Thorac Surg 2011;**91**(6):1836-42; discussion 1842-3.
526. Sedrakyan A, Wu AW, Parashar A, Bass EB, Treasure T. Off-pump surgery is associated with reduced occurrence of stroke and other morbidity as compared with traditional coronary artery bypass grafting: a meta-analysis of systematically reviewed trials. Stroke 2006;**37**(11):2759-69.
527. Altarabsheh SE, Deo SV, Rababa'h AM, Lim JY, Cho YH, Sharma V, Jung SH, Shin E, Markowitz AH, Park SJ. Off-pump coronary artery bypass reduces early stroke in octogenarians: a meta-analysis of 18,000 patients. Ann Thorac Surg 2015;**99**(5):1568-75.
528. Chawla LS, Zhao Y, Lough FC, Schroeder E, Seneff MG, Brennan JM. Off-pump versus on-pump coronary artery bypass grafting outcomes stratified by preoperative renal function. J Am Soc Nephrol 2012;**23**(8):1389-97.
529. Head SJ, Borgermann J, Osnabrugge RL, Kieser TM, Falk V, Taggart DP, Puskas JD, Gummert JF, Kappetein AP. Coronary artery bypass grafting: Part 2--optimizing outcomes and future prospects. Eur Heart J 2013;**34**(37):2873-86.
530. Diegeler A, Walther T, Metz S, Falk V, Krakor R, Autschbach R, Mohr FW. Comparison of MIDCAP versus conventional CABG surgery regarding pain and quality of life. Heart Surg Forum 1999;**2**(4):290-5; discussion 295-6.
531. Groh MA, Sutherland SE, Burton HG, 3rd, Johnson AM, Ely SW. Port-access coronary artery bypass grafting: technique and comparative results. Ann Thorac Surg 1999;**68**(4):1506-8.
532. Lapierre H, Chan V, Sohmer B, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting via a small thoracotomy versus off-pump: a case-matched study. Eur J Cardiothorac Surg 2011;**40**(4):804-10.
533. Deppe AC, Liakopoulos OJ, Kuhn EW, Slottosch I, Scherner M, Choi YH, Rahmanian PB, Wahlers T. Minimally invasive direct coronary bypass grafting versus percutaneous coronary intervention for single-vessel disease: a meta-analysis of 2885 patients. Eur J Cardiothorac Surg 2015;**47**(3):397-406; discussion 406.
534. Wang XW, Qu C, Huang C, Xiang XY, Lu ZQ. Minimally invasive direct coronary bypass compared with percutaneous coronary intervention for left anterior descending artery disease: a meta-analysis. J Cardiothorac Surg 2016;**11**(1):125.
535. Gasior M, Zembala MO, Tajstra M, Filipiak K, Gierlotka M, Hrapkowicz T, Hawranek M, Polonski L, Zembala M, Investigato P-MHS. Hybrid Revascularization for Multivessel Coronary Artery Disease. Jacc-Cardiovascular Interventions 2014;**7**(11):1277-1283.
536. Bonatti JO, Zimrin D, Lehr EJ, Vesely M, Kon ZN, Wehman B, de Biasi AR, Hofauer B, Weidinger F, Schachner T, Bonaros N, Friedrich G. Hybrid coronary revascularization using robotic

totally endoscopic surgery: perioperative outcomes and 5-year results. Ann Thorac Surg 2012;**94**(6):1920-6; discussion 1926.
537. Shen L, Hu S, Wang H, Xiong H, Zheng Z, Li L, Xu B, Yan H, Gao R. One-stop hybrid coronary revascularization versus coronary artery bypass grafting and percutaneous coronary intervention for the treatment of multivessel coronary artery disease: 3-year follow-up results from a single institution. J Am Coll Cardiol 2013;**61**(25):2525-33.
538. Harskamp RE, Bonatti JO, Zhao DX, Puskas JD, de Winter RJ, Alexander JH, Halkos ME. Standardizing definitions for hybrid coronary revascularization. J Thorac Cardiovasc Surg 2014;**147**(2):556-60.
539. Zembala M, Tajstra M, Filipiak K, Knapik P, Hrapkowicz T, Gierlotka M, Hawranek M, Polonski L, Gasior M. Prospective randomised pilOt study evaLuating the safety and efficacy of hybrid revascularisation in MultI-vessel coronary artery DisEaSe (POLMIDES) - study design. Kardiol Pol 2011;**69**(5):460-6.
540. Zembala M. Hybrid Revascularization for Multivessel Coronary Artery Disease: 5-year results [in press]. JACC Cardiovasc Interv 2018.
541. Panoulas VF, Colombo A, Margonato A, Maisano F. Hybrid coronary revascularization: promising, but yet to take off. J Am Coll Cardiol 2015;**65**(1):85-97.
542. Siregar S, Groenwold RH, de Mol BA, Speekenbrink RG, Versteegh MI, Brandon Bravo Bruinsma GJ, Bots ML, van der Graaf Y, van Herwerden LA. Evaluation of cardiac surgery mortality rates: 30-day mortality or longer follow-up? Eur J Cardiothorac Surg 2013;**44**(5):875-83.
543. Zhao DF, Edelman JJ, Seco M, Bannon PG, Wilson MK, Byrom MJ, Thourani V, Lamy A, Taggart DP, Puskas JD, Vallely MP. Coronary Artery Bypass Grafting With and Without Manipulation of the Ascending Aorta: A Network Meta-Analysis. J Am Coll Cardiol 2017;**69**(8):924-936.
544. Moss E, Puskas JD, Thourani VH, Kilgo P, Chen EP, Leshnower BG, Lattouf OM, Guyton RA, Glas KE, Halkos ME. Avoiding aortic clamping during coronary artery bypass grafting reduces postoperative stroke. J Thorac Cardiovasc Surg 2015;**149**(1):175-80.
545. Hlatky MA, Boothroyd DB, Reitz BA, Shilane DA, Baker LC, Go AS. Adoption and effectiveness of internal mammary artery grafting in coronary artery bypass surgery among Medicare beneficiaries. J Am Coll Cardiol 2014;**63**(1):33-9.
546. Kieser TM, Lewin AM, Graham MM, Martin BJ, Galbraith PD, Rabi DM, Norris CM, Faris PD, Knudtson ML, Ghali WA, Investigators A. Outcomes associated with bilateral internal thoracic artery grafting: the importance of age. Ann Thorac Surg 2011;**92**(4):1269-75; discussion 1275-6.
547. Yi G, Shine B, Rehman SM, Altman DG, Taggart DP. Effect of bilateral internal mammary artery grafts on long-term survival: a meta-analysis approach. Circulation 2014;**130**(7):539-45.
548. Taggart DP, Altman DG, Flather M, Gerry S, Gray A, Lees B, Benedetto U, Investigators ART. Associations Between Adding a Radial Artery Graft to Single and Bilateral Internal Thoracic Artery Grafts and Outcomes: Insights From the Arterial Revascularization Trial. Circulation 2017;**136**(5):454-463.
549. Yamasaki M, Deb S, Tsubota H, Moussa F, Kiss A, Cohen EA, Radhakrishnan S, Dubbin J, Ko D, Schwartz L, Fremes SE, Radial Artery Patency Study I. Comparison of Radial Artery and Saphenous Vein Graft Stenosis More Than 5 Years After Coronary Artery Bypass Grafting. Ann Thorac Surg 2016;**102**(3):712-719.
550. Taggart DP, Altman DG, Gray AM, Lees B, Gerry S, Benedetto U, Flather M, Investigators ART. Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med 2016;**375**(26):2540-9.
551. Benedetto U, Amrani M, Raja SG, Harefield Cardiac Outcomes Research G. Guidance for the use of bilateral internal thoracic arteries according to survival benefit across age groups. J Thorac Cardiovasc Surg 2014;**148**(6):2706-11.
552. Pu A, Ding L, Shin J, Price J, Skarsgard P, Wong DR, Bozinovski J, Fradet G, Abel JG. Long-term Outcomes of Multiple Arterial Coronary Artery Bypass Grafting: A Population-Based Study of Patients in British Columbia, Canada. JAMA Cardiol 2017;**2**(11):1187-1196.

553. Desai ND, Cohen EA, Naylor CD, Fremes SE, Radial Artery Patency Study I. A randomized comparison of radial-artery and saphenous-vein coronary bypass grafts. N Engl J Med 2004;**351**(22):2302-9.
554. Gaudino M, Tondi P, Benedetto U, Milazzo V, Flore R, Glieca F, Ponziani FR, Luciani N, Girardi LN, Crea F, Massetti M. Radial Artery as a Coronary Artery Bypass Conduit: 20-Year Results. J Am Coll Cardiol 2016;**68**(6):603-10.
555. Dacey LJ, Braxton JH, Jr., Kramer RS, Schmoker JD, Charlesworth DC, Helm RE, Frumiento C, Sardella GL, Clough RA, Jones SR, Malenka DJ, Olmstead EM, Ross CS, O'Connor GT, Likosky DS, Northern New England Cardiovascular Disease Study G. Long-term outcomes of endoscopic vein harvesting after coronary artery bypass grafting. Circulation 2011;**123**(2):147-53.
556. Sen O, Gonca S, Solakoglu S, Dalcik H, Dalcik C, Ozkara A. Comparison of conventional and no-touch techniques in harvesting saphenous vein for coronary artery bypass grafting in view of endothelial damage. Heart Surg Forum 2013;**16**(4):E177-83.
557. Kim YH, Oh HC, Choi JW, Hwang HY, Kim KB. No-Touch Saphenous Vein Harvesting May Improve Further the Patency of Saphenous Vein Composite Grafts: Early Outcomes and 1-Year Angiographic Results. Ann Thorac Surg 2017;**103**(5):1489-1497.
558. Benedetto U, Lau C, Caputo M, Kim L, Feldman DN, Ohmes LB, Di Franco A, Soletti G, Angelini GD, Girardi LN, Gaudino M. Comparison of Outcomes for Off-Pump Versus On-Pump Coronary Artery Bypass Grafting in Low-Volume and High-Volume Centers and by Low-Volume and High-Volume Surgeons. Am J Cardiol 2017.
559. Lapar DJ, Mery CM, Kozower BD, Kern JA, Kron IL, Stukenborg GJ, Ailawadi G. The effect of surgeon volume on mortality for off-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg 2012;**143**(4):854-63.
560. Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. Eur Heart J 2012;**33**(10):1257-67.
561. Lemma MG, Coscioni E, Tritto FP, Centofanti P, Fondacone C, Salica A, Rossi A, De Santo T, Di Benedetto G, Piazza L, Rinaldi M, Schinosa AL, De Paulis R, Contino M, Genoni M. On-pump versus off-pump coronary artery bypass surgery in high-risk patients: operative results of a prospective randomized trial (on-off study). J Thorac Cardiovasc Surg 2012;**143**(3):625-31.
562. Rosenblum JM, Harskamp RE, Hoedemaker N, Walker P, Liberman HA, de Winter RJ, Vassiliades TA, Puskas JD, Halkos ME. Hybrid coronary revascularization versus coronary artery bypass surgery with bilateral or single internal mammary artery grafts. J Thorac Cardiovasc Surg 2016;**151**(4):1081-9.
563. Harskamp RE, Brennan JM, Xian Y, Halkos ME, Puskas JD, Thourani VH, Gammie JS, Taylor BS, de Winter RJ, Kim S, O'Brien S, Peterson ED, Gaca JG. Practice patterns and clinical outcomes after hybrid coronary revascularization in the United States: an analysis from the society of thoracic surgeons adult cardiac database. Circulation 2014;**130**(11):872-9.
564. Puskas JD, Halkos ME, DeRose JJ, Bagiella E, Miller MA, Overbey J, Bonatti J, Srinivas VS, Vesely M, Sutter F, Lynch J, Kirkwood K, Shapiro TA, Boudoulas KD, Crestanello J, Gehrig T, Smith P, Ragosta M, Hoff SJ, Zhao D, Gelijns AC, Szeto WY, Weisz G, Argenziano M, Vassiliades T, Liberman H, Matthai W, Ascheim DD. Hybrid Coronary Revascularization for the Treatment of Multivessel Coronary Artery Disease: A Multicenter Observational Study. J Am Coll Cardiol 2016;**68**(4):356-65.
565. Gasior M, Zembala MO, Tajstra M, Filipiak K, Gierlotka M, Hrapkowicz T, Hawranek M, Polonski L, Zembala M, Investigators P-MS. Hybrid revascularization for multivessel coronary artery disease. JACC Cardiovasc Interv 2014;**7**(11):1277-83.
566. Brophy JM, Belisle P, Joseph L. Evidence for use of coronary stents. A hierarchical bayesian meta-analysis. Ann Intern Med 2003;**138**(10):777-86.
567. Mehran R, Baber U, Steg PG, Ariti C, Weisz G, Witzenbichler B, Henry TD, Kini AS, Stuckey T, Cohen DJ, Berger PB, Iakovou I, Dangas G, Waksman R, Antoniucci D, Sartori S, Krucoff MW, Hermiller JB, Shawl F, Gibson CM, Chieffo A, Alu M, Moliterno DJ, Colombo A, Pocock S. Cessation of dual antiplatelet treatment and cardiac events after percutaneous coronary intervention (PARIS): 2 year results from a prospective observational study. Lancet 2013;**382**(9906):1714-22.

568. Silber S, Kirtane AJ, Belardi JA, Liu M, Brar S, Rothman M, Windecker S. Lack of association between dual antiplatelet therapy use and stent thrombosis between 1 and 12 months following resolute zotarolimus-eluting stent implantation. Eur Heart J 2014;**35**(29):1949-56.
569. Kastrati A, Mehilli J, Dirschinger J, Dotzer F, Schuhlen H, Neumann FJ, Fleckenstein M, Pfafferott C, Seyfarth M, Schomig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. Circulation 2001;**103**(23):2816-21.
570. Pache J, Kastrati A, Mehilli J, Schuhlen H, Dotzer F, Hausleiter J, Fleckenstein M, Neumann FJ, Sattelberger U, Schmitt C, Muller M, Dirschinger J, Schomig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. J Am Coll Cardiol 2003;**41**(8):1283-8.
571. Kastrati A, Mehilli J, Pache J, Kaiser C, Valgimigli M, Kelbaek H, Menichelli M, Sabate M, Suttorp MJ, Baumgart D, Seyfarth M, Pfisterer ME, Schomig A. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007;**356**(10):1030-9.
572. Stone GW, Moses JW, Ellis SG, Schofer J, Dawkins KD, Morice MC, Colombo A, Schampaert E, Grube E, Kirtane AJ, Cutlip DE, Fahy M, Pocock SJ, Mehran R, Leon MB. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007;**356**(10):998-1008.
573. Raber L, Magro M, Stefanini GG, Kalesan B, van Domburg RT, Onuma Y, Wenaweser P, Daemen J, Meier B, Juni P, Serruys PW, Windecker S. Very late coronary stent thrombosis of a newer-generation everolimus-eluting stent compared with early-generation drug-eluting stents: a prospective cohort study. Circulation 2012;**125**(9):1110-21.
574. Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, Doostzadeh J, Cao S, Simonton CA, Sudhir K, Lansky AJ, Cutlip DE, Kereiakes DJ. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med 2010;**362**(18):1663-74.
575. Serruys PW, Silber S, Garg S, van Geuns RJ, Richardt G, Buszman PE, Kelbaek H, van Boven AJ, Hofma SH, Linke A, Klauss V, Wijns W, Macaya C, Garot P, DiMario C, Manoharan G, Kornowski R, Ischinger T, Bartorelli A, Ronden J, Bressers M, Gobbens P, Negoita M, van Leeuwen F, Windecker S. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. N Engl J Med 2010;**363**(2):136-46.
576. Christiansen EH, Jensen LO, Thayssen P, Tilsted HH, Krusell LR, Hansen KN, Kaltoft A, Maeng M, Kristensen SD, Botker HE, Terkelsen CJ, Villadsen AB, Ravkilde J, Aaroe J, Madsen M, Thuesen L, Lassen JF, Scandinavian Organization for Randomized Trials with Clinical Outcome Vi. Biolimus-eluting biodegradable polymer-coated stent versus durable polymer-coated sirolimus-eluting stent in unselected patients receiving percutaneous coronary intervention (SORT OUT V): a randomised non-inferiority trial. Lancet 2013;**381**(9867):661-9.
577. Byrne RA, Kastrati A, Kufner S, Massberg S, Birkmeier KA, Laugwitz KL, Schulz S, Pache J, Fusaro M, Seyfarth M, Schomig A, Mehilli J. Randomized, non-inferiority trial of three limus agent-eluting stents with different polymer coatings: the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents (ISAR-TEST-4) Trial. Eur Heart J 2009;**30**(20):2441-9.
578. Smits PC, Hofma S, Togni M, Vazquez N, Valdes M, Voudris V, Slagboom T, Goy JJ, Vuillomenet A, Serra A, Nouche RT, den Heijer P, van der Ent M. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. Lancet 2013;**381**(9867):651-60.
579. Massberg S, Byrne RA, Kastrati A, Schulz S, Pache J, Hausleiter J, Ibrahim T, Fusaro M, Ott I, Schomig A, Laugwitz KL, Mehilli J, Intracoronary S, Angiographic Results: Test Efficacy of S, Probucol-Eluting Versus Zotarolimus- Eluting Stents I. Polymer-free sirolimus- and probucol-eluting versus new generation zotarolimus-eluting stents in coronary artery disease: the Intracoronary Stenting and Angiographic Results: Test Efficacy of Sirolimus- and Probucol-Eluting versus Zotarolimus-eluting Stents (ISAR-TEST 5) trial. Circulation 2011;**124**(5):624-32.
580. Byrne RA, Serruys PW, Baumbach A, Escaned J, Fajadet J, James S, Joner M, Oktay S, Juni P, Kastrati A, Sianos G, Stefanini GG, Wijns W, Windecker S. Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions task force on the evaluation of coronary stents in Europe: executive summary. Eur Heart J 2015;**36**(38):2608-20.

581. Bonaa KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, Nilsen DW, Klow NE, Uchto M, Trovik T, Bendz B, Stavnes S, Bjornerheim R, Larsen AI, Slette M, Steigen T, Jakobsen OJ, Bleie O, Fossum E, Hanssen TA, Dahl-Eriksen O, Njolstad I, Rasmussen K, Wilsgaard T, Nordrehaug JE, Investigators N. Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease. N Engl J Med 2016.
582. Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits PC, Vlachojannis GJ, Jensen LO, Christiansen EH, Berencsi K, Valgimigli M, Orlandi C, Petrou M, Rapezzi C, Stone GW. Long-Term Safety of Drug-Eluting and Bare-Metal Stents: Evidence From a Comprehensive Network Meta-Analysis. J Am Coll Cardiol 2015;**65**(23):2496-507.
583. Varenne O, Cook S, Sideris G, Kedev S, Cuisset T, Carrie D, Hovasse T, Garot P, El Mahmoud R, Spaulding C, Helft G, Diaz Fernandez JF, Brugaletta S, Pinar-Bermudez E, Mauri Ferre J, Commeau P, Teiger E, Bogaerts K, Sabate M, Morice MC, Sinnaeve PR, investigators S. Drug-eluting stents in elderly patients with coronary artery disease (SENIOR): a randomised single-blind trial. Lancet 2018;**391**(10115):41-50.
584. Kang SH, Park KW, Kang DY, Lim WH, Park KT, Han JK, Kang HJ, Koo BK, Oh BH, Park YB, Kandzari DE, Cohen DJ, Hwang SS, Kim HS. Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: a systematic review and Bayesian approach network meta-analysis. Eur Heart J 2014;**35**(17):1147-58.
585. Pilgrim T, Heg D, Roffi M, Tuller D, Muller O, Vuilliomenet A, Cook S, Weilenmann D, Kaiser C, Jamshidi P, Fahrni T, Moschovitis A, Noble S, Eberli FR, Wenaweser P, Juni P, Windecker S. Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial. Lancet 2014;**384**(9960):2111-22.
586. Kaiser C, Galatius S, Jeger R, Gilgen N, Skov Jensen J, Naber C, Alber H, Wanitschek M, Eberli F, Kurz DJ, Pedrazzini G, Moccetti T, Rickli H, Weilenmann D, Vuillomenet A, Steiner M, Von Felten S, Vogt DR, Wadt Hansen K, Rickenbacher P, Conen D, Muller C, Buser P, Hoffmann A, Pfisterer M, group B-PIs. Long-term efficacy and safety of biodegradable-polymer biolimus-eluting stents: main results of the Basel Stent Kosten-Effektivitats Trial-PROspective Validation Examination II (BASKET-PROVE II), a randomized, controlled noninferiority 2-year outcome trial. Circulation 2015;**131**(1):74-81.
587. Raungaard B, Jensen LO, Tilsted HH, Christiansen EH, Maeng M, Terkelsen CJ, Krusell LR, Kaltoft A, Kristensen SD, Botker HE, Thuesen L, Aaroe J, Jensen SE, Villadsen AB, Thayssen P, Veien KT, Hansen KN, Junker A, Madsen M, Ravkilde J, Lassen JF, Scandinavian Organization for Randomized Trials with Clinical O. Zotarolimus-eluting durable-polymer-coated stent versus a biolimus-eluting biodegradable-polymer-coated stent in unselected patients undergoing percutaneous coronary intervention (SORT OUT VI): a randomised non-inferiority trial. Lancet 2015;**385**(9977):1527-35.
588. von Birgelen C, Kok MM, van der Heijden LC, Danse PW, Schotborgh CE, Scholte M, Gin RM, Somi S, van Houwelingen KG, Stoel MG, de Man FH, Louwerenburg JH, Hartmann M, Zocca P, Linssen GC, van der Palen J, Doggen CJ, Lowik MM. Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial. Lancet 2016;**388**(10060):2607-2617.
589. Kereiakes DJ, Meredith IT, Windecker S, Lee Jobe R, Mehta SR, Sarembock IJ, Feldman RL, Stein B, Dubois C, Grady T, Saito S, Kimura T, Christen T, Allocco DJ, Dawkins KD. Efficacy and safety of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent: the EVOLVE II Randomized Trial. Circ Cardiovasc Interv 2015;**8**(4).
590. Natsuaki M, Kozuma K, Morimoto T, Kadota K, Muramatsu T, Nakagawa Y, Akasaka T, Igarashi K, Tanabe K, Morino Y, Ishikawa T, Nishikawa H, Awata M, Abe M, Okada H, Takatsu Y, Ogata N, Kimura K, Urasawa K, Tarutani Y, Shiode N, Kimura T, Investigators N. Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial. J Am Coll Cardiol 2013;**62**(3):181-90.
591. Saito S, Valdes-Chavarri M, Richardt G, Moreno R, Iniguez Romo A, Barbato E, Carrie D, Ando K, Merkely B, Kornowski R, Eltchaninoff H, James S, Wijns W, Investigators CI. A randomized, prospective, intercontinental evaluation of a bioresorbable polymer sirolimus-eluting coronary stent

system: the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) trial. Eur Heart J 2014;**35**(30):2021-31.
592. Kandzari DE, Mauri L, Koolen JJ, Massaro JM, Doros G, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE, Waksman R, Investigators BV. Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation (BIOFLOW V): a randomised trial. Lancet 2017.
593. Kufner S, Sorges J, Mehilli J, Cassese S, Repp J, Wiebe J, Lohaus R, Lahmann A, Rheude T, Ibrahim T, Massberg S, Laugwitz KL, Kastrati A, Byrne RA, Investigators I-T-. Randomized Trial of Polymer-Free Sirolimus- and Probucol-Eluting Stents Versus Durable Polymer Zotarolimus-Eluting Stents: 5-Year Results of the ISAR-TEST-5 Trial. JACC Cardiovasc Interv 2016;**9**(8):784-92.
594. Kufner S, Byrne RA, Valeskini M, Schulz S, Ibrahim T, Hoppmann P, Schneider S, Laugwitz KL, Schunkert H, Kastrati A, Intracoronary S, Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents I. Five-year outcomes from a trial of three limus-eluting stents with different polymer coatings in patients with coronary artery disease: final results from the ISAR-TEST 4 randomised trial. EuroIntervention 2016;**11**(12):1372-9.
595. Vlachojannis GJ, Smits PC, Hofma SH, Togni M, Vazquez N, Valdes M, Voudris V, Slagboom T, Goy JJ, den Heijer P, van der Ent M. Biodegradable Polymer Biolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in Patients With Coronary Artery Disease: Final 5-Year Report From the COMPARE II Trial (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent). JACC Cardiovasc Interv 2017;**10**(12):1215-1221.
596. Vlachojannis GJ, Puricel S, Natsuaki M, Morimoto T, Smits PC, Kimura T. Biolimus-eluting versus everolimus-eluting stents in coronary artery disease: a pooled analysis from the NEXT (NOBORI biolimus-eluting versus XIENCE/PROMUS everolimus-eluting stent) and COMPARE II (Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent) randomised trials. EuroIntervention 2017;**12**(16):1970-1977.
597. Wiebe J, Nef HM, Hamm CW. Current status of bioresorbable scaffolds in the treatment of coronary artery disease. J Am Coll Cardiol 2014;**64**(23):2541-51.
598. Sorrentino S, Giustino G, Mehran R, Kini AS, Sharma SK, Faggioni M, Farhan S, Vogel B, Indolfi C, Dangas GD. Everolimus-Eluting Bioresorbable Scaffolds Versus Everolimus-Eluting Metallic Stents. J Am Coll Cardiol 2017;**69**(25):3055-3066.
599. Montone RA, Niccoli G, De Marco F, Minelli S, D'Ascenzo F, Testa L, Bedogni F, Crea F. Temporal Trends in Adverse Events After Everolimus-Eluting Bioresorbable Vascular Scaffold Versus Everolimus-Eluting Metallic Stent Implantation: A Meta-Analysis of Randomized Controlled Trials. Circulation 2017;**135**(22):2145-2154.
600. Bondesson P, Lagerqvist B, James SK, Olivecrona GK, Venetsanos D, Harnek J. Comparison of two drug-eluting balloons: a report from the SCAAR registry. EuroIntervention 2012;**8**(4):444-9.
601. Latib A, Colombo A, Castriota F, Micari A, Cremonesi A, De Felice F, Marchese A, Tespili M, Presbitero P, Sgueglia GA, Buffoli F, Tamburino C, Varbella F, Menozzi A. A randomized multicenter study comparing a paclitaxel drug-eluting balloon with a paclitaxel-eluting stent in small coronary vessels: the BELLO (Balloon Elution and Late Loss Optimization) study. J Am Coll Cardiol 2012;**60**(24):2473-80.
602. Cortese B, Micheli A, Picchi A, Coppolaro A, Bandinelli L, Severi S, Limbruno U. Paclitaxel-coated balloon versus drug-eluting stent during PCI of small coronary vessels, a prospective randomised clinical trial. The PICCOLETO study. Heart 2010;**96**(16):1291-6.
603. Stella PR, Belkacemi A, Dubois C, Nathoe H, Dens J, Naber C, Adriaenssens T, van Belle E, Doevendans P, Agostoni P. A multicenter randomized comparison of drug-eluting balloon plus bare-metal stent versus bare-metal stent versus drug-eluting stent in bifurcation lesions treated with a single-stenting technique: six-month angiographic and 12-month clinical results of the drug-eluting balloon in bifurcations trial. Catheter Cardiovasc Interv 2012;**80**(7):1138-46.
604. Abdel-Wahab M, Richardt G, Joachim Buttner H, Toelg R, Geist V, Meinertz T, Schofer J, King L, Neumann FJ, Khattab AA. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational

Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. JACC Cardiovasc Interv 2013;**6**(1):10-9.
605. Parise H, Maehara A, Stone GW, Leon MB, Mintz GS. Meta-analysis of randomized studies comparing intravascular ultrasound versus angiographic guidance of percutaneous coronary intervention in pre-drug-eluting stent era. Am J Cardiol 2011;**107**(3):374-82.
606. Lodi-Junqueira L, de Sousa MR, da Paixao LC, Kelles SM, Amaral CF, Ribeiro AL. Does intravascular ultrasound provide clinical benefits for percutaneous coronary intervention with bare-metal stent implantation? A meta-analysis of randomized controlled trials. Syst Rev 2012;**1**:42.
607. Nerlekar N, Cheshire CJ, Verma KP, Ihdayhid AR, McCormick LM, Cameron JD, Bennett MR, Malaiapan Y, Meredith IT, Brown AJ. Intravascular ultrasound guidance improves clinical outcomes during implantation of both first- and second-generation drug-eluting stents: a meta-analysis. EuroIntervention 2017;**12**(13):1632-1642.
608. Buccheri S, Franchina G, Romano S, Puglisi S, Venuti G, D'Arrigo P, Francaviglia B, Scalia M, Condorelli A, Barbanti M, Capranzano P, Tamburino C, Capodanno D. Clinical Outcomes Following Intravascular Imaging-Guided Versus Coronary Angiography-Guided Percutaneous Coronary Intervention With Stent Implantation: A Systematic Review and Bayesian Network Meta-Analysis of 31 Studies and 17,882 Patients. JACC Cardiovasc Interv 2017;**10**(24):2488-2498.
609. Prati F, Di Vito L, Biondi-Zoccai G, Occhipinti M, La Manna A, Tamburino C, Burzotta F, Trani C, Porto I, Ramazzotti V, Imola F, Manzoli A, Materia L, Cremonesi A, Albertucci M. Angiography alone versus angiography plus optical coherence tomography to guide decision-making during percutaneous coronary intervention: the Centro per la Lotta contro l'Infarto-Optimisation of Percutaneous Coronary Intervention (CLI-OPCI) study. EuroIntervention 2012;**8**(7):823-9.
610. Wijns W, Shite J, Jones MR, Lee SW, Price MJ, Fabbiocchi F, Barbato E, Akasaka T, Bezerra H, Holmes D. Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study. Eur Heart J 2015.
611. Prati F, Guagliumi G, Mintz GS, Costa M, Regar E, Akasaka T, Barlis P, Tearney GJ, Jang IK, Arbustini E, Bezerra HG, Ozaki Y, Bruining N, Dudek D, Radu M, Erglis A, Motreff P, Alfonso F, Toutouzas K, Gonzalo N, Tamburino C, Adriaenssens T, Pinto F, Serruys PW, Di Mario C, Expert's OCTRD. Expert review document part 2: methodology, terminology and clinical applications of optical coherence tomography for the assessment of interventional procedures. Eur Heart J 2012;**33**(20):2513-20.
612. Radu MD, Raber L, Heo J, Gogas BD, Jorgensen E, Kelbaek H, Muramatsu T, Farooq V, Helqvist S, Garcia-Garcia HM, Windecker S, Saunamaki K, Serruys PW. Natural history of optical coherence tomography-detected non-flow-limiting edge dissections following drug-eluting stent implantation. EuroIntervention 2014;**9**(9):1085-94.
613. Ali ZA, Maehara A, Genereux P, Shlofmitz RA, Fabbiocchi F, Nazif TM, Guagliumi G, Meraj PM, Alfonso F, Samady H, Akasaka T, Carlson EB, Leesar MA, Matsumura M, Ozan MO, Mintz GS, Ben-Yehuda O, Stone GW, Investigators IIOP. Optical coherence tomography compared with intravascular ultrasound and with angiography to guide coronary stent implantation (ILUMIEN III: OPTIMIZE PCI): a randomised controlled trial. Lancet 2016;**388**(10060):2618-2628.
614. Meneveau N, Souteyrand G, Motreff P, Caussin C, Amabile N, Ohlmann P, Morel O, Lefrancois Y, Descotes-Genon V, Silvain J, Braik N, Chopard R, Chatot M, Ecarnot F, Tauzin H, Van Belle E, Belle L, Schiele F. Optical Coherence Tomography to Optimize Results of Percutaneous Coronary Intervention in Patients with Non-ST-Elevation Acute Coronary Syndrome: Results of the Multicenter, Randomized DOCTORS Study (Does Optical Coherence Tomography Optimize Results of Stenting). Circulation 2016;**134**(13):906-17.
615. Taniwaki M, Radu MD, Zaugg S, Amabile N, Garcia-Garcia HM, Yamaji K, Jorgensen E, Kelbaek H, Pilgrim T, Caussin C, Zanchin T, Veugeois A, Abildgaard U, Juni P, Cook S, Koskinas KC, Windecker S, Raber L. Mechanisms of Very Late Drug-Eluting Stent Thrombosis Assessed by Optical Coherence Tomography. Circulation 2016;**133**(7):650-60.
616. Souteyrand G, Amabile N, Mangin L, Chabin X, Meneveau N, Cayla G, Vanzetto G, Barnay P, Trouillet C, Rioufol G, Range G, Teiger E, Delaunay R, Dubreuil O, Lhermusier T, Mulliez A, Levesque S, Belle L, Caussin C, Motreff P, Investigators P. Mechanisms of stent thrombosis analysed by optical

coherence tomography: insights from the national PESTO French registry. Eur Heart J 2016;**37**(15):1208-16.
617. Kang SJ, Mintz GS, Akasaka T, Park DW, Lee JY, Kim WJ, Lee SW, Kim YH, Whan Lee C, Park SW, Park SJ. Optical coherence tomographic analysis of in-stent neoatherosclerosis after drug-eluting stent implantation. Circulation 2011;**123**(25):2954-63.
618. Malle C, Tada T, Steigerwald K, Ughi GJ, Schuster T, Nakano M, Massberg S, Jehle J, Guagliumi G, Kastrati A, Virmani R, Byrne RA, Joner M. Tissue characterization after drug-eluting stent implantation using optical coherence tomography. Arterioscler Thromb Vasc Biol 2013;**33**(6):1376-83.
619. Gao XF, Zhang YJ, Tian NL, Wu W, Li MH, Bourantas CV, Jiang XM, Wang ZM, Li B, Mao WX, Zhang JJ, Chen SL. Stenting strategy for coronary artery bifurcation with drug-eluting stents: a meta-analysis of nine randomised trials and systematic review. EuroIntervention 2014;**10**(5):561-9.
620. Behan MW, Holm NR, de Belder AJ, Cockburn J, Erglis A, Curzen NP, Niemela M, Oldroyd KG, Kervinen K, Kumsars I, Gunnes P, Stables RH, Maeng M, Ravkilde J, Jensen JS, Christiansen EH, Cooter N, Steigen TK, Vikman S, Thuesen L, Lassen JF, Hildick-Smith D. Coronary bifurcation lesions treated with simple or complex stenting: 5-year survival from patient-level pooled analysis of the Nordic Bifurcation Study and the British Bifurcation Coronary Study. Eur Heart J 2016;**37**(24):1923-8.
621. Hildick-Smith D, Behan MW, Lassen JF, Chieffo A, Lefevre T, Stankovic G, Burzotta F, Pan M, Ferenc M, Bennett L, Hovasse T, Spence MJ, Oldroyd K, Brunel P, Carrie D, Baumbach A, Maeng M, Skipper N, Louvard Y. The EBC TWO Study (European Bifurcation Coronary TWO): A Randomized Comparison of Provisional T-Stenting Versus a Systematic 2 Stent Culotte Strategy in Large Caliber True Bifurcations. Circ Cardiovasc Interv 2016;**9**(9).
622. Chen SL, Zhang JJ, Han Y, Kan J, Chen L, Qiu C, Jiang T, Tao L, Zeng H, Li L, Xia Y, Gao C, Santoso T, Paiboon C, Wang Y, Kwan TW, Ye F, Tian N, Liu Z, Lin S, Lu C, Wen S, Hong L, Zhang Q, Sheiban I, Xu Y, Wang L, Rab TS, Li Z, Cheng G, Cui L, Leon MB, Stone GW. Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial. J Am Coll Cardiol 2017;**70**(21):2605-2617.
623. Erglis A, Kumsars I, Niemela M, Kervinen K, Maeng M, Lassen JF, Gunnes P, Stavnes S, Jensen JS, Galloe A, Narbute I, Sondore D, Makikallio T, Ylitalo K, Christiansen EH, Ravkilde J, Steigen TK, Mannsverk J, Thayssen P, Hansen KN, Syvanne M, Helqvist S, Kjell N, Wiseth R, Aaroe J, Puhakka M, Thuesen L. Randomized comparison of coronary bifurcation stenting with the crush versus the culotte technique using sirolimus eluting stents: the Nordic stent technique study. Circ Cardiovasc Interv 2009;**2**(1):27-34.
624. Zheng XW, Zhao DH, Peng HY, Fan Q, Ma Q, Xu ZY, Fan C, Liu LY, Liu JH. Randomized Comparison of the Crush Versus the Culotte Stenting for Coronary Artery Bifurcation Lesions. Chin Med J (Engl) 2016;**129**(5):505-10.
625. Adriaenssens T, Byrne RA, Dibra A, Iijima R, Mehilli J, Bruskina O, Schomig A, Kastrati A. Culotte stenting technique in coronary bifurcation disease: angiographic follow-up using dedicated quantitative coronary angiographic analysis and 12-month clinical outcomes. Eur Heart J 2008;**29**(23):2868-76.
626. Ferenc M, Gick M, Comberg T, Rothe J, Valina C, Toma A, Loffelhardt N, Hochholzer W, Riede F, Kienzle RP, Achtari A, Neumann FJ. Culotte stenting vs. TAP stenting for treatment of de-novo coronary bifurcation lesions with the need for side-branch stenting: the Bifurcations Bad Krozingen (BBK) II angiographic trial. Eur Heart J 2016;**37**(45):3399-3405.
627. Chen SL, Xu B, Han YL, Sheiban I, Zhang JJ, Ye F, Kwan TW, Paiboon C, Zhou YJ, Lv SZ, Dangas GD, Xu YW, Wen SY, Hong L, Zhang RY, Wang HC, Jiang TM, Wang Y, Chen F, Yuan ZY, Li WM, Leon MB. Comparison of double kissing crush versus Culotte stenting for unprotected distal left main bifurcation lesions: results from a multicenter, randomized, prospective DKCRUSH-III study. J Am Coll Cardiol 2013;**61**(14):1482-8.
628. Niemela M, Kervinen K, Erglis A, Holm NR, Maeng M, Christiansen EH, Kumsars I, Jegere S, Dombrovskis A, Gunnes P, Stavnes S, Steigen TK, Trovik T, Eskola M, Vikman S, Romppanen H, Makikallio T, Hansen KN, Thayssen P, Aberge L, Jensen LO, Hervold A, Airaksinen J, Pietila M, Frobert O, Kellerth T, Ravkilde J, Aaroe J, Jensen JS, Helqvist S, Sjogren I, James S, Miettinen H, Lassen JF,

Thuesen L. Randomized comparison of final kissing balloon dilatation versus no final kissing balloon dilatation in patients with coronary bifurcation lesions treated with main vessel stenting: the Nordic-Baltic Bifurcation Study III. Circulation 2011;**123**(1):79-86.
629. Gwon HC, Hahn JY, Koo BK, Song YB, Choi SH, Choi JH, Lee SH, Jeong MH, Kim HS, Seong IW, Yang JY, Rha SW, Jang Y, Yoon JH, Tahk SJ, Seung KB, Park SJ. Final kissing ballooning and long-term clinical outcomes in coronary bifurcation lesions treated with 1-stent technique: results from the COBIS registry. Heart 2012;**98**(3):225-31.
630. Généreux P, Kumsars I, Lesiak M, Kini A, Fontos G, Slagboom T, Ungi I, Metzger DC, Wykrzykowska JJ, Stella PR, Bartorelli AL, Fearon WF, Lefèvre T, Feldman RL, LaSalle L, Francese DP, Onuma Y, Grundeken MJ, Garcia-Garcia HM, Laak LL, Cutlip DE, Kaplan AV, Serruys PW, Leon MB. A Randomized Trial of a Dedicated Bifurcation Stent Versus Provisional Stenting in the Treatment of Coronary Bifurcation Lesions. J Am Coll Cardiol 2015;**65**(6):533-543.
631. Lassen JF, Holm NR, Banning A, Burzotta F, Lefevre T, Chieffo A, Hildick-Smith D, Louvard Y, Stankovic G. Percutaneous coronary intervention for coronary bifurcation disease: 11th consensus document from the European Bifurcation Club. EuroIntervention 2016;**12**(1):38-46.
632. Henriques JPS, Hoebers LP, Råmunddal T, Laanmets P, Eriksen E, Bax M, Ioanes D, Suttorp MJ, Strauss BH, Barbato E, Nijveldt R, van Rossum AC, Marques KM, Elias J, van Dongen IM, Claessen BEPM, Tijssen JG, van der Schaaf RJ, Henriques JPS, van der Schaaf R, Tijssen JGP, Zijlstra F, de Boer M-J, Michels R, Meuwissen M, Agostoni P, van Houwelingen KG, Verberne HJ, Hirsch A, Henriques JPS, Piek JJ, de Winter RJ, Koch KT, Vis MM, Baan J, Wykrzykowska J, Råmunddal T, Ioanes D, Laanmets P, van der Schaaf RJ, Slagboom T, Amoroso G, Eriksen E, Tuseth V, Bax M, Schotborgh CE, Suttorp MJ, Strauss BH, Barbato E, Marques KM, Bertrand O, Meuwissen M, van der Ent M, Koolen J. Percutaneous Intervention for Concurrent Chronic Total Occlusions in Patients With STEMI: The EXPLORE Trial. J Am Coll Cardiol 2016;**68**(15):1622-1632.
633. Christakopoulos GE, Christopoulos G, Carlino M, Jeroudi OM, Roesle M, Rangan BV, Abdullah S, Grodin J, Kumbhani DJ, Vo M, Luna M, Alaswad K, Karmpaliotis D, Rinfret S, Garcia S, Banerjee S, Brilakis ES. Meta-analysis of clinical outcomes of patients who underwent percutaneous coronary interventions for chronic total occlusions. Am J Cardiol 2015;**115**(10):1367-75.
634. Brilakis ES, Banerjee S, Karmpaliotis D, Lombardi WL, Tsai TT, Shunk KA, Kennedy KF, Spertus JA, Holmes DR, Jr., Grantham JA. Procedural outcomes of chronic total occlusion percutaneous coronary intervention: a report from the NCDR (National Cardiovascular Data Registry). JACC Cardiovasc Interv 2015;**8**(2):245-53.
635. Maeremans J, Walsh S, Knaapen P, Spratt JC, Avran A, Hanratty CG, Faurie B, Agostoni P, Bressollette E, Kayaert P, Bagnall AJ, Egred M, Smith D, Chase A, McEntegart MB, Smith WHT, Harcombe A, Kelly P, Irving J, Smith EJ, Strange JW, Dens J. The Hybrid Algorithm for Treating Chronic Total Occlusions in Europe: The RECHARGE Registry. J Am Coll Cardiol 2016;**68**(18):1958-1970.
636. Galassi AR, Sianos G, Werner GS, Escaned J, Tomasello SD, Boukhris M, Castaing M, Buttner JH, Bufe A, Kalnins A, Spratt JC, Garbo R, Hildick-Smith D, Elhadad S, Gagnor A, Lauer B, Bryniarski L, Christiansen EH, Thuesen L, Meyer-Gessner M, Goktekin O, Carlino M, Louvard Y, Lefevre T, Lismanis A, Gelev VL, Serra A, Marza F, Di Mario C, Reifart N, Euro CTOC. Retrograde Recanalization of Chronic Total Occlusions in Europe: Procedural, In-Hospital, and Long-Term Outcomes From the Multicenter ERCTO Registry. J Am Coll Cardiol 2015;**65**(22):2388-400.
637. Koh JS, Koo BK, Kim JH, Yang HM, Park KW, Kang HJ, Kim HS, Oh BH, Park YB. Relationship between fractional flow reserve and angiographic and intravascular ultrasound parameters in ostial lesions: major epicardial vessel versus side branch ostial lesions. JACC Cardiovasc Interv 2012;**5**(4):409-15.
638. Arnous S, Shakhshir N, Wiper A, Ordoubadi FF, Williams P, Clarke B, Mahadavan V, El-Omar M, Mamas M, Fraser D. Incidence and mechanisms of longitudinal stent deformation associated with Biomatrix, Resolute, Element, and Xience stents: Angiographic and case-by-case review of 1,800 PCIs. Catheter Cardiovasc Interv 2015;**86**(6):1002-11.
639. Szabo S, Abramowitz B, Vaitkus P. New technique of aorto-ostial stent placement. Am J Cardiol 2005;**96**:212H.

640. Gutierrez-Chico JL, Villanueva-Benito I, Villanueva-Montoto L, Vazquez-Fernandez S, Kleinecke C, Gielen S, Iniguez-Romo A. Szabo technique versus conventional angiographic placement in bifurcations 010-001 of Medina and in aorto-ostial stenting: angiographic and procedural results. EuroIntervention 2010;**5**(7):801-8.
641. Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P, Budaj A, Niemela M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afzal R, Joyner CD, Chrolavicius S, Mehta SR. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011;**377**(9775):1409-20.
642. Hamon M, Pristipino C, Di Mario C, Nolan J, Ludwig J, Tubaro M, Sabate M, Mauri-Ferre J, Huber K, Niemela K, Haude M, Wijns W, Dudek D, Fajadet J, Kiemeneij F, European Association of Percutaneous Cardiovascular I, Working Group on Acute Cardiac Care of the European Society of C, Working Group on Thrombosis on the European Society of C. Consensus document on the radial approach in percutaneous cardiovascular interventions: position paper by the European Association of Percutaneous Cardiovascular Interventions and Working Groups on Acute Cardiac Care** and Thrombosis of the European Society of Cardiology. EuroIntervention 2013;**8**(11):1242-51.
643. Bonaa KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, Nilsen DW, Klow NE, Uchto M, Trovik T, Bendz B, Stavnes S, Bjornerheim R, Larsen AI, Slette M, Steigen T, Jakobsen OJ, Bleie O, Fossum E, Hanssen TA, Dahl-Eriksen O, Njolstad I, Rasmussen K, Wilsgaard T, Nordrehaug JE, Investigators N. Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease. N Engl J Med 2016;**375**(13):1242-52.
644. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F, Kimura T, Briguori C, Sabate M, Kim HS, De Waha A, Kedhi E, Smits PC, Kaiser C, Sardella G, Marullo A, Kirtane AJ, Leon MB, Stone GW. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. Lancet 2012;**379**(9824):1393-402.
645. Ferrante G, Rao SV, Juni P, Da Costa BR, Reimers B, Condorelli G, Anzuini A, Jolly SS, Bertrand OF, Krucoff MW, Windecker S, Valgimigli M. Radial Versus Femoral Access for Coronary Interventions Across the Entire Spectrum of Patients With Coronary Artery Disease: A Meta-Analysis of Randomized Trials. JACC Cardiovasc Interv 2016;**9**(14):1419-34.
646. Sabate M, Windecker S, Iniguez A, Okkels-Jensen L, Cequier A, Brugaletta S, Hofma SH, Raber L, Christiansen EH, Suttorp M, Pilgrim T, Anne van Es G, Sotomi Y, Garcia-Garcia HM, Onuma Y, Serruys PW. Everolimus-eluting bioresorbable stent vs. durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. Eur Heart J 2016;**37**(3):229-40.
647. Cassese S, Byrne RA, Ndrepepa G, Kufner S, Wiebe J, Repp J, Schunkert H, Fusaro M, Kimura T, Kastrati A. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic stents: a meta-analysis of randomised controlled trials. Lancet 2016;**387**(10018):537-44.
648. Serruys PW, Chevalier B, Dudek D, Cequier A, Carrie D, Iniguez A, Dominici M, van der Schaaf RJ, Haude M, Wasungu L, Veldhof S, Peng L, Staehr P, Grundeken MJ, Ishibashi Y, Garcia-Garcia HM, Onuma Y. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. Lancet 2015;**385**(9962):43-54.
649. Puricel S, Arroyo D, Corpataux N, Baeriswyl G, Lehmann S, Kallinikou Z, Muller O, Allard L, Stauffer J-C, Togni M, Goy J-J, Cook S. Comparison of Everolimus- and Biolimus-Eluting Coronary Stents With Everolimus-Eluting Bioresorbable Vascular Scaffolds. J Am Coll Cardiol 2015;**65**(8):791-801.
650. Kimura T, Kozuma K, Tanabe K, Nakamura S, Yamane M, Muramatsu T, Saito S, Yajima J, Hagiwara N, Mitsudo K, Popma JJ, Serruys PW, Onuma Y, Ying S, Cao S, Staehr P, Cheong WF, Kusano H, Stone GW, Investigators AJ. A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan. Eur Heart J 2015;**36**(47):3332-42.
651. Gao R, Yang Y, Han Y, Huo Y, Chen J, Yu B, Su X, Li L, Kuo HC, Ying SW, Cheong WF, Zhang Y, Su X, Xu B, Popma JJ, Stone GW, Investigators AC. Bioresorbable Vascular Scaffolds Versus Metallic

Stents in Patients With Coronary Artery Disease: ABSORB China Trial. J Am Coll Cardiol 2015;**66**(21):2298-309.
652. Ellis SG, Kereiakes DJ, Metzger DC, Caputo RP, Rizik DG, Teirstein PS, Litt MR, Kini A, Kabour A, Marx SO, Popma JJ, McGreevy R, Zhang Z, Simonton C, Stone GW, Investigators AI. Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease. N Engl J Med 2015;**373**(20):1905-15.
653. Wykrzykowska JJ, Kraak RP, Hofma SH, van der Schaaf RJ, Arkenbout EK, AJ IJ, Elias J, van Dongen IM, Tijssen RYG, Koch KT, Baan J, Jr., Vis MM, de Winter RJ, Piek JJ, Tijssen JGP, Henriques JPS, Investigators A. Bioresorbable Scaffolds versus Metallic Stents in Routine PCI. N Engl J Med 2017;**376**(24):2319-2328.
654. Cassese S, Byrne RA, Juni P, Wykrzykowska JJ, Puricel S, Ndrepepa G, Schunkert H, Fusaro M, Cook S, Kimura T, Henriques JPS, Serruys PW, Windecker S, Kastrati A. Midterm clinical outcomes with everolimus-eluting bioresorbable scaffolds versus everolimus-eluting metallic stents for percutaneous coronary interventions: a meta-analysis of randomised trials. EuroIntervention 2018;**13**(13):1565-1573.
655. Casella G, Klauss V, Ottani F, Siebert U, Sangiorgio P, Bracchetti D. Impact of intravascular ultrasound-guided stenting on long-term clinical outcome: a meta-analysis of available studies comparing intravascular ultrasound-guided and angiographically guided stenting. Catheter Cardiovasc Interv 2003;**59**(3):314-21.
656. Witzenbichler B, Maehara A, Weisz G, Neumann FJ, Rinaldi MJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Brodie BR, Stuckey TD, Mazzaferri EL, Jr., Xu K, Parise H, Mehran R, Mintz GS, Stone GW. Relationship Between Intravascular Ultrasound Guidance and Clinical Outcomes After Drug-Eluting Stents: The Assessment of Dual Antiplatelet Therapy With Drug-Eluting Stents (ADAPT-DES) Study. Circulation 2014;**129**(4):463-70.
657. Maehara A, Ben-Yehuda O, Ali Z, Wijns W, Bezerra HG, Shite J, Genereux P, Nichols M, Jenkins P, Witzenbichler B, Mintz GS, Stone GW. Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound: The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention). JACC Cardiovasc Interv 2015;**8**(13):1704-14.
658. Maeng M, Holm NR, Erglis A, Kumsars I, Niemela M, Kervinen K, Jensen JS, Galloe A, Steigen TK, Wiseth R, Narbute I, Gunnes P, Mannsverk J, Meyerdierks O, Rotevatn S, Nikus K, Vikman S, Ravkilde J, James S, Aaroe J, Ylitalo A, Helqvist S, Sjogren I, Thayssen P, Virtanen K, Puhakka M, Airaksinen J, Christiansen EH, Lassen JF, Thuesen L. Long-term results after simple versus complex stenting of coronary artery bifurcation lesions: Nordic Bifurcation Study 5-year follow-up results. J Am Coll Cardiol 2013;**62**(1):30-4.
659. Hildick-Smith D, de Belder AJ, Cooter N, Curzen NP, Clayton TC, Oldroyd KG, Bennett L, Holmberg S, Cotton JM, Glennon PE, Thomas MR, Maccarthy PA, Baumbach A, Mulvihill NT, Henderson RA, Redwood SR, Starkey IR, Stables RH. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. Circulation 2010;**121**(10):1235-43.
660. Behan MW, Holm NR, Curzen NP, Erglis A, Stables RH, de Belder AJ, Niemela M, Cooter N, Chew DP, Steigen TK, Oldroyd KG, Jensen JS, Lassen JF, Thuesen L, Hildick-Smith D. Simple or complex stenting for bifurcation coronary lesions: a patient-level pooled-analysis of the Nordic Bifurcation Study and the British Bifurcation Coronary Study. Circ Cardiovasc Interv 2011;**4**(1):57-64.
661. Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, Kan J, Paiboon C, Zhou Y, Ding SQ, Kwan TW. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions) trial. J Am Coll Cardiol 2011;**57**(8):914-20.
662. Katritsis DG, Siontis GC, Ioannidis JP. Double versus single stenting for coronary bifurcation lesions: a meta-analysis. Circ Cardiovasc Interv 2009;**2**(5):409-15.
663. Mehran R, Claessen BE, Godino C, Dangas GD, Obunai K, Kanwal S, Carlino M, Henriques JP, Di Mario C, Kim YH, Park SJ, Stone GW, Leon MB, Moses JW, Colombo A. Long-term outcome of

percutaneous coronary intervention for chronic total occlusions. JACC Cardiovasc Interv 2011;**4**(9):952-61.
664. Claessen BE, Dangas GD, Godino C, Lee SW, Obunai K, Carlino M, Suh JW, Leon MB, Di Mario C, Park SJ, Stone GW, Moses JW, Colombo A, Mehran R. Long-term clinical outcomes of percutaneous coronary intervention for chronic total occlusions in patients with versus without diabetes mellitus. Am J Cardiol 2011;**108**(7):924-31.
665. Jones DA, Weerackody R, Rathod K, Behar J, Gallagher S, Knight CJ, Kapur A, Jain AK, Rothman MT, Thompson CA, Mathur A, Wragg A, Smith EJ. Successful recanalization of chronic total occlusions is associated with improved long-term survival. JACC Cardiovasc Interv 2012;**5**(4):380-8.
666. Grantham JA, Jones PG, Cannon L, Spertus JA. Quantifying the early health status benefits of successful chronic total occlusion recanalization: Results from the FlowCardia's Approach to Chronic Total Occlusion Recanalization (FACTOR) Trial. Circ Cardiovasc Qual Outcomes 2010;**3**(3):284-90.
667. Joyal D, Afilalo J, Rinfret S. Effectiveness of recanalization of chronic total occlusions: a systematic review and meta-analysis. Am Heart J 2010;**160**(1):179-87.
668. Ndrepepa G, Berger PB, Mehilli J, Seyfarth M, Neumann FJ, Schomig A, Kastrati A. Periprocedural bleeding and 1-year outcome after percutaneous coronary interventions: appropriateness of including bleeding as a component of a quadruple end point. J Am Coll Cardiol 2008;**51**(7):690-7.
669. Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, Walter H, Zitzmann-Roth EM, Richardt G, Alt E, Schmitt C, Ulm K. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 1996;**334**(17):1084-9.
670. Sibbing D, Kastrati A, Berger PB. Pre-treatment with P2Y12 inhibitors in ACS patients: who, when, why, and which agent? Eur Heart J 2016;**37**(16):1284-95.
671. Steinhubl SR, Berger PB, Mann JT, 3rd, Fry ET, DeLago A, Wilmer C, Topol EJ, Observation CICftRoED. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. JAMA 2002;**288**(19):2411-20.
672. Bellemain-Appaix A, O'Connor SA, Silvain J, Cucherat M, Beygui F, Barthelemy O, Collet JP, Jacq L, Bernasconi F, Montalescot G, Group A. Association of clopidogrel pretreatment with mortality, cardiovascular events, and major bleeding among patients undergoing percutaneous coronary intervention: a systematic review and meta-analysis. JAMA 2012;**308**(23):2507-16.
673. Lincoff AM, Kleiman NS, Kereiakes DJ, Feit F, Bittl JA, Jackman JD, Sarembock IJ, Cohen DJ, Spriggs D, Ebrahimi R, Keren G, Carr J, Cohen EA, Betriu A, Desmet W, Rutsch W, Wilcox RG, de Feyter PJ, Vahanian A, Topol EJ. Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization: REPLACE-2 randomized trial. JAMA: the journal of the American Medical Association 2004;**292**(6):696-703.
674. Kastrati A, Neumann FJ, Mehilli J, Byrne RA, Iijima R, Buttner HJ, Khattab AA, Schulz S, Blankenship JC, Pache J, Minners J, Seyfarth M, Graf I, Skelding KA, Dirschinger J, Richardt G, Berger PB, Schomig A, Investigators I-RT. Bivalirudin versus unfractionated heparin during percutaneous coronary intervention. N Engl J Med 2008;**359**(7):688-96.
675. Schulz S, Mehilli J, Neumann FJ, Schuster T, Massberg S, Valina C, Seyfarth M, Pache J, Laugwitz KL, Buttner HJ, Ndrepepa G, Schomig A, Kastrati A, Intracoronary S, Antithrombotic Regimen: Rapid Early Action for Coronary Treatment ATI. ISAR-REACT 3A: a study of reduced dose of unfractionated heparin in biomarker negative patients undergoing percutaneous coronary intervention. Eur Heart J 2010;**31**(20):2482-91.
676. Montalescot G, White HD, Gallo R, Cohen M, Steg PG, Aylward PE, Bode C, Chiariello M, King SB, 3rd, Harrington RA, Desmet WJ, Macaya C, Steinhubl SR. Enoxaparin versus unfractionated heparin in elective percutaneous coronary intervention. N Engl J Med 2006;**355**(10):1006-17.
677. Steg PG, Bhatt DL, Hamm CW, Stone GW, Gibson CM, Mahaffey KW, Leonardi S, Liu T, Skerjanec S, Day JR, Iwaoka RS, Stuckey TD, Gogia HS, Gruberg L, French WJ, White HD, Harrington RA, Investigators C. Effect of cangrelor on periprocedural outcomes in percutaneous coronary interventions: a pooled analysis of patient-level data. Lancet 2013;**382**(9909):1981-92.

678. Valgimigli M, Percoco G, Barbieri D, Ferrari F, Guardigli G, Parrinello G, Soukhomovskaia O, Ferrari R. The additive value of tirofiban administered with the high-dose bolus in the prevention of ischemic complications during high-risk coronary angioplasty: the ADVANCE Trial. Journal of the American College of Cardiology 2004;**44**(1):14-19.
679. Kastrati A, Mehilli J, Schuhlen H, Dirschinger J, Dotzer F, ten Berg JM, Neumann FJ, Bollwein H, Volmer C, Gawaz M, Berger PB, Schomig A, Intracoronary S, Antithrombotic Regimen-Rapid Early Action for Coronary Treatment Study I. A clinical trial of abciximab in elective percutaneous coronary intervention after pretreatment with clopidogrel. N Engl J Med 2004;**350**(3):232-8.
680. Winchester DE, Wen X, Brearley WD, Park KE, Anderson RD, Bavry AA. Efficacy and safety of glycoprotein IIb/IIIa inhibitors during elective coronary revascularization: a meta-analysis of randomized trials performed in the era of stents and thienopyridines. J Am Coll Cardiol 2011;**57**(10):1190-9.
681. Valgimigli M. 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease Eur Heart J 2017;**39**.
682. Iakovou I, Schmidt T, Bonizzoni E, Ge L, Sangiorgi GM, Stankovic G, Airoldi F, Chieffo A, Montorfano M, Carlino M, Michev I, Corvaja N, Briguori C, Gerckens U, Grube E, Colombo A. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA 2005;**293**(17):2126-30.
683. Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, Diaz R, Alings M, Lonn EM, Anand SS, Widimsky P, Hori M, Avezum A, Piegas LS, Branch KRH, Probstfield J, Bhatt DL, Zhu J, Liang Y, Maggioni AP, Lopez-Jaramillo P, O'Donnell M, Kakkar AK, Fox KAA, Parkhomenko AN, Ertl G, Stork S, Keltai M, Ryden L, Pogosova N, Dans AL, Lanas F, Commerford PJ, Torp-Pedersen C, Guzik TJ, Verhamme PB, Vinereanu D, Kim JH, Tonkin AM, Lewis BS, Felix C, Yusoff K, Steg PG, Metsarinne KP, Cook Bruns N, Misselwitz F, Chen E, Leong D, Yusuf S, Investigators C. Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. N Engl J Med 2017;**377**(14):1319-1330.
684. Di Sciascio G, Patti G, Pasceri V, Gatto L, Colonna G, Montinaro A. Effectiveness of in-laboratory high-dose clopidogrel loading versus routine pre-load in patients undergoing percutaneous coronary intervention: results of the ARMYDA-5 PRELOAD (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) randomized trial. Journal of the American College of Cardiology 2010;**56**(7):550-557.
685. Widimsky P, Motovska Z, Simek S, Kala P, Pudil R, Holm F, Petr R, Bilkova D, Skalicka H, Kuchynka P, Poloczek M, Miklik R, Maly M, Aschermann M. Clopidogrel pre-treatment in stable angina: for all patients > 6 h before elective coronary angiography or only for angiographically selected patients a few minutes before PCI? A randomized multicentre trial PRAGUE-8. Eur Heart J 2008;**29**(12):1495-503.
686. Antiplatelet tc. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ 2002;**324**:71-86.
687. Collaborative overview of randomised trials of antiplatelet therapy--I: Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients. Antiplatelet Trialists' Collaboration. BMJ (Clinical research ed) 1994;**308**(6921):81-106.
688. Antithrombotic Trialists C, Baigent C, Blackwell L, Collins R, Emberson J, Godwin J, Peto R, Buring J, Hennekens C, Kearney P, Meade T, Patrono C, Roncaglioni MC, Zanchetti A. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. Lancet 2009;**373**(9678):1849-60.
689. Bertrand ME, Rupprecht HJ, Urban P, Gershlick AH. Double-blind study of the safety of clopidogrel with and without a loading dose in combination with aspirin compared with ticlopidine in combination with aspirin after coronary stenting : the clopidogrel aspirin stent international cooperative study (CLASSICS). Circulation 2000;**102**(6):624-9.
690. Taniuchi M, Kurz HI, Lasala JM. Randomized comparison of ticlopidine and clopidogrel after intracoronary stent implantation in a broad patient population. Circulation 2001;**104**(5):539-43.
691. Muller C, Buttner HJ, Petersen J, Roskamm H. A randomized comparison of clopidogrel and aspirin versus ticlopidine and aspirin after the placement of coronary-artery stents. Circulation 2000;**101**(6):590-3.

692. von Beckerath N, Taubert D, Pogatsa-Murray G, Schomig E, Kastrati A, Schomig A. Absorption, metabolization, and antiplatelet effects of 300-, 600-, and 900-mg loading doses of clopidogrel: results of the ISAR-CHOICE (Intracoronary Stenting and Antithrombotic Regimen: Choose Between 3 High Oral Doses for Immediate Clopidogrel Effect) Trial. Circulation 2005;**112**(19):2946-50.
693. Montalescot G, Sideris G, Meuleman C, Bal-dit-Sollier C, Lellouche N, Steg PG, Slama M, Milleron O, Collet JP, Henry P, Beygui F, Drouet L. A randomized comparison of high clopidogrel loading doses in patients with non-ST-segment elevation acute coronary syndromes: the ALBION (Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation and Ongoing Necrosis) trial. J Am Coll Cardiol 2006;**48**(5):931-8.
694. Silvain J, Beygui F, Barthélémy O, Pollack C, Jr., Cohen M, Zeymer U, Huber K, Goldstein P, Cayla G, Collet J-P, Vicaut E, Montalescot G. Efficacy and safety of enoxaparin versus unfractionated heparin during percutaneous coronary intervention: systematic review and meta-analysis. BMJ 2012;**344**.
695. Valgimigli M, Campo G, Monti M, Vranckx P, Percoco G, Tumscitz C, Castriota F, Colombo F, Tebaldi M, Fuca G, Kubbajeh M, Cangiano E, Minarelli M, Scalone A, Cavazza C, Frangione A, Borghesi M, Marchesini J, Parrinello G, Ferrari R, Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia Study I. Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. Circulation 2012;**125**(16):2015-26.
696. Schulz-Schupke S, Byrne RA, Ten Berg JM, Neumann FJ, Han Y, Adriaenssens T, Tolg R, Seyfarth M, Maeng M, Zrenner B, Jacobshagen C, Mudra H, von Hodenberg E, Wohrle J, Angiolillo DJ, von Merzljak B, Rifatov N, Kufner S, Morath T, Feuchtenberger A, Ibrahim T, Janssen PW, Valina C, Li Y, Desmet W, Abdel-Wahab M, Tiroch K, Hengstenberg C, Bernlochner I, Fischer M, Schunkert H, Laugwitz KL, Schomig A, Mehilli J, Kastrati A, Intracoronary S, Antithrombotic Regimen S, Investigators EFoMDATAD-EST. ISAR-SAFE: a randomized, double-blind, placebo-controlled trial of 6 vs. 12 months of clopidogrel therapy after drug-eluting stenting. Eur Heart J 2015;**36**(20):1252-63.
697. Han Y, Xu B, Xu K, Guan C, Jing Q, Zheng Q, Li X, Zhao X, Wang H, Zhao X, Li X, Yu P, Zang H, Wang Z, Cao X, Zhang J, Pang W, Li J, Yang Y, Dangas GD. Six Versus 12 Months of Dual Antiplatelet Therapy After Implantation of Biodegradable Polymer Sirolimus-Eluting Stent: Randomized Substudy of the I-LOVE-IT 2 Trial. Circ Cardiovasc Interv 2016;**9**(2):e003145.
698. Hong SJ, Shin DH, Kim JS, Kim BK, Ko YG, Choi D, Her AY, Kim YH, Jang Y, Hong MK. 6-Month Versus 12-Month Dual-Antiplatelet Therapy Following Long Everolimus-Eluting Stent Implantation: The IVUS-XPL Randomized Clinical Trial. JACC Cardiovasc Interv 2016;**9**(14):1438-46.
699. Kereiakes DJ, Yeh RW, Massaro JM, Driscoll-Shempp P, Cutlip DE, Steg PG, Gershlick AH, Darius H, Meredith IT, Ormiston J, Tanguay JF, Windecker S, Garratt KN, Kandzari DE, Lee DP, Simon DI, Iancu AC, Trebacz J, Mauri L, for the DAPT Study Investigators. Antiplatelet therapy duration following bare metal or drug-eluting coronary stents: the dual antiplatelet therapy randomized clinical trial. JAMA 2015;**313**(11):1113-21.
700. Kim BK, Hong MK, Shin DH, Nam CM, Kim JS, Ko YG, Choi D, Kang TS, Park BE, Kang WC, Lee SH, Yoon JH, Hong BK, Kwon HM, Jang Y, Investigators R. A new strategy for discontinuation of dual antiplatelet therapy: the RESET Trial (REal Safety and Efficacy of 3-month dual antiplatelet Therapy following Endeavor zotarolimus-eluting stent implantation). J Am Coll Cardiol 2012;**60**(15):1340-8.
701. Feres F, Costa RA, Abizaid A, Leon MB, Marin-Neto JA, Botelho RV, King SB, 3rd, Negoita M, Liu M, de Paula JE, Mangione JA, Meireles GX, Castello HJ, Jr., Nicolela EL, Jr., Perin MA, Devito FS, Labrunie A, Salvadori D, Jr., Gusmao M, Staico R, Costa JR, Jr., de Castro JP, Abizaid AS, Bhatt DL, for the OPTIMIZE Trial investigators. Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: the OPTIMIZE randomized trial. JAMA 2013;**310**(23):2510-22.
702. Palmerini T, Benedetto U, Bacchi-Reggiani L, Riva DD, Biondi-Zoccai G, Feres F, Abizaid A, Hong MK, Kim BK, Jang Y, Kim HS, Park KW, Genereux P, Bhatt DL, Orlandi C, De Servi S, Petrou M, Rapezzi C, Stone GW. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. Lancet 2015.

703. Giustino G, Baber U, Sartori S, Mehran R, Mastoris I, Kini AS, Sharma SK, Pocock SJ, Dangas GD. Duration of dual antiplatelet therapy after drug-eluting stent implantation: a systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol 2015;**65**(13):1298-1310.
704. Navarese EP, Andreotti F, Schulze V, Kolodziejczak M, Buffon A, Brouwer M, Costa F, Kowalewski M, Parati G, Lip GY, Kelm M, Valgimigli M. Optimal duration of dual antiplatelet therapy after percutaneous coronary intervention with drug eluting stents: meta-analysis of randomised controlled trials. BMJ 2015;**350**:h1618.
705. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2007;**357**(20):2001-15.
706. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA, Investigators P, Freij A, Thorsen M. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;**361**(11):1045-57.
707. Eikelboom JW, Anand SS, Malmberg K, Weitz JI, Ginsberg JS, Yusuf S. Unfractionated heparin and low-molecular-weight heparin in acute coronary syndrome without ST elevation: a meta-analysis. Lancet 2000;**355**(9219):1936-42.
708. Cohen M, Mahaffey KW, Pieper K, Pollack CV, Jr., Antman EM, Hoekstra J, Goodman SG, Langer A, Col JJ, White HD, Califf RM, Ferguson JJ. A subgroup analysis of the impact of prerandomization antithrombin therapy on outcomes in the SYNERGY trial: enoxaparin versus unfractionated heparin in non-ST-segment elevation acute coronary syndromes. Journal of the American College of Cardiology 2006;**48**(7):1346-1354.
709. Ferguson JJ, Califf RM, Antman EM, Cohen M, Grines CL, Goodman S, Kereiakes DJ, Langer A, Mahaffey KW, Nessel CC, Armstrong PW, Avezum A, Aylward P, Becker RC, Biasucci L, Borzak S, Col J, Frey MJ, Fry E, Gulba DC, Guneri S, Gurfinkel E, Harrington R, Hochman JS, Kleiman NS, Leon MB, Lopez-Sendon JL, Pepine CJ, Ruzyllo W, Steinhubl SR, Teirstein PS, Toro-Figueroa L, White H. Enoxaparin vs unfractionated heparin in high-risk patients with non-ST-segment elevation acute coronary syndromes managed with an intended early invasive strategy: primary results of the SYNERGY randomized trial. JAMA 2004;**292**(1):45-54.
710. Cavender MA, Sabatine MS. Bivalirudin versus heparin in patients planned for percutaneous coronary intervention: a meta-analysis of randomised controlled trials. Lancet 2014;**384**(9943):599-606.
711. Cassese S, Byrne RA, Laugwitz KL, Schunkert H, Berger PB, Kastrati A. Bivalirudin versus heparin in patients treated with percutaneous coronary intervention: a meta-analysis of randomised trials. EuroIntervention 2015;**11**(2):196-203.
712. Zhang S, Gao W, Li H, Zou M, Sun S, Ba Y, Liu Y, Cheng G. Efficacy and safety of bivalirudin versus heparin in patients undergoing percutaneous coronary intervention: A meta-analysis of randomized controlled trials. Int J Cardiol 2016;**209**:87-95.
713. Erlinge D, Omerovic E, Frobert O, Linder R, Danielewicz M, Hamid M, Swahn E, Henareh L, Wagner H, Hardhammar P, Sjogren I, Stewart J, Grimfjard P, Jensen J, Aasa M, Robertsson L, Lindroos P, Haupt J, Wikstrom H, Ulvenstam A, Bhiladvala P, Lindvall B, Lundin A, Todt T, Ioanes D, Ramunddal T, Kellerth T, Zagozdzon L, Gotberg M, Andersson J, Angeras O, Ostlund O, Lagerqvist B, Held C, Wallentin L, Schersten F, Eriksson P, Koul S, James S. Bivalirudin versus Heparin Monotherapy in Myocardial Infarction. N Engl J Med 2017;**377**(12):1132-1142.
714. Fifth Organization to Assess Strategies in Acute Ischemic Syndromes I, Yusuf S, Mehta SR, Chrolavicius S, Afzal R, Pogue J, Granger CB, Budaj A, Peters RJG, Bassand J-P, Wallentin L, Joyner C, Fox KAA. Comparison of fondaparinux and enoxaparin in acute coronary syndromes. The New England journal of medicine 2006;**354**(14):1464-1476.
715. Boersma E, Harrington RA, Moliterno DJ, White H, Theroux P, Van de Werf F, de Torbal A, Armstrong PW, Wallentin LC, Wilcox RG, Simes J, Califf RM, Topol EJ, Simoons ML. Platelet glycoprotein IIb/IIIa inhibitors in acute coronary syndromes: a meta-analysis of all major randomised clinical trials. Lancet 2002;**359**(9302):189-98.

716. Giugliano RP, White JA, Bode C, Armstrong PW, Montalescot G, Lewis BS, van 't Hof A, Berdan LG, Lee KL, Strony JT, Hildemann S, Veltri E, Van de Werf F, Braunwald E, Harrington RA, Califf RM, Newby LK, Investigators EA. Early versus delayed, provisional eptifibatide in acute coronary syndromes. N Engl J Med 2009;**360**(21):2176-90.
717. Stone GW, McLaurin BT, Cox DA, Bertrand ME, Lincoff AM, Moses JW, White HD, Pocock SJ, Ware JH, Feit F, Colombo A, Aylward PE, Cequier AR, Darius H, Desmet W, Ebrahimi R, Hamon M, Rasmussen LH, Rupprecht HJ, Hoekstra J, Mehran R, Ohman EM, Investigators A. Bivalirudin for patients with acute coronary syndromes. N Engl J Med 2006;**355**(21):2203-16.
718. Hahn JY, Song YB, Oh JH, Cho DK, Lee JB, Doh JH, Kim SH, Jeong JO, Bae JH, Kim BO, Cho JH, Suh IW, Kim DI, Park HK, Park JS, Choi WG, Lee WS, Kim J, Choi KH, Park TK, Lee JM, Yang JH, Choi JH, Choi SH, Gwon HC, investigators S-D. 6-month versus 12-month or longer dual antiplatelet therapy after percutaneous coronary intervention in patients with acute coronary syndrome (SMART-DATE): a randomised, open-label, non-inferiority trial. Lancet 2018.
719. Cuisset T, Deharo P, Quilici J, Johnson TW, Deffarges S, Bassez C, Bonnet G, Fourcade L, Mouret JP, Lambert M, Verdier V, Morange PE, Alessi MC, Bonnet JL. Benefit of switching dual antiplatelet therapy after acute coronary syndrome: the TOPIC (timing of platelet inhibition after acute coronary syndrome) randomized study. Eur Heart J 2017;**38**(41):3070-3078.
720. Sibbing D, Aradi D, Jacobshagen C, Gross L, Trenk D, Geisler T, Orban M, Hadamitzky M, Merkely B, Kiss RG, Komocsi A, Dezsi CA, Holdt L, Felix SB, Parma R, Klopotowski M, Schwinger RHG, Rieber J, Huber K, Neumann FJ, Koltowski L, Mehilli J, Huczek Z, Massberg S, Investigators T-A. Guided de-escalation of antiplatelet treatment in patients with acute coronary syndrome undergoing percutaneous coronary intervention (TROPICAL-ACS): a randomised, open-label, multicentre trial. Lancet 2017;**390**(10104):1747-1757.
721. Angiolillo DJ, Rollini F, Storey RF, Bhatt DL, James S, Schneider DJ, Sibbing D, So DYF, Trenk D, Alexopoulos D, Gurbel PA, Hochholzer W, De Luca L, Bonello L, Aradi D, Cuisset T, Tantry US, Wang TY, Valgimigli M, Waksman R, Mehran R, Montalescot G, Franchi F, Price MJ. International Expert Consensus on Switching Platelet P2Y12 Receptor-Inhibiting Therapies. Circulation 2017;**136**(20):1955-1975.
722. Grines CL, Bonow RO, Casey DE, Jr., Gardner TJ, Lockhart PB, Moliterno DJ, O'Gara P, Whitlow P, American Heart A, American College of C, Society for Cardiovascular A, Interventions, American College of S, American Dental A, American College of P. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. Circulation 2007;**115**:813-8.
723. Mega JL, Braunwald E, Wiviott SD, Bassand JP, Bhatt DL, Bode C, Burton P, Cohen M, Cook-Bruns N, Fox KA, Goto S, Murphy SA, Plotnikov AN, Schneider D, Sun X, Verheugt FW, Gibson CM, Investigators AAT. Rivaroxaban in patients with a recent acute coronary syndrome. N Engl J Med 2012;**366**(1):9-19.
724. Patrono C, Andreotti F, Arnesen H, Badimon L, Baigent C, Collet JP, De Caterina R, Gulba D, Huber K, Husted S, Kristensen SD, Morais J, Neumann FJ, Rasmussen LH, Siegbahn A, Steg PG, Storey RF, Van de Werf F, F V. Antiplatelet agents for the treatment and prevention of atherothrombosis. Eur Heart J 2011;**32(23)**:2922-32.
725. Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, Natarajan MK, Malmberg K, Rupprecht H, Zhao F, Chrolavicius S, Copland I, Fox KA, Clopidogrel in Unstable angina to prevent Recurrent Events trial I. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. Lancet 2001;**358**(9281):527-33.
726. Mehta S, Tanguay JF, Eikelboom JW, Jolly SS, Joyner CD, Granger CB, Faxon DP, Rupprecht HJ, Budaj A, Avezum A, Widimsky P, Steg PG, Bassand JP, Montalescot G, Macaya C, Di Pasquale G, Niemela K, Ajani AE, White HD, Chrolavicius S, Gao P, Fox KAA, Yusuf S, on behalf of the CI. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals

undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. Lancet 2010;**376**:1233-43.
727. Oler A, Whooley MA, Oler J, Grady D. Adding heparin to aspirin reduces the incidence of myocardial infarction and death in patients with unstable angina. A meta-analysis. JAMA 1996;**276**(10):811-5.
728. Group FO-T, Steg PG, Jolly SS, Mehta SR, Afzal R, Xavier D, Rupprecht HJ, Lopez-Sendon JL, Budaj A, Diaz R, Avezum A, Widimsky P, Rao SV, Chrolavicius S, Meeks B, Joyner C, Pogue J, Yusuf S. Low-dose vs standard-dose unfractionated heparin for percutaneous coronary intervention in acute coronary syndromes treated with fondaparinux: the FUTURA/OASIS-8 randomized trial. JAMA 2010;**304**(12):1339-49.
729. Valgimigli M, Frigoli E, Leonardi S, Rothenbuhler M, Gagnor A, Calabro P, Garducci S, Rubartelli P, Briguori C, Ando G, Repetto A, Limbruno U, Garbo R, Sganzerla P, Russo F, Lupi A, Cortese B, Ausiello A, Ierna S, Esposito G, Presbitero P, Santarelli A, Sardella G, Varbella F, Tresoldi S, de Cesare N, Rigattieri S, Zingarelli A, Tosi P, van 't Hof A, Boccuzzi G, Omerovic E, Sabate M, Heg D, Juni P, Vranckx P, Investigators M. Bivalirudin or Unfractionated Heparin in Acute Coronary Syndromes. N Engl J Med 2015;**373**(11):997-1009.
730. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK, Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;**345**(7):494-502.
731. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA, for the PLATO Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;**361**(11):1045-57.
732. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson CM, Antman EM, for the TRITON TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2007;**357**(20):2001-15.
733. Palmerini T, Della Riva D, Benedetto U, Reggiani LB, Feres F, Abizaid A, Gilard M, Morice M, Valgimigli M, Hong M, Kim B, Jang Y, Kim H, Park KW, Colombo A, Chieffo A, Sangiorgi D, Biondi-Zoccai G, Genereux P, Angelini GD, White, Bhatt DL, Stone GW. Three, six or twelve months of dual antiplatelet therapy after drug-eluting stent implantation in patients with or without acute coronary syndromes: an individual patient data pairwise and network meta-analysis of six randomized trials and 11,473 patients. Eur Heart J 2016:ehw627.
734. Costa F, van Klaveren D, James S, Heg D, Raber L, Feres F, Pilgrim T, Hong MK, Kim HS, Colombo A, Steg G, Zanchin T, Palmerini T, Wallentin L, Bhatt DL, Stone GW, Windecker S, Steyerberg EW, Valgimigli M. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet 2017;**389**.
735. Mauri L, Kereiakes DJ, Yeh RW, Driscoll-Shempp P, Cutlip DE, Steg PG, Normand SL, Braunwald E, Wiviott SD, Cohen DJ, Holmes DR, Jr., Krucoff MW, Hermiller J, Dauerman HL, Simon DI, Kandzari DE, Garratt KN, Lee DP, Pow TK, Ver Lee P, Rinaldi MJ, Massaro JM, for the DAPT Study Investigators. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014;**371**(23):2155-66.
736. Bonaca MP, Bhatt DL, Steg PG, Storey RF, Cohen M, Im K, Oude Ophuis T, Budaj A, Goto S, Lopez-Sendon J, Diaz R, Dalby A, Van de Werf F, Ardissino D, Montalescot G, Aylward P, Magnani G, Jensen EC, Held P, Braunwald E, Sabatine MS. Ischaemic risk and efficacy of ticagrelor in relation to time from P2Y12 inhibitor withdrawal in patients with prior myocardial infarction: insights from PEGASUS-TIMI 54. Eur Heart J 2016;**37**(14):1133-42.
737. Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Oude Ophuis T, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS, for the PEGASUS-TIMI 54 Steering Committee and Investigators. Long-term use of ticagrelor in patients with prior myocardial infarction. N Engl J Med 2015;**372**(19):1791-800.

738. Costa F, Adamo M, Ariotti S, Navarese EP, Biondi-Zoccai G, Valgimigli M. Impact of greater than 12-month dual antiplatelet therapy duration on mortality: Drug-specific or a class-effect? A meta-analysis. Int J Cardiol 2015;**201**:179-81.
739. Hermiller JB, Krucoff MW, Kereiakes DJ, Windecker S, Steg PG, Yeh RW, Cohen DJ, Cutlip DE, Massaro JM, Hsieh WH, Mauri L, for the DAPT Study Investigators. Benefits and Risks of Extended Dual Antiplatelet Therapy After Everolimus-Eluting Stents. JACC Cardiovasc Interv 2016;**9**(2):138-47.
740. Motovska Z, Hlinomaz O, Miklik R, Hromadka M, Varvarovsky I, Dusek J, Knot J, Jarkovsky J, Kala P, Rokyta R, Tousek F, Kramarikova P, Majtan B, Simek S, Branny M, Mrozek J, Cervinka P, Ostransky J, Widimsky P. Prasugrel versus Ticagrelor in Patients with Acute Myocardial Infarction Treated with Primary Percutaneous Coronary Intervention: Multicenter Randomized PRAGUE-18 Study. Circulation 2016.
741. Montalescot G, van 't Hof AW, Lapostolle F, Silvain J, Lassen JF, Bolognese L, Cantor WJ, Cequier A, Chettibi M, Goodman SG, Hammett CJ, Huber K, Janzon M, Merkely B, Storey RF, Zeymer U, Stibbe O, Ecollan P, Heutz WM, Swahn E, Collet JP, Willems FF, Baradat C, Licour M, Tsatsaris A, Vicaut E, Hamm CW, Investigators A. Prehospital ticagrelor in ST-segment elevation myocardial infarction. N Engl J Med 2014;**371**(11):1016-27.
742. Montalescot G, Zeymer U, Silvain J, Boulanger B, Cohen M, Goldstein P, Ecollan P, Combes X, Huber K, Pollack C, Jr., Benezet JF, Stibbe O, Filippi E, Teiger E, Cayla G, Elhadad S, Adnet F, Chouihed T, Gallula S, Greffet A, Aout M, Collet JP, Vicaut E, Investigators A. Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction: the international randomised open-label ATOLL trial. Lancet 2011;**378**(9792):693-703.
743. Montalescot G, Barragan P, Wittenberg O, Ecollan P, Elhadad S, Villain P, Boulenc JM, Morice MC, Maillard L, Pansieri M, Choussat R, Pinton P, Angioplasty AIAbD, Stenting in Myocardial Infarction Regarding A, Long-Term F-u. Platelet glycoprotein IIb/IIIa inhibition with coronary stenting for acute myocardial infarction. N Engl J Med 2001;**344**(25):1895-903.
744. Stone GW, Grines CL, Cox DA, Garcia E, Tcheng JE, Griffin JJ, Guagliumi G, Stuckey T, Turco M, Carroll JD, Rutherford BD, Lansky AJ, Controlled A, Device Investigation to Lower Late Angioplasty Complications I. Comparison of angioplasty with stenting, with or without abciximab, in acute myocardial infarction. N Engl J Med 2002;**346**(13):957-66.
745. De Luca G, Navarese E, Marino P. Risk profile and benefits from Gp IIb-IIIa inhibitors among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: a meta-regression analysis of randomized trials. Eur Heart J 2009;**30**(22):2705-13.
746. Ellis SG, Tendera M, de Belder MA, van Boven AJ, Widimsky P, Janssens L, Andersen HR, Betriu A, Savonitto S, Adamus J, Peruga JZ, Kosmider M, Katz O, Neunteufl T, Jorgova J, Dorobantu M, Grinfeld L, Armstrong P, Brodie BR, Herrmann HC, Montalescot G, Neumann FJ, Effron MB, Barnathan ES, Topol EJ, Investigators F. Facilitated PCI in patients with ST-elevation myocardial infarction. N Engl J Med 2008;**358**(21):2205-17.
747. Van't Hof AW, Ten Berg J, Heestermans T, Dill T, Funck RC, van Werkum W, Dambrink JH, Suryapranata H, van Houwelingen G, Ottervanger JP, Stella P, Giannitsis E, Hamm C, Ongoing Tirofiban In Myocardial infarction Evaluation 2 study g. Prehospital initiation of tirofiban in patients with ST-elevation myocardial infarction undergoing primary angioplasty (On-TIME 2): a multicentre, double-blind, randomised controlled trial. Lancet 2008;**372**(9638):537-46.
748. Herrmann HC, Lu J, Brodie BR, Armstrong PW, Montalescot G, Betriu A, Neuman F-J, Effron MB, Barnathan ES, Topol EJ, Ellis SG, Investigators F. Benefit of facilitated percutaneous coronary intervention in high-risk ST-segment elevation myocardial infarction patients presenting to nonpercutaneous coronary intervention hospitals. JACC Cardiovascular interventions 2009;**2**(10):917-924.
749. Steg PG, James S, Harrington RA, Ardissino D, Becker RC, Cannon CP, Emanuelsson H, Finkelstein A HS, Katus H, Kilhamn J, Olofsson S, Storey RF, Weaver WD, Wallentin L, for the PSG. Ticagrelor Versus Clopidogrel in Patients With ST-Elevation Acute Coronary Syndromes Intended for Reperfusion With Primary Percutaneous Coronary Intervention: A Platelet Inhibition and Patient Outcomes (PLATO) Trial Subgroup Analysis. Circulation 2010;**122(21)**:2131-2141.

750. Steg PG, van 't Hof A, Hamm CW, Clemmensen P, Lapostolle F, Coste P, Ten Berg J, Van Grunsven P, Eggink GJ, Nibbe L, Zeymer U, Campo dell' Orto M, Nef H, Steinmetz J, Soulat L, Huber K, Deliargyris EN, Bernstein D, Schuette D, Prats J, Clayton T, Pocock S, Hamon M, Goldstein P, Investigators E. Bivalirudin started during emergency transport for primary PCI. N Engl J Med 2013;**369**(23):2207-17.
751. Stone GW, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Kornowski R, Hartmann F, Gersh BJ, Pocock SJ, Dangas G, Wong SC, Kirtane AJ, Parise H, Mehran R, Investigators H-AT. Bivalirudin during primary PCI in acute myocardial infarction. N Engl J Med 2008;**358**(21):2218-30.
752. Shahzad A, Kemp I, Mars C, Wilson K, Roome C, Cooper R, Andron M, Appleby C, Fisher M, Khand A, Kunadian B, Mills JD, Morris JL, Morrison WL, Munir S, Palmer ND, Perry RA, Ramsdale DR, Velavan P, Stables RH, investigators H-Pt. Unfractionated heparin versus bivalirudin in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. Lancet 2014;**384**(9957):1849-58.
753. Hansson EC, Jideus L, Aberg B, Bjursten H, Dreifaldt M, Holmgren A, Ivert T, Nozohoor S, Barbu M, Svedjeholm R, Jeppsson A. Coronary artery bypass grafting-related bleeding complications in patients treated with ticagrelor or clopidogrel: a nationwide study. Eur Heart J 2016;**37**(2):189-97.
754. Tomsic A, Schotborgh MA, Manshanden JS, Li WW, de Mol BA. Coronary artery bypass grafting-related bleeding complications in patients treated with dual antiplatelet treatment. Eur J Cardiothorac Surg 2016;**50**(5):849-856.
755. Gherli R, Mariscalco G, Dalen M, Onorati F, Perrotti A, Chocron S, Verhoye JP, Gulbins H, Reichart D, Svenarud P, Faggian G, Santarpino G, Fischlein T, Maselli D, Dominici C, Musumeci F, Rubino AS, Mignosa C, De Feo M, Bancone C, Gatti G, Maschietto L, Santini F, Nicolini F, Gherli T, Zanobini M, Kinnunen EM, Ruggieri VG, Rosato S, Biancari F. Safety of Preoperative Use of Ticagrelor With or Without Aspirin Compared With Aspirin Alone in Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Grafting. JAMA Cardiol 2016;**1**(8):921-928.
756. Kwak YL, Kim JC, Choi YS, Yoo KJ, Song Y, Shim JK. Clopidogrel responsiveness regardless of the discontinuation date predicts increased blood loss and transfusion requirement after off-pump coronary artery bypass graft surgery. J Am Coll Cardiol 2010;**56**(24):1994-2002.
757. Ranucci M, Baryshnikova E, Soro G, Ballotta A, De Benedetti D, Conti D, Surgical, Clinical Outcome Research G. Multiple electrode whole-blood aggregometry and bleeding in cardiac surgery patients receiving thienopyridines. Ann Thorac Surg 2011;**91**(1):123-9.
758. Ranucci M, Colella D, Baryshnikova E, Di Dedda U, Surgical, Clinical Outcome Research G. Effect of preoperative P2Y12 and thrombin platelet receptor inhibition on bleeding after cardiac surgery. Br J Anaesth 2014;**113**(6):970-6.
759. Lamberts M, Gislason GH, Olesen JB, Kristensen SL, Schjerning Olsen AM, Mikkelsen A, Christensen CB, Lip GY, Kober L, Torp-Pedersen C, Hansen ML. Oral anticoagulation and antiplatelets in atrial fibrillation patients after myocardial infarction and coronary intervention. J Am Coll Cardiol 2013;**62**(11):981-9.
760. Dewilde WJ, Oirbans T, Verheugt FW, Kelder JC, De Smet BJ, Herrman JP, Adriaenssens T, Vrolix M, Heestermans AA, Vis MM, Tijsen JG, van 't Hof AW, ten Berg JM, investigators Ws. Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial. Lancet 2013;**381**(9872):1107-15.
761. Fiedler KA, Maeng M, Mehilli J, Schulz-Schupke S, Byrne RA, Sibbing D, Hoppmann P, Schneider S, Fusaro M, Ott I, Kristensen SD, Ibrahim T, Massberg S, Schunkert H, Laugwitz KL, Kastrati A, Sarafoff N. Duration of Triple Therapy in Patients Requiring Oral Anticoagulation After Drug-Eluting Stent Implantation: The ISAR-TRIPLE Trial. J Am Coll Cardiol 2015;**65**(16):1619-29.
762. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt FW, Wildgoose P, Birmingham M, Ianus J, Burton P, van Eickels M, Korjian S, Daaboul Y, Lip GY, Cohen M, Husted S, Peterson ED, Fox KA. Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI. N Engl J Med 2016;**375**(25):2423-2434.
763. Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T, Maeng M, Merkely B, Zeymer U, Gropper S, Nordaby M, Kleine E, Harper R, Manassie J, Januzzi JL, Ten Berg JM, Steg PG, Hohnloser

SH, Committee R-DPS, Investigators. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. N Engl J Med 2017;**377**(16):1513-1524.
764. Post PN, Kuijpers M, Ebels T, Zijlstra F. The relation between volume and outcome of coronary interventions: a systematic review and meta-analysis. Eur Heart J 2010;**31**(16):1985-92.
765. Kim LK, Looser P, Feldman DN. Peri- and postoperative care after coronary artery bypass grafting in low versus high volume centers. J Thorac Cardiovasc Surg 2016;**152**(4):1205.
766. Kim LK, Looser P, Swaminathan RV, Minutello RM, Wong SC, Girardi L, Feldman DN. Outcomes in patients undergoing coronary artery bypass graft surgery in the United States based on hospital volume, 2007 to 2011. J Thorac Cardiovasc Surg 2016;**151**(6):1686-92.
767. Gonzalez AA, Dimick JB, Birkmeyer JD, Ghaferi AA. Understanding the volume-outcome effect in cardiovascular surgery: the role of failure to rescue. JAMA Surg 2014;**149**(2):119-23.
768. Birkmeyer JD, Stukel TA, Siewers AE, Goodney PP, Wennberg DE, Lucas FL. Surgeon volume and operative mortality in the United States. N Engl J Med 2003;**349**(22):2117-27.
769. Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A, Papadimos TJ, Engoren M, Habib RH. Is hospital procedure volume a reliable marker of quality for coronary artery bypass surgery? A comparison of risk and propensity adjusted operative and midterm outcomes. Ann Thorac Surg 2005;**79**(6):1961-9.
770. Kurlansky PA, Argenziano M, Dunton R, Lancey R, Nast E, Stewart A, Williams T, Zapolanski A, Chang H, Tingley J, Smith CR. Quality, not volume, determines outcome of coronary artery bypass surgery in a university-based community hospital network. J Thorac Cardiovasc Surg 2012;**143**(2):287-93.
771. Auerbach AD, Hilton JF, Maselli J, Pekow PS, Rothberg MB, Lindenauer PK. Shop for quality or volume? Volume, quality, and outcomes of coronary artery bypass surgery. Ann Intern Med 2009;**150**(10):696-704.
772. Pagano D, Kappetein AP, Sousa-Uva M, Beyersdorf F, Klautz R, Mohr F, Falk V, European Association for Cardio-Thoracic S, the EQIP. EACTS clinical statement: guidance for the provision of adult cardiac surgery. Eur J Cardiothorac Surg 2016;**50**(6):1006-1009.
773. Hannan EL, Wu C, Walford G, King SB, 3rd, Holmes DR, Jr., Ambrose JA, Sharma S, Katz S, Clark LT, Jones RH. Volume-outcome relationships for percutaneous coronary interventions in the stent era. Circulation 2005;**112**(8):1171-9.
774. McGrath PD, Wennberg DE, Dickens JD, Jr., Siewers AE, Lucas FL, Malenka DJ, Kellett MA, Jr., Ryan TJ, Jr. Relation between operator and hospital volume and outcomes following percutaneous coronary interventions in the era of the coronary stent. JAMA 2000;**284**(24):3139-44.
775. Nallamothu BK, Wang Y, Magid DJ, McNamara RL, Herrin J, Bradley EH, Bates ER, Pollack CV, Jr., Krumholz HM. Relation between hospital specialization with primary percutaneous coronary intervention and clinical outcomes in ST-segment elevation myocardial infarction: National Registry of Myocardial Infarction-4 analysis. Circulation 2006;**113**(2):222-9.
776. Spaulding C, Morice MC, Lancelin B, El Haddad S, Lepage E, Bataille S, Tresca JP, Mouranche X, Fosse S, Monchi M, de Vernejoul N. Is the volume-outcome relation still an issue in the era of PCI with systematic stenting? Results of the greater Paris area PCI registry. Eur Heart J 2006;**27**(9):1054-60.
777. Vakili BA, Kaplan R, Brown DL. Volume-outcome relation for physicians and hospitals performing angioplasty for acute myocardial infarction in New York state. Circulation 2001;**104**(18):2171-6.
778. Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD, French WJ, Tiefenbrunn AJ, Misra VK, Kiefe CI, Barron HV. The volume of primary angioplasty procedures and survival after acute myocardial infarction. National Registry of Myocardial Infarction 2 Investigators. N Engl J Med 2000;**342**(21):1573-80.
779. Xu B, Redfors B, Yang Y, Qiao S, Wu Y, Chen J, Liu H, Chen J, Xu L, Zhao Y, Guan C, Gao R, Genereux P. Impact of Operator Experience and Volume on Outcomes After Left Main Coronary Artery Percutaneous Coronary Intervention. JACC Cardiovasc Interv 2016;**9**(20):2086-2093.
780. Di Mario C, Di Sciascio G, Dubois-Rande JL, Michels R, Mills P. Curriculum and syllabus for Interventional Cardiology subspecialty training in Europe. EuroIntervention 2006;**2**(1):31-6.

781. Anderson L, Oldridge N, Thompson DR, Zwisler AD, Rees K, Martin N, Taylor RS. Exercise-Based Cardiac Rehabilitation for Coronary Heart Disease: Cochrane Systematic Review and Meta-Analysis. J Am Coll Cardiol 2016;**67**(1):1-12.
782. Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. Ann Intern Med 2005;**143**(9):659-72.
783. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. JAMA 2003;**290**(1):86-97.
784. Estruch R, Ros E, Salas-Salvado J, Covas MI, Corella D, Aros F, Gomez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pinto X, Basora J, Munoz MA, Sorli JV, Martinez JA, Martinez-Gonzalez MA, Investigators PS. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013;**368**(14):1279-90.
785. Cholesterol Treatment Trialists C, Baigent C, Blackwell L, Emberson J, Holland LE, Reith C, Bhala N, Peto R, Barnes EH, Keech A, Simes J, Collins R. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet 2010;**376**(9753):1670-81.
786. Patrono C, Morais J, Baigent C, Collet JP, Fitzgerald D, Halvorsen S, Rocca B, Siegbahn A, Storey RF, Vilahur G. Antiplatelet Agents for the Treatment and Prevention of Coronary Atherothrombosis. J Am Coll Cardiol 2017;**70**(14):1760-1776.
787. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016;**387**(10022):957-967.
788. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, Golden SH. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004;**141**(6):421-31.
789. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;**352**(9131):854-65.
790. Harb SC, Marwick TH. Prognostic value of stress imaging after revascularization: a systematic review of stress echocardiography and stress nuclear imaging. Am Heart J 2014;**167**(1):77-85.