Temporal patterns, characteristics, and predictors of clinical outcomes in patients undergoing percutaneous coronary intervention for stent thrombosis

Running title: Outcomes of PCI for stent thrombosis

Mohamed O. Mohamed, PhD[1], Alex Sirker, PhD[2], Alaide Chieffo, MD[3], Pablo Avanzas, MD, PhD[4], James Nolan, MD[5], Muhammad Rashid, MRCP[1,5], Mohamed Dafaalla, MRCP [1,5], Saadiq Moledina, MRCP(UK)[1,5], Peter Ludman, MD[6], Tim Kinnaird, MD[7], Mamas A. Mamas, DPhil[1,5]

1. Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, United Kingdom
2. Department of Cardiology, University College London Hospitals NHS Foundation Trust, London, United Kingdom
3. Department of Cardiology, San Raffaele Hospital, Milan, Italy
4. Department of Cardiology, Hospital Universitario Central de Asturias, Oviedo, Spain
5. Department of Cardiology, Royal Stoke University Hospital, Stoke-on-Trent, United Kingdom
6. Institute of Cardiovascular Sciences, University of Birmingham, United Kingdom
7. Department of Cardiology, University Hospital of Wales, Cardiff, UK

Correspondence to:

Mamas A. Mamas
Professor of Cardiology
Keele Cardiovascular Research Group,
Centre for Prognosis Research,
Institute for Primary Care and Health Sciences,
Keele University, UK
mamasmamas1@yahoo.co.uk

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Head and shoulder portrait of the first author (300 DPI)

Abstract

Background: There are limited data on the outcomes of PCI following stent thrombosis (ST) and differences exist based on timing.

Aim: To study the rates and characteristics of patients with a ST indication for PCI and compare procedural outcomes based on ST timing.

Methods: All PCI procedures in England and Wales (2014-2020) were retrospectively analysed, stratified by the presence of ST, into four groups: non-ST, early-ST:0-30 days, late-ST:>30-360 days, very late-ST:>360 days. Multivariable logistic regression models were performed to assess the odds ratios (OR) of in-hospital MACCE (major acute cardiovascular and cerebrovascular complications; composite of mortality, acute stroke and reinfarction) and mortality.

Results: Overall, 7,923 (1.4%) procedures were for ST indication, most commonly for early-ST (n=4,171, 52.6%) followed by very late-ST (n=2,801, 35.4%) and late-ST (n=951, 12.0%). The rate of PCI for ST declined between 2014 and 2020 (1.7 to 1.4%, $p<0.001$). Early-ST was the only subgroup associated with increased odds of MACCE (1.22 95%CI 1.05-1.41), all-cause mortality (1.21 95%CI 1.07-1.36) and reinfarction (2.48 95%CI 1.48-4.14), compared with non-ST indication. The odds of mortality were significantly reduced in ST patients with the use of intravascular imaging (0.66 95%CI 0.48-0.92) and newer P2Y12 inhibitors (ticagrelor: 0.69 95%CI 0.49-0.95; prasugrel: 0.54 95%CI 0.30-0.96).

Conclusion: PCI for ST has declined in frequency over a 7-year period, with most procedures performed for early-ST. Among the different times of ST onset, only early-ST is associated with worse clinical outcomes after PCI. Routine use of intravascular imaging and newer P2Y12 inhibitors could further improve outcomes in this high-risk procedural group.

Condensed Abstract (112 words)

Limited data exists around the frequency and outcomes of PCI for ST of different time onset compared with non-ST PCI. The present study of all PCI procedures nationally for ACS (2014-2020) shows that PCI for ST indication has declined over 7 years with the most common subtype being early ST. Only early ST was associated with higher risk of in-hospital mortality and reinfarction, while late and very late ST had similar outcomes compared with non-ST PCI. Certain factors were associated with better outcomes among the ST groups including the use of intravascular imaging (IVUS/OCT) and newer P2Y12 inhibitors. However, intravascular imaging was only utilised in up to a third of ST cases.

Introduction

Percutaneous coronary intervention (PCI) is the most common means of coronary revascularisation.[1, 2] A rare yet serious complication of PCI is stent thrombosis (ST), which can occur at different time points post-procedure, ranging in onset from acute (0-24h) to subacute (24h-30 days), late (31-360 days) and very late (>360 days).[3] The incidence of ST is estimated be up to 1% within the first year, declining to rates between 0.2% and 0.4% thereafter. [4-7] Risk factors for ST differ according to time of onset, as does the overall prognosis.[8]

ST often presents with an acute myocardial infarction (AMI) and requires urgent PCI[9], although there are limited data around the characteristics, management and outcomes of these patients when undergoing PCI, and whether this varies according to the timing of ST in relation to the index PCI. Furthermore, whilst patients suffering ST have been shown to be at a very high risk of mortality, little is known about the predictors of in-hospital adverse outcomes.[10, 11] Finally, there are limited data around the frequency of PCI for ST from a national perspective and whether this has changed in recent years, commensurate with advances in stent platforms, procedural techniques (e.g. use of intracoronary imaging), and the greater use of newer P2Y12 inhibitors.[12-14]

The present study sought to examine the rates, characteristics and in-hospital outcomes in patients presenting with ST undergoing PCI, compared with PCI for non-ST indication, with further stratification according to different timing of ST onset, in a nationwide cohort of PCI procedures in England and Wales between April 2014 and March 2020.

Methods

Data Source, Study Design and Population

All adult (aged ≥18 years) PCI procedures for acute coronary syndrome (ACS) between 1st April 2014 and 31st March 2020 in England and Wales were retrospectively analysed from

the British Cardiovascular Intervention Society (BCIS) registry, stratified by indication for PCI into two groups: ST and no-ST. Further stratification was performed based on the timing of ST from index PCI: early (0-30 days), late (>30 days to 360 days) and very late (>360 days). The BCIS registry comprises clinical and procedural data, and in-hospital outcomes (death, bleeding, arterial complications) for all procedures undertaken in the England and Wales.[15, 16] There were no specified exclusion criteria except missing data for death (n=14,150, 2.4% of the original cohort) and stent thrombosis (n=18,008, 3.0% of the original cohort). (**see Supplementary Figure 1 for study flow diagram**)

Outcomes

The main outcomes were in-hospital major adverse cardiovascular and cerebrovascular events (MACCE; composite of death, acute stroke/transient ischaemic attack and reinfarction), all-cause mortality and bleeding academic research consortium (BARC) stage 3-5 bleeding, as per the standard definition.[17]

Statistical Analysis

Patient and procedural characteristics of patients undergoing PCI for ACS were compared according to indication (ST and no-ST) and further by timing of ST (Early ST, Late ST and Very Late) as part of the exploratory analysis. Continuous variables were normally distributed and therefore presented as mean values with standard deviation (SD), compared using the t-test. Categorical variables are summarised as percentages and analysed using the chi squared (X^2) test. Multivariable logistic regression models were performed to 1) assess the association between ST (overall and different onsets) and in-hospital adverse outcomes, namely MACCE, mortality, BARC 3-5 bleeding and acute stroke, and 2) examine predictors of in-hospital adverse outcomes among patients undergoing PCI for ST indication. All associations are reported as odds ratios (OR) with corresponding 95% confidence intervals (CI).

Variables adjusted for in the models included: age, sex, race, clinical syndrome (ST-elevation myocardial infarction (STEMI) vs. non-STEMI), previous AMI, previous PCI, previous coronary artery bypass graft surgery (CABG), previous non coronary surgery, diabetes mellitus, renal failure (Creatinine > 200 µmol/l and/or dialysis), cardiac transplant, family history of ischaemic heart disease (IHD), left ventricular (LV) function, hypercholesterolaemia, peripheral vascular disease (PVD), previous cerebrovascular accident (CVA; stroke or transient ischaemic attack), hypertension, smoking, valvular heart disease (VHD), out of hospital cardiac arrest (OHCA), mechanical ventilation, circulatory support (intra-aortic balloon pump or LV assist device), vascular access (radial vs. femoral), number of vessels and lesions attempted, number of stents, drug eluting stent (DES), DES stent generation (1^{st} vs. $2^{nd}/3^{rd}$ generation), use of fractional flow reserve (FFR), intravascular imaging (intravascular ultrasound (IVUS) or optimal coherence tomography (OCT)) or calcium modification (rotablation, laser angioplasty), vessel attempted (prognostic targets: left main stem (LMS), proximal left anterior descending (LAD), graft), and in-hospital pharmacotherapy (aspirin, clopidogrel, ticagrelor, prasugrel, warfarin, glycoprotein IIb/IIIa inhibitor (GP-2b3a), bivalirudin).

Multiple imputation with chained equations was performed for variables with missing data (except ST and death) prior to model fitting, with a total of 10 imputations. Model estimates were later combined using Rubin's rules.[18] All statistical analyses were performed using Stata 16 MP (College Station, TX).

Results

A total of 571,949 procedures performed in England and Wales between 1^{st} April 2014 and 31^{st} March 2020, of which 351,735 (61.5%) were for an ACS indication. Among those with ACS, 7,923 cases (~1.4% of total cohort, 2.3% of ACS cohort) were for ST indication

including 4,171 (52.6%) cases for early ST, 951 (12.0%) cases for late ST, and 2,801 (35.4%) cases for very Late ST. Both the rate and frequency of ST among all PCI indications decreased over the study period in the overall cohort (**2014 to 2020**; rate: 1.7% to 1.4%, frequency: 2.4 to 2.2 per 100,000 population, p_{trend} <0.01 for both). (**Figure 1**) Similar findings were observed in both sexes, although ST indication was more frequent in males than females throughout the study period (**2014 to 2020**: rate: 1.8% to 1.5% for males, 1.3% to 1.0% for females; frequency: 3.8 to 3.6 per 100,000 population for males and 1.0 to 0.8 per 100,000 population for females, $p_{trend} \leq 0.01$ for all). The frequency of ST per 100,000 population was also higher among those aged >60 years throughout the study period.

Patient characteristics

Several differences in patient characteristics were observed between patients undergoing PCI for non-ST indication and ST indication of different time of onset. (**Table 1**) Patients with an ST indication were general younger (mean age 64.6 to 64.9 years vs. 65.4 years) and were more likely to be males (74.2 to 81.2% vs. 73.0%), from non-White background (White: 77.7 to 84.7% vs. 85.0%) and to present with STEMI (46.8 to 74.7% vs. 40.0%). ST patients had a higher prevalence of renal failure (2.7 to 7.8% vs. 2.4%), especially in the Late ST group (7.8%), as well as diabetes mellitus (25.3 to 38.0% vs. 22.0%), hypertension (53.7 to 68.8% vs. 51.5%), PVD (4.5 to 8.7% vs. 3.9%), hypercholesterolaemia (51.4 to 66.0% vs. 43.9%) and previous CVA (4.4 to 8.8% vs. 4.1%) and MI (45.7 to 82.1% vs. 19.3%). ST patients were also more likely to have LV impairment (Good LV function: 46.9 to 59.8% vs. 61.7%), experience out of hospital cardiac arrest (Early ST: 6.7% and Very Late ST 5.5% vs. 4.5% for non-ST) as well as pre-procedure cardiogenic shock (7.0 to 11.0% vs. 4.2%).

Procedural characteristics

Patients with an ST indication for PCI were more likely to require mechanical ventilation (3.3 to 6.0% vs. 3.1%), circulatory support (4.2 to 6.1% vs. 2.4%), and femoral access for intervention (26.4 to 38.2% vs. 17.2%) compared with the non-ST indication group. Procedures for patients with Early ST and Very Late ST more commonly involved the proximal LAD (31.4 and 32.8%, respectively vs. 29.9%) while those with Late ST were more likely to undergo a LMS intervention (8.0%). The utilisation of IVUS/OCT was significantly higher in patients with an ST indication (21.5 to 30.5% vs. 8.4%). Patients with ST indication were less likely to receive DES (54.3 to 66.9% vs. 84.6%) and more likely to be managed with drug coated balloons (0.4 to 1.8% vs. 0.2%) compared with those with a non-ST indication. Patients with an ST indication were more also likely to receive intraprocedural GP-2b3a inhibitor (34.2 to 46.4% vs. 19.8%) as well as newer P2Y12 agents such as prasugrel (6.6 to 8.2% vs. 4.8%) and ticagrelor (42.9 to 47.9% vs. 41.9%) as part of their antithrombotic regime.

Similar patterns in patient and procedural characteristic were observed between the overall ST indication and non-ST indication groups. (**Supplementary Table 1**)

In-hospital outcomes

Overall, patients undergoing PCI for a ST indication experienced higher crude rates of MACCE (6.4% vs. 3.5%) compared with non-ST indication PCI, (**Supplementary Table 2**) a pattern that was consistent across all ST time onset groups and highest in the Early ST group (Early: 8.1%, Late: 4.8%, Very Late: 4.0%). (**Table 2, Figure 2**) This was primarily driven by higher all-cause mortality (Overall ST: 5.7%, Early ST: 7.2%, Late ST: 4.6%, Very Late ST: 3.7% vs. non-ST: 3.0%). All other adverse outcomes were higher in the ST onset groups compared with the non-ST group, including BARC 3-5 bleeding and reinfarction. However, no difference in acute stroke/TIA was observed between the non-ST indication groups and overall ST group (p=0.784) and across all the ST onset groups (p=0.326). While the rates of

MACCE, all-cause mortality and reinfarction were stable in the non-ST group over the study years (from 2014-2015 to 2019-2020), they declined in the ST group. (**Table 3**)

After adjustment for baseline differences, only patients with Early ST were associated with increased odds of MACCE (OR 1.22 95% CI 1.05-1.41), all-cause mortality (OR 1.21 95% CI 1.07-1.36) and reinfarction (OR 2.48 95% CI 1.48-4.14) compared with the non-ST indication groups while other ST onset groups (Late, Very Late) were not associated with increased odds of adverse outcomes. (**Figure 3, Table 4)** Similarly, the overall ST indication group was not associated with increased odds of MACCE, mortality or reinfarction compared with the non-ST indication group.

Predictors of adverse outcomes in ST indication PCI

In multivariable analysis, several factors were predictive of MACCE and mortality in the ST group. (**Table 5)** The strongest correlates of all-cause mortality included STEMI presentation (OR 3.07 95% CI 2.07-4.56), renal failure (OR 3.49 95% CI 2.19-5.55), moderate-poor LV function (OR moderate: 1.56 95% CI 1.14-2.13; poor: 3.98 95% CI 2.64-6.00), OHCA (OR 1.78 95% CI 1.20-2.64), circulatory support (OR 2.19 95% CI 1.57-3.05), as well as procedure-related variables including femoral access (OR 3.14 95% CI 1.75-5.64), proximal LAD PCI (OR 1.62 95% CI 1.19-2.21).

In contrast, the odds of mortality were reduced with the use of newer P_2Y_{12} inhibitors (OR ticagrelor: 0.69 95% CI 0.49-0.95; prasugrel: 0.54 95% CI 0.30-0.96) and the use of intravascular imaging (IVUS or OCT) (OR 0.66 95% CI 0.48-0.92).

Discussion

This national analysis is by far the largest to examine the frequency, characteristics and outcomes of patients presenting with stent thrombosis undergoing PCI over a 7-year period.

Our key findings can be summarised as follows (**Central Illustration**). First, we find that ST represents 1.4% of all indications for PCI, but its frequency has decreased over the study period, from 1.7% in 2014 to 1.4% in 2020. The most common form of ST among those undergoing PCI was early ST (0-30 days, 52.6%), followed by very late ST (>1 year, 35.4%) and late ST (>30 days to 1 year, 12.0%). Second, we show that ST patients have a worse risk profile compared with those undergoing PCI for a non-ST indication, with a higher prevalence of cardiovascular risk factors, and are more critically ill during admission with greater need for mechanical ventilation and circulatory support. Importantly we show that intravascular imaging is under-utilised in this group of patients, with less than a third of procedures using either IVUS or OCT. We report worse prognosis among patients with early ST whose odds of in-hospital mortality and reinfarction were ~20% and 150% higher, respectively, compared to those without ST, despite adjustment for baseline risk profile, while those with late and very late ST were not associated with an increased risk of adverse outcomes. Finally, our study reports several important patient and procedure-related predictors of mortality and adverse outcomes in patients with ST undergoing PCI and find that use of intravascular imaging and newer P_2Y_{12} agents are independently associated with reduced odds of mortality.

Stent thrombosis is a rare complication of PCI, which is known to be associated with a high rate of mortality and morbidity. [4-7] Patients presenting with ST are often critically unwell and some may die prior to PCI, which is the definitive treatment for this complication.[11, 19] Therefore, the characteristics and outcomes of patients with ST undergoing PCI will differ to those who are not invasively managed due to survivorship bias. While there are many reports on the incidence of ST, limited data exists for the frequency and characteristics of ST patients undergoing PCI and how they differ from those undergoing PCI for other indications. Furthermore, there are no data on how the frequency of PCI for ST has changed in recent years. A study of 415,306 DES procedures (2013 from Medicare claims data in the US, which was

linked to the NCDR (National Cardiovascular Data Registry) CathPCI Registry, reported only 1,346 PCI procedures for stent thrombosis (i.e., ~0.3%). [20] This is significantly lower than our reported frequency (~1.4%), although this could be explained by two reasons. First, the authors were only able to link ~86% of procedures to the NCDR CathPCI Registry. Second, their cohort was exclusively aged >65 years when more than a third of stent thrombosis cases are in patients ages <60 years as shown in our analysis. Since age is an important predictor of mortality among patients with stent thrombosis, it is possible that many elderly patients will have died before an intervention and would not have been captured in their analysis.

In the absence of any previously published temporal data, our study is the first to report a decline in the frequency/rate of ST as an indication for PCI over a 7-year period. This is likely attributed to advances in stent technologies and deployment techniques, and antithrombotic strategies (e.g., newer P_2Y_{12} inhibitors, low-dose rivaroxaban) in the past decade, all of which are associated with a reduced incidence of stent thrombosis. [12-14, 21]

We find that patients undergoing PCI for ST indication are more critically unwell, with a higher proportion presenting with OHCA or pre-procedural cardiogenic shock or requiring circulatory support, which may account for the poorer outcomes associated with ST particularly in the early and late groups.

Differences in procedural management were also observed between PCI indication groups where there was a higher rate of utilisation of IVUS, OCT for patients presenting with ST. The routine use of intravascular imaging has been recommended by major interventional societies for the management of stent thrombosis due to its ability to define the mechanism of stent thrombosis (e.g., stent malapposition, underexpansion, or neoatherosclerosis), as well as ensure that adequate stent expansion and apposition is achieved during PCI. [22-24] Interestingly, only ~30% of ST patients were managed with intravascular imaging, more frequently in the

late and very late ST groups, and this was associated with reduced odds of mortality in our analysis.

ST has been previously attributed to clopidogrel resistance in previous studies and is associated with a high risk of mortality and ischaemic complications, warranting more potent antithrombotic therapy.[22, 25] We find that ST patients were indeed more likely to be offered GP-2b3a inhibitors and newer P_2Y_{12} inhibitors (ticagrelor and prasugrel) instead of clopidogrel and while GP-2b3a inhibitor therapy was not associated with a reduction of in-hospital mortality in our analysis, ticagrelor and prasugrel were associated with a 31% and 46% reduction in odds of all-cause mortality, respectively. These findings reaffirm those observed in an observational study by Ferero et al. where GP-2b3a inhibitor use was not associated with better survival or reduced MACE at 60 months among 695 patients with definite ST, while newer P_2Y_{12} inhibitor use was associated with reduced risk of re-infarction at 60 months (hazard ratio 0.56 95% CI 0.32-0.99).[26]

In totality, ST was not associated with an increased risk of MACCE, mortality or reinfarction following PCI after adjustment for differences in baseline characteristics (when compared to PCI undertaken for ACS indications). A study by Ohno et al. from the Japanese PCI (J-PCI) registry that compared in-hospital outcomes between PCI for ACS cases with and without ST found no difference in mortality higher reinfarction between ST and non-ST ACS in a 1:1 matched cohort of 1,898 patients, which is consistent with our findings. [27] However, they reported higher rates of recurrent ST, unlike in our analysis, which may be related to their sample size or their balancing of covariates since differences in certain characteristics remained unbalanced after matching in their analysis (e.g., higher rates of LMS/LAD culprit vessel in ST group).

Importantly, we observe differences in prognosis between different times of ST onset. Early ST was the only onset group associated with increased odds of mortality and reinfarction

(21% and 148% increase in odds, respectively). It is difficult to place our findings within context of other studies since none have previously compared procedural outcomes between non-ST PCI and ST PCI stratified by time of ST onset. However, the increased risk of post-procedural adverse outcomes among specific ST onset groups such as early ST has been previously demonstrated in previous studies. In a meta-analysis by Yang et al., patients with early ST were associated with an increased risk of in-hospital and 30-day mortality (risk ratio (RR) 1.67 95% CI 1.17, 2.37 and 2.05 95% CI 1.58, 2.67, respectively). [28] The increased risk of complications among this specific ST onset group, despite adjustment for their higher risk profile at baseline, could be possibly attributed to differences in the aetiology and vascular bed status at different times of ST onset. Early ST is more commonly caused by stent under-expansion and acute malapposition as well as early discontinuation of antiplatelet therapy especially at a time when re-endothelialisation has not occurred, while late and very late ST have been previously attributed to late stent malapposition, delayed endothelialisation and neoatherosclerosis. [8, 29, 30] Coronary collateral circulation, which can limit myocardial damage, is less likely to be established in the acute phase, as is myocardial healing, possibly contributing to their higher risk of mortality and reinfarction. [31, 32] In contrast, in cases of very late ST, which are driven by neoatherosclerosis, coronary collaterals are more likely to develop, contributing to their relatively better outcomes in comparison to those with a non-ST indication. Previous studies have demonstrated a higher thrombotic burden among those with early ST, that has a higher risk of no-reflow that is known to portend to worse outcomes, thereby necessitating a greater need of more aggressive antithrombotic therapy as seen in our analysis, with concomitant increased peri-procedural bleeding risk. [33, 34]

Previous studies have examined predictors of ST after PCI, such as heart failure, diabetes mellitus, type of stent implanted, indication for the index PCI and antithrombotic therapy. [10, 11, 35, 36] However, it is unclear what the predictors are for adverse outcomes among

patients undergoing PCI for ST. We find that several patient and procedure-related factors are associated with increased odds of any in-hospital complication (MACCE) as well as mortality, including patient age (>60 years), STEMI presentation, renal failure, diabetes mellitus, moderate-poor LV function, OHCA, circulatory support, femoral (vs. radial) access as well as proximal LAD PCI. While many of these factors are non-modifiable, increased uptake of radial access, intravascular imaging during PCI and newer P_2Y_{12} inhibitor use in patients with ST may help further improve their post-procedural outcomes.

Limitations

There are several limitations to the present study. First, whilst the BCIS dataset captures cardiovascular risk factors and procedural characteristics, it does not capture measures of comorbidity or frailty that are important determinants of mortality post PCI.[37, 38] Second, the observational nature of our analysis means that residual unmeasured confounders may not be accounted for. Several factors such as the type of stent used in the index PCI, indication of index PCI, and differences in antithrombotic regime prior to admission for ST PCI, were not captured in our dataset. Third, specific information on ST management (e.g. balloon angioplasty or DEB/additional stent use) was not captured in our dataset. Finally, our findings were based on the study of in-hospital outcomes, and more significant differences in outcomes may become evident on longer follow-up. For example, the use of overlapping or two-layer stents to manage ST could increase the risk of target vessel failure and/or revascularisation. [39]

Conclusions

Our temporal analysis of all PCI procedures in England and Wales shows a decline in the frequency of procedures for a ST indication over a 7-year period. The prognosis of ST patients undergoing PCI, compared with non-ST indication procedures, differs between

different times of onset, with early ST being the only onset group associated with an increased risk of mortality and reinfarction. Our analysis demonstrates that intravascular imaging is under-utilised in this high-risk group, with less than a third of cases receiving IVUS or OCT, even though its use is associated with better outcomes.

Impact on daily practice (92 words)

The present study provides operators with contemporary data on the frequency of ST PCI according to time of onset. Our findings suggest that, while the rate of ST PCI has declined, early ST is the most common subtype and is associated with an increased risk of in-hospital mortality and reinfarction. Furthermore, our findings remind operators of the benefits of intravascular imaging use in ST cases, which was shown to correlate with improved in-hospital survival and lower rates of reinfaction in our analysis and yet remains significantly underutilised in this high-risk patient group.

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Conflict of interest

The authors report no conflicts of interest relevant to the current study.

References

1. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J 2019;**40**(2):87-165.
2. Weiss AJ, Elixhauser A. Trends in Operating Room Procedures in U.S. Hospitals, 2001-2011: Statistical Brief #171. In. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006.

3. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, Fearon WF, Taggart D, Kappetein AP, Krucoff MW, Vranckx P, Windecker S, Cutlip D, Serruys PW. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. Circulation 2018;**137**(24):2635-2650.
4. Airoldi F, Colombo A, Morici N, Latib A, Cosgrave J, Buellesfeld L, Bonizzoni E, Carlino M, Gerckens U, Godino C, Melzi G, Michev I, Montorfano M, Sangiorgi GM, Qasim A, Chieffo A, Briguori C, Grube E. Incidence and Predictors of Drug-Eluting Stent Thrombosis During and After Discontinuation of Thienopyridine Treatment. Circulation 2007;**116**(7):745-754.
5. Räber L, Magro M, Stefanini GG, Kalesan B, van Domburg RT, Onuma Y, Wenaweser P, Daemen J, Meier B, Jüni 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.
6. Stone GW, Witzenbichler B, Weisz G, Rinaldi MJ, Neumann FJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Mazzaferri E, Gurbel PA, Xu K, Parise H, Kirtane AJ, Brodie BR, Mehran R, Stuckey TD. Platelet reactivity and clinical outcomes after coronary artery implantation of drug-eluting stents (ADAPT-DES): a prospective multicentre registry study. Lancet 2013;**382**(9892):614-23.
7. 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.
8. Claessen BE, Henriques JPS, Jaffer FA, Mehran R, Piek JJ, Dangas GD. Stent Thrombosis: A Clinical Perspective. JACC: Cardiovascular Interventions 2014;**7**(10):1081-1092.
9. Burzotta F, Parma A, Pristipino C, Manzoli A, Belloni F, Sardella G, Rigattieri S, Danesi A, Mazzarotto P, Summaria F, Romagnoli E, Prati F, Trani C, Crea F. Angiographic and clinical outcome of invasively managed patients with thrombosed coronary bare metal or drug-eluting stents: the OPTIMIST study. European Heart Journal 2008;**29**(24):3011-3021.
10. 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.
11. Kirtane AJ, Stone GW. How to Minimize Stent Thrombosis. Circulation 2011;**124**(11):1283-1287.
12. 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.
13. Weisz G, Leon MB, Holmes DR, Jr., Kereiakes DJ, Popma JJ, Teirstein PS, Cohen SA, Wang H, Cutlip DE, Moses JW. Five-year follow-up after sirolimus-eluting stent implantation results of the SIRIUS (Sirolimus-Eluting Stent in De-Novo Native Coronary Lesions) Trial. J Am Coll Cardiol 2009;**53**(17):1488-97.
14. Wenaweser P, Daemen J, Zwahlen M, van Domburg R, Jüni P, Vaina S, Hellige G, Tsuchida K, Morger C, Boersma E, Kukreja N, Meier B, Serruys PW, Windecker S. Incidence and correlates of drug-eluting stent thrombosis in routine clinical practice. 4-year results from a large 2-institutional cohort study. J Am Coll Cardiol 2008;**52**(14):1134-40.

15. Ludman PF. British Cardiovascular Intervention Society Registry for audit and quality assessment of percutaneous coronary interventions in the United Kingdom. Heart 2011;**97**(16):1293-7.
16. Mamas MA, Nolan J, de Belder MA, Zaman A, Kinnaird T, Curzen N, Kwok CS, Buchan I, Ludman P, Kontopantelis E. Changes in Arterial Access Site and Association With Mortality in the United Kingdom: Observations From a National Percutaneous Coronary Intervention Database. Circulation 2016;**133**(17):1655-67.
17. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, Kaul S, Wiviott SD, Menon V, Nikolsky E, Serebruany V, Valgimigli M, Vranckx P, Taggart D, Sabik JF, Cutlip DE, Krucoff MW, Ohman EM, Steg PG, White H. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. Circulation 2011;**123**(23):2736-47.
18. Rubin DB. *Multiple Imputation for Nonresponse in Surveys.* : John Wiley & Sons Inc., New York; 1987.
19. Byrne RA, Joner M, Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. European Heart Journal 2015;**36**(47):3320-3331.
20. Dhruva SS, Parzynski CS, Gamble GM, Curtis JP, Desai NR, Yeh RW, Masoudi FA, Kuntz R, Shaw RE, Marinac-Dabic D, Sedrakyan A, Normand ST, Krumholz HM, Ross JS. Attribution of Adverse Events Following Coronary Stent Placement Identified Using Administrative Claims Data. J Am Heart Assoc 2020;**9**(4):e013606.
21. Camenzind E, Steg PG, Wijns W. A Cause for Concern. Circulation 2007;**115**(11):1440-1455.
22. Stefanini GG, Alfonso F, Barbato E, Byrne RA, Capodanno D, Colleran R, Escaned J, Giacoppo D, Kunadian V, Lansky A, Mehilli J, Neumann FJ, Regazzoli D, Sanz-Sanchez J, Wijns W, Baumbach A. Management of myocardial revascularisation failure: an expert consensus document of the EAPCI. EuroIntervention 2020;**16**(11):e875-e890.
23. Souteyrand G, Amabile N, Mangin L, Chabin X, Meneveau N, Cayla G, Vanzetto G, Barnay P, Trouillet C, Rioufol G, Rangé G, Teiger E, Delaunay R, Dubreuil O, Lhermusier T, Mulliez A, Levesque S, Belle L, Caussin C, Motreff P, the PI. Mechanisms of stent thrombosis analysed by optical coherence tomography: insights from the national PESTO French registry. European Heart Journal 2016;**37**(15):1208-1216.
24. 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. 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.
25. Mega JL, Simon T, Collet JP, Anderson JL, Antman EM, Bliden K, Cannon CP, Danchin N, Giusti B, Gurbel P, Horne BD, Hulot JS, Kastrati A, Montalescot G, Neumann FJ, Shen L, Sibbing D, Steg PG, Trenk D, Wiviott SD, Sabatine MS. Reduced-function CYP2C19 genotype and risk of adverse clinical outcomes among patients treated with clopidogrel predominantly for PCI: a meta-analysis. Jama 2010;**304**(16):1821-30.
26. Maria Natalia Tovar F, Thomas Z, Kaneshka M, Laurens JCVZ, Isabella K, Felix Z, Jonas H, Stephan W, Nicolas MVM, Lorenz R, Joost D. Incidence and predictors of outcomes after a first definite coronary stent thrombosis. EuroIntervention 2020;**16**(4):e344-e350.
27. Ohno Y, Yamaji K, Kohsaka S, Inohara T, Amano T, Ishii H, Kadota K, Nakamura M, Nakazawa G, Yoshimachi F, Ikari Y. Incidence and In-Hospital Outcomes of Patients

Presenting With Stent Thrombosis (from the Japanese Nationwide Percutaneous Coronary Intervention Registry). Am J Cardiol 2020;**125**(5):720-726.
28. Yang Y-X, Liu Y, Li X-W, Lu P-J, Wang J, Li C-P, Gao J. Clinical outcomes after percutaneous coronary intervention for early versus late and very late stent thrombosis: a systematic review and meta-analysis. Journal of Thrombosis and Thrombolysis 2021;**51**(3):682-692.
29. Parodi G, La Manna A, Di Vito L, Valgimigli M, Fineschi M, Bellandi B, Niccoli G, Giusti B, Valenti R, Cremonesi A, Biondi-Zoccai G, Prati F. Stent-related defects in patients presenting with stent thrombosis: differences at optical coherence tomography between subacute and late/very late thrombosis in the Mechanism Of Stent Thrombosis (MOST) study. EuroIntervention 2013;**9**(8):936-44.
30. Ong DS, Jang I-K. Causes, assessment, and treatment of stent thrombosis—intravascular imaging insights. Nature Reviews Cardiology 2015;**12**(6):325-336.
31. Cui K, Lyu S, Song X, Yuan F, Xu F, Zhang M, Zhang M, Wang W, Zhang D, Tian J. Effect of Coronary Collaterals on Prognosis in Patients Undergoing Primary Percutaneous Coronary Intervention for Acute ST-Segment Elevation Myocardial Infarction: A Meta-Analysis. Angiology 2018;**69**(9):803-811.
32. Feistritzer HJ, Jobs A, de Waha-Thiele S, Eitel I, Freund A, Abdel-Wahab M, Desch S, Thiele H. Multivessel versus culprit-only PCI in STEMI patients with multivessel disease: meta-analysis of randomized controlled trials. Clin Res Cardiol 2020;**109**(11):1381-1391.
33. Chechi T, Vecchio S, Vittori G, Giuliani G, Lilli A, Spaziani G, Consoli L, Baldereschi G, Biondi-Zoccai GGL, Sheiban I, Margheri M. ST-Segment Elevation Myocardial Infarction Due to Early and Late Stent Thrombosis: A New Group of High-Risk Patients. Journal of the American College of Cardiology 2008;**51**(25):2396-2402.
34. Sianos G, Papafaklis MI, Daemen J, Vaina S, van Mieghem CA, van Domburg RT, Michalis LK, Serruys PW. Angiographic Stent Thrombosis After Routine Use of Drug-Eluting Stents in ST-Segment Elevation Myocardial Infarction: The Importance of Thrombus Burden. Journal of the American College of Cardiology 2007;**50**(7):573-583.
35. Dangas GD, Caixeta A, Mehran R, Parise H, Lansky AJ, Cristea E, Brodie BR, Witzenbichler B, Guagliumi G, Peruga JZ, Dudek D, Möeckel M, Stone GW. Frequency and Predictors of Stent Thrombosis After Percutaneous Coronary Intervention in Acute Myocardial Infarction. Circulation 2011;**123**(16):1745-1756.
36. Leibundgut G, Nietlispach F, Pittl U, Rocca HB-L, Kaiser CA, Pfisterer ME. Stent thrombosis up to 3 years after stenting for ST-segment elevation myocardial infarction versus for stable angina—Comparison of the effects of drug-eluting versus bare-metal stents. American Heart Journal 2009;**158**(2):271-276.
37. Mamas MA, Fath-Ordoubadi F, Danzi GB, Spaepen E, Kwok CS, Buchan I, Peek N, de Belder MA, Ludman PF, Paunovic D, Urban P. Prevalence and Impact of Co-morbidity Burden as Defined by the Charlson Co-morbidity Index on 30-Day and 1- and 5-Year Outcomes After Coronary Stent Implantation (from the Nobori-2 Study). Am J Cardiol 2015;**116**(3):364-71.
38. Potts J, Nagaraja V, Al Suwaidi J, Brugaletta S, Martinez SC, Alraies C, Fischman D, Kwok CS, Nolan J, Mylotte D, Mamas MA. The influence of Elixhauser comorbidity index on percutaneous coronary intervention outcomes. Catheter Cardiovasc Interv 2019;**94**(2):195-203.
39. Räber L, Jüni P, Löffel L, Wandel S, Cook S, Wenaweser P, Togni M, Vogel R, Seiler C, Eberli F, Lüscher T, Meier B, Windecker S. Impact of Stent Overlap on Angiographic and Long-Term Clinical Outcome in Patients Undergoing Drug-Eluting Stent Implantation. Journal of the American College of Cardiology 2010;**55**(12):1178-1188.

Figure titles and legends:

Figure 1. Frequency of PCI procedures per 100,000 population according to indication (2014 to 2020)

Figure 2. In-hospital post-procedural adverse outcomes according to indication for PCI

Legend: ST: Stent thrombosis; $p<0.01$ for all except acute ischemic stroke ($p=0.256$ for overall ST vs. no ST groups, $p=0.784$ for ST onset vs. no ST groups)

Figure 3. Odds ratios (OR) of adverse events in ST group (vs. no ST)

Central Illustration. Summary of study findings

Legend: MACE: Major acute cardiovascular events; ST: Stent thrombosis

Table 1. Patient and procedural characteristics according to PCI indication and onset of ST in ACS only groups

	No Stent thrombosis (n=343,812)	Early ST (n=4,171)	Late ST (n=951)	Very Late ST (n=2,801)	p-value
Patient characteristics					
Age, mean (SD)	65.4 (12.5)	64.7 (12.3)	64.9 (12.0)	64.6 (11.8)	<0.001
Age groups (years), %					0.107
<60	34.7	37.2	35.1	37.6	
60-69	27.0	27.2	26.2	27.7	
70-79	24.3	23.0	27.2	23.5	
≥80	14.1	12.6	11.5	11.3	
Males, %	73.0	75.9	74.2	81.2	<0.001
Ethnicity, %					<0.001
White	85.0	79.4	77.7	84.7	
Black	4.1	4.9	5.3	4.5	
Asian	6.5	9.4	13.0	7.4	
Other	4.3	6.2	4.0	3.3	
Clinical Indication, %					<0.001
NSTE-ACS	60.0	25.3	53.2	27.8	
STEMI	40.0	74.7	46.8	72.2	
Previous MI, %	19.3	45.7	77.6	82.1	<0.001
Previous PCI, %	15.1	100	100	100	<0.001
Previous CABG, %	5.9	6.8	15.6	9.4	<0.001
Previous CVA, %	4.1	4.4	8.8	6.5	<0.001
Previous non-coronary cardiac surgery, %	0.5	1.2	0.9	0.8	0.257
Diabetes Mellitus, %	22.0	25.3	38.0	25.3	<0.001
Renal Failure, %	2.4	2.9	7.8	2.7	<0.001
Functioning renal transplant, %	0.3	0.4	0.6	0.4	0.639

Cardiac transplant, %	0.0	0.0	0.1	0.1	0.799
Family history of IHD, %	37.8	34.5	42.2	43.5	<0.001
LV function (ejection fraction), %*					<0.001
Good (>50%)	61.7	59.8	51.8	46.9	
Moderate (30-50%)	34.8	34.9	41.1	47.4	
Poor (<30%)	3.4	5.3	7.0	5.7	
Hypercholesterolaemia, %	43.9	51.4	65.9	66.0	<0.001
Peripheral Vascular Disease, %	3.9	4.5	8.7	5.9	<0.001
Hypertension, %	51.5	53.7	68.8	66.2	<0.001
Current/Previous smoker, %	61.4	61.1	68.2	74.5	<0.001
Valvular Heart Disease, %	1.7	1.4	1.8	1.4	0.667
Cardiogenic Shock (pre-procedure), %	4.2	11.0	7.0	7.3	<0.001
Out of hospital cardiac arrest, %	4.5	6.7	4.5	5.5	0.012
Procedural characteristics					
Mechanical Ventilation, %	3.1	6.0	3.8	3.3	<0.001
Mechanical circulatory support, %	2.4	6.1	3.7	4.2	<0.001
Access route*					<0.001
Radial, %	85.2	63.5	69.7	76.4	
Femoral, %	17.2	38.2	32.1	26.4	
No. of vessels, %					0.053
1	80.1	83.6	79.9	84.7	
2	16.3	13.7	16.6	12.9	
3	3.1	2.4	3.0	2.0	
4	0.6	0.4	0.4	0.3	
No. of lesions, %					0.028
1	72.5	74.6	70.8	76.4	

2	21.1	20.1	24.0	18.6	
3	5.0	4.4	4.5	4.1	
4+	1.4	0.9	0.7	0.9	
No. of stents, mean (SD)	2.4 (1)	2.1 (1)	1.9 (1)	2.0 (1)	<0.001
Drug eluting stents (DES), %	84.6	66.9	54.3	65.1	<0.001
1st generation DES, %**	40.7	40.3	28.6	30.5	<0.001
2nd/3rd generation DES, %**	65.1	56.1	42.4	52.2	<0.001
Drug coated balloon, %	0.2	0.4	1.8	0.7	<0.001
Fractional Flow Reserve, %	7.8	1.6	1.6	1.7	0.946
Intravascular imaging (IVUS/OCT), %	8.4	21.5	30.5	28.4	<0.001
Thrombus aspiration catheter use, %	11.5	28.8	20.7	31.9	<0.001
Calcium modification, %	2.5	2.4	3.7	2.4	0.053
LMS, %	4.8	4.3	8.0	3.8	<0.001
LAD proximal, %	29.9	32.8	30.0	31.4	0.160
Grafts, %	2.6	1.6	5.3	4.4	<0.001
Aspirin, %	88.5	90.3	91.5	91.3	0.286
Clopidogrel. %	43.8	38.7	44.3	36.2	<0.001
Ticagrelor, %	41.9	47.9	42.9	45.3	0.008
Prasugrel, %	4.8	7.2	6.6	8.2	0.144
Warfarin, %	0.9	1.1	2.1	1.0	0.026
Glycoprotein 2b/3a inhibitor, %	19.8	44.2	34.2	46.4	<0.001
Bivalirudin, %	1.5	0.8	1.6	2.3	<0.001

*patients had more than one access route in some cases; ** there was an overlap in stent generations in a subset of cases

Table 2. Unadjusted rates of in-hospital complications according to PCI indication and onset of ST in ACS only groups

	No Stent thrombosis (n=343,812)	Early ST (n=4,171)	Late ST (n=951)	Very Late ST (n=2,801)	p-value
MACCE*, %	3.5	8.1	4.8	4.0	<0.001
All-cause mortality, %	3.0	7.2	4.6	3.7	<0.001
Acute stroke/TIA, %	0.5	0.6	0.3	0.4	0.326
BARC 3-5 bleeding, %	0.2	0.4	1.2	0.0	<0.001
Reinfarction, %	0.1	0.5	0.0	0.0	<0.001

*major acute cardiovascular and cerebrovascular outcomes: composite of death, acute stroke/transient ischaemic attack and reinfarction

Table 3. In-hospital complications according to PCI indication over the study period

	2014-2015			2016-2018			2019-2020		
	No ST	ST	p-value	No ST	ST	p-value	No ST	ST	p-value
MACCE*	3.5	6.9	<0.001	3.5	6.4	<0.001	3.4	5.2	<0.001
All-cause mortality, %	3.0	6.2	<0.001	3.0	5.7	<0.001	2.9	4.9	<0.001
Acute stroke/TIA, %	0.6	0.6	0.952	0.5	0.5	0.549	0.5	0.2	0.103
BARC 3-5 bleeding, %	0.2	0.3	0.224	0.2	0.4	0.020	0.2	0.3	0.295
Reinfarction, %	0.1	0.2	0.043	0.1	0.3	<0.001	0.1	0.2	0.042

*major acute cardiovascular and cerebrovascular outcomes: composite of death, acute stroke/transient ischaemic attack and reinfarction

Table 4. Odds ratio (OR) of in-hospital complications in patients undergoing PCI for ST indication*

Outcome	OR [95% CI]	p-value
MACCE**		
Overall	0.95 [0.84, 1.08]	0.430
Early ST	1.22 [1.05, 1.41]	0.010
Late ST	0.79 [0.55, 1.13]	0.201
Very Late ST	0.60 [0.47, 0.76]	<0.001
All-cause mortality		
Overall	0.99 [0.86, 1.14]	0.882
Early ST	1.21 [1.07,1.36]	0.019
Late ST	0.90 [0.61, 1.33]	0.597
Very Late ST	0.65 [0.50, 0.84]	<0.001
Reinfarction		
Overall	1.47 [0.88, 2.44]	0.141
Early ST	2.48 [1.48, 4.14]	<0.001
Late ST	***	***
Very Late ST	0.16 [0.02, 1.17]	0.071

*reference in non-ST indication for each outcome; **major acute cardiovascular and cerebrovascular outcomes: composite of death, acute stroke/transient ischaemic attack and reinfarction; ***perfect predictor (i.e. complete separation of data points)

Table 5. Predictors of adverse outcomes in patients undergoing PCI for stent thrombosis indication

	OR [95% CI]	
	MACCE*	**All-cause mortality**
Age group		
<60	reference	
60-69	1.56 [1.12,2.18]	1.97 [1.36,2.85]
70-79	2.06 [1.49,2.85]	2.38 [1.65,3.43]
≥80	2.89 [1.99,4.18]	3.69 [2.46,5.56]
Males	0.93 [0.70,1.23]	0.93 [0.69,1.26]
Ethnicity		
White	reference	
Black	0.50 [0.26,0.95]	0.50 [0.25,0.98]
Asian	1.00 [0.65,1.53]	0.97 [0.61,1.54]
Other	1.31 [0.78,2.19]	1.40 [0.81,2.42]
STEMI	2.84 [1.98,4.10]	3.07 [2.07,4.56]
Stent thrombosis onset		
Very Late	reference	
Late	2.54 [1.88,3.43]	2.30 [1.65,3.20]
Early	1.29 [0.83,2.01]	1.33 [0.83,2.13]
Previous MI	0.98 [0.71,1.35]	1.16 [0.80,1.66]
Previous PCI	1.54 [1.04,2.28]	1.33 [0.86,2.05]
Previous CABG	1.30 [0.82,2.08]	1.61 [0.98,2.65]
Previous CVA	1.54 [1.02,2.31]	1.59 [1.03,2.46]
Diabetes Mellitus	1.35 [1.03,1.76]	1.56 [1.17,2.09]
Renal failure	3.47 [2.24,5.36]	3.49 [2.19,5.55]
LVEF category (ejection fraction)		
Good (>50%)	reference	
Moderate (30-50%)	1.42 [1.07,1.88]	1.56 [1.14,2.13]
Poor (<30%)	3.71 [2.55,5.42]	3.98 [2.64,6.00]
Hypercholesterolaemia	0.80 [0.61,1.05]	0.74 [0.55,0.99]
PVD	1.12 [0.72,1.74]	1.15 [0.72,1.85]
Hypertension	1.14 [0.86,1.50]	1.14 [0.84,1.55]
OHCA	1.55 [1.06,2.26]	1.78 [1.20,2.64]
Mechanical ventilation	4.22 [2.94,6.07]	4.19 [2.87,6.11]
Circulatory support	2.04 [1.48,2.81]	2.19 [1.57,3.05]
Radial access	1.66 [0.98,2.79]	1.23 [0.69,2.18]
Femoral access	3.59 [2.11,6.09]	3.14 [1.75,5.64]
Number of vessels attempted	1.15 [0.85,1.56]	1.18 [0.85,1.62]
Number of stents	1.25 [1.06,1.47]	1.20 [1.00,1.43]
Drug eluting stents	0.53 [0.33,0.83]	0.55 [0.33,0.90]
Drug coated balloon	0.25 [0.03,2.14]	0.28 [0.03,2.44]
Fractional Flow Reserve	0.82 [0.19,3.52]	0.69 [0.09,5.24]
IVUS/OCT	0.81 [0.60,1.08]	0.66 [0.48,0.92]
Calcium modification	1.89 [0.96,3.72]	2.30 [1.11,4.79]

LMS	1.32 [0.82,2.15]	1.28 [0.77,2.14]
LAD proximal	1.46 [1.11,1.94]	1.62 [1.19,2.21]
Aspirin	1.21 [0.80,1.83]	1.27 [0.81,2.01]
Clopidogrel	0.91 [0.65,1.28]	0.96 [0.66,1.39]
Ticagrelor	0.69 [0.48,1.00]	0.69 [0.49,0.95]
Prasugrel	0.60 [0.32,1.13]	0.54 [0.30,0.96]
Warfarin	1.01 [0.42,2.45]	1.19 [0.48,2.94]
Glycoprotein 2b/3a inhibitor	1.08 [0.84,1.40]	0.88 [0.67,1.17]
Bivalirudin	1.34 [0.48,3.71]	1.61 [0.56,4.59]

*Major acute cardiovascular and cerebrovascular outcomes, composite of death, acute stroke/transient ischaemic attack and reinfarction; **zero events recorded