Assessment of Paclitaxel Drug Coated Balloon Only Angioplasty in STEMI

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ABSTRACT

Background: Primary percutaneous coronary intervention (pPCI) with drug eluting stents (DES) has emerged as the standard of care, but stent related events have persisted. Drug coated balloon (DCB)-only angioplasty is an emerging technology, although not fully evaluated compared with DES in context of pPCI. We aimed to investigate the safety of DCB-only angioplasty compared to 2nd generation DES in pPCI.

Methods: We compared all-cause mortality and net adverse cardiac events (cardiovascular mortality, acute coronary syndrome, ischaemic stroke or transient ischaemic attack, major bleeding and unplanned target lesion revascularisation (TLR)) of all patients treated with DCB-only or 2nd generation DES-only for first presentation of STEMI due to de novo disease between 1st January 2016 and 15th November 2019. Patients treated with both DCB and DES were excluded. Data were analysed with Cox regression models, Kaplan Meier estimator plots and propensity score matching.

Results: Among 1139 patients with STEMI due to de novo disease; 452 were treated with DCB and 687 were treated with DES. After a median follow up of >3 years, the all-cause mortality was 49/452 and 62/687 in the DCB and DES group respectively (p=0.18). On multivariable Cox regression analysis, there was no difference in mortality between DCB and DES, in the full and propensity score-matched cohorts. Age, frailty risk, history of heart failure and family history of ischaemic heart disease remained significant independent predictors of mortality. There was no difference in any of the secondary endpoints including unplanned TLR.

Conclusion: DCB-only angioplasty appears safe when compared to DES for STEMI, in terms of all-cause mortality and all net adverse cardiac events including unplanned TLR. DCB may be an efficacious and safe alternative to DES in selected patient groups.

Registration

https://clinicaltrials.gov/ct2/show/NCT04482972 Unique identifier: NCT04482972

KEY WORDS: DCB, STEMI, DES

CONDENSED ABSTRACT

There are limited data about the safety of DCB-only angioplasty in STEMI and how it compares with 2nd generation DES. In this study, we report 1139 patients treated in our institution; 452 with DCB and 687 with DES for STEMI due to de novo disease between 1st January 2016 and 15th November 2019. We obtained patient outcomes from the Hospital Episodes Statistics of NHS digital. There was no difference in all-cause mortality or any of net adverse cardiac events including unplanned TLR after a median >3 years. The results remained unchanged after propensity score matched analysis. In conclusion DCB-only angioplasty for STEMI appears safe and may be considered in selected patients.

ABBREVIATIONS ANDN ACRONYMS

ACS: Acute Coronary Syndrome

CABG: Coronary Artery Bypass Graft

DCB: Drug Coated Balloon

DES: Drug Eluting Stent

TIA: Transient Ischaemic Attack

TLR: Target Lesion Revascularisation

INTRODUCTION

Primary percutaneous coronary intervention (pPCI) is the guideline recommended treatment strategy for patients with ST Elevation Myocardial Infarction (STEMI), with studies demonstrating improved patient outcomes including mortality compared to thrombolysis [1]. Stents were initially developed to treat acute complications of balloon angioplasty, such as flow limiting dissections and acute vessel recoil. Since then, implantation of a drug eluting stent (DES) has emerged as the standard of care [1]. Despite great advances in stent technology over the years and evolution of 2nd generation DES with significantly better patient outcomes and reduced stent-related events [2], stent-related complications such as stent thrombosis and in-stent restenosis have persisted. This in turn has stimulated the concept of 'leaving nothing behind' PCI [3]. Drug coated balloons (DCB) combine the benefits of local drug delivery without the complications of a permanent stent implantation in cases where stenting was not mandated following the initial balloon angioplasty [4].

The safety and efficacy of DCB-only angioplasty has already been demonstrated in in-stent restenosis, small vessel disease and high-bleeding risk cohorts with emerging data in large vessels as well [5 6 7 8 9 10]. However, only a few, predominantly small studies have evaluated the safety of DCB-only angioplasty in the setting of pPCI [7 11 12 13]. The present study sought to assess the safety of DCB-only angioplasty in pPCI as compared with newer generation DES.

METHODS

The safety of paclitaxel drug coated balloon only angioplasty for ST elevation myocardial infarction was an investigator-initiated, single centre, retrospective, propensity matched, cohort study. In our institution, patients undergoing PCI are prospectively entered in a dedicated clinical database. The study received approval from the Northwest Haydock (17/NW/0278), UK research

ethics committee and Institutional Board approval by the Norfolk and Norwich University Hospital. The confidentiality advisory group waived the need for patient consent due to the retrospective nature of our study (17/CAG/0145). In our institution, usage of DCB has steadily increased and usage of second-generation DES has steadily decreased over the last ten years as shown in **Supplementary Figure 1**. From 2016 onwards more than 100 patients per year with first presentation of STEMI and de novo disease were treated with DCB-only angioplasty, representing at least 35% of all the STEMI patients. Hence, for the purposes of this study we considered patients from 2016 onwards, so that the two groups were more balanced in terms of frequency and follow up. We excluded patients with cardiac arrest, intubation or cardiogenic shock as their outcomes are determined mainly by the severity of the clinical presentation rather than the treatment strategy (Fig 1). Clinical and angiographic data were obtained from our prospectively collated database supplemented with data from electronic hospital records as required. An operator (NC) blinded to the outcomes reviewed all angiograms to confirm accuracy of treatment strategy, classify bifurcation disease, TIMI flow before and after PCI as well as coronary artery dissection post DCB implantation. A lesion was defined as bifurcation if there was a side branch more than 2mm in diameter within 5mm of the lesion. Medina subtypes 1.1.1, 1.0.1 and 0.1.1 were considered as true bifurcations. The vessel diameter was considered as the largest pre/post-dilatation balloon, DCB or DES used and lesion length was based on the DCB or DES length. Calcification was assessed by angiographic visualisation.

The primary endpoint was all-cause mortality. The secondary endpoints were cardiovascular mortality, acute coronary syndrome (ACS), stroke or transient ischaemic attack, major bleeding and target lesion revascularisation. Patient outcomes were obtained from the Hospital Episodes Statistics from NHS digital. Hospital Episode Statistics is a data warehouse

containing details of all admissions, outpatient appointments and accident & emergency attendances at NHS hospitals in England. Supplementary table 1 demonstrates the ICD-10 diagnostic codes used to identify patients' outcomes. We obtained mortality data for all patients from NHS digital. All deaths were classified as cardiovascular or non-cardiovascular by three blinded adjudicators according to academic research consortium 2 consensus [14]. We used the validated Hospital Frailty Risk Score based on ICD-10 diagnostic codes to calculate the patients' frailty index [15]. We estimated the well validated 'acuity' score based on gender, age, serum creatinine, white blood cell count, anaemia, clinical presentation and antithrombotic medications [16]. Unplanned TLR was identified following review of all patients' angiograms who had repeat PCIs.

Statistical analysis was undertaken by an independent statistician in program R (version 3.6.0). Nominal variables are reported as counts (percentages) and compared by the Pearson's Chi-squared test. Kolmogorov and Shapiro tests were used to assess normal distribution of continuous variables. Continuous variables not normally distributed are reported as median (interquartile range (IQR)). Wilcoxon rank sum test or Fisher's exact test were used to compare variables as appropriate. Univariable Cox regression analyses were performed to identify predictors of mortality. Predictors with p-value <0.05 were introduced into the multivariable Cox regression model. A p-value <0.05 was considered significant. Kaplan Meier estimator curve and the log-rank test were used to plot and compare survival. Propensity score matching was done using the MatchIt package for R (v4.5), specifically utilising the optimal pair matching algorithm (*https://kosukeimai.github.io/MatchIt/reference/method_optimal.html*) to achieve a 1:1 match. This algorithm was chosen over the typical nearest neighbour matching method due to better overall matching performance (by enabling less within-pair distance variation). Variables that

were shown to be significant predictors of all-cause mortality in the univariate cox-regression models were used in the propensity score matching process. These were: age, hypertension, peripheral vascular disease, stroke, previous ACS, history of heart failure, atrial fibrillation, family history of coronary artery disease, chronic obstructive pulmonary disease, diabetes, glomerular filtration rate, LMS treatment, bifurcation disease, frailty score, heavy calcification and acuity score. The performance of the match was assessed by visually inspecting the dimensionally reduced jitter plot (Supplementary figure 4) and density curves of the variables.

RESULTS

A total of 452 consecutive patients treated with paclitaxel DCB only and 687 consecutive patients treated with 2nd generation DES only were identified (Fig 1). There were 24 patients who required bailout stenting (21 for worsening dissection and 3 for worsening acute vessel recoil following DCB). These patients have not been included in the analysis as they were identified during the index procedure and received a DES – hence excluded. The mean age was 66 (±13) and 66 (±11) years old for the DCB and DES groups, respectively. Male patients accounted for 73% and 74% for the DCB and DES groups, respectively. The groups were well balanced in baseline patient characteristics as shown in table 1. There were very few differences; the DCB group had more patients with previous stroke and higher frailty index while the DES group had more patients with history of smoking.

Table 2 shows the angiographic characteristics of the target vessels treated. Overall, the groups were well balanced with very few differences. The DCB group had significantly more patients with bifurcation and true bifurcation disease treated. The DES group had a significantly larger median vessel diameter but both groups had median vessel diameter more than 3 mm.

The median follow-up for the DCB group was 2.9 years (interquartile range: 2 – 4.2) while for the DES group it was 3.4 years (IQR: 2.3 – 4.3) ($p<0.001$). The incidence of death was 49/452 (10.8%) in the DCB group and 62/687 (9%) in the DES group (hazard ratio (HR)=0.77; CI: 0.53-1.12; p=0.18). Kaplan Meier estimator plot showed that there was no significant difference in all-cause mortality associated with paclitaxel DCB compared to DES (Fig 2). Furthermore, there were no significant differences in any of the secondary endpoints, cardiovascular mortality, ACS, stroke, major bleeding or unplanned TLR (**Supplementary Figure 2**). The median length of hospitalisation post-pPCI was 2.22 days (IQR: 1.63, 2.87) for the DCB group and 2.19 days (IQR: 1.57, 2.69) for the DES group. There were six in-hospital deaths (1.3%) in the DCB group and five in the DES group (0.7%). The difference was not statistically significant (p=0.56). There were no planned or unplanned in-hospital TLR in the DCB group, while there were five unplanned in-hospital TLR in the DES group. Three patients had acute stent thrombosis while another two patients had ongoing chest pain requiring stent optimisation. Furthermore, there was no difference in all-cause mortality or unplanned TLR within 30 days. The 30-day mortality was 2% vs 1.5% (p=0.49) while the 30-day unplanned TLR was 0.2% vs 0.7% (p=0.41) for the DCB and DES group respectively. Analysis of net adverse cardiac events at the short term after propensity score matching, did not show any significant differences between DCB and DES at 30 days or 1 year.

Univariable Cox regression analysis (table 3) identified the following adverse prognostic factors for all-cause mortality: increasing age, hypertension, peripheral vascular disease, stroke, previous myocardial infarction, coronary artery bypass graft (CABG), heart failure, atrial fibrillation (AF), chronic obstructive pulmonary disease (COPD), diabetes, decreasing estimated glomerular filtration rate (eGFR), frailty, vessel treated and true bifurcation. On multivariable

Cox regression analysis (table 4), only age, history of heart failure, frailty and family history of IHD remained independent predictors of mortality.

Propensity score matched analysis for all positive variables in univariable Cox regression analysis demonstrated no difference in mortality between DCB and DES (Fig 3). There were no significant differences in any of the net adverse cardiac events including unplanned TLR (supplementary figure 3). Multivariable Cox regression analysis for the propensity matched population identified frailty score, acuity score, history of heart failure and family history of IHD as independent predictors of mortality (Table 5).

Subgroup analysis according to vessel size (more or less than 3mm) or bifurcation disease demonstrated that the results were consistent in these subgroups.

DISCUSISON

This is the largest cohort analysis assessing the safety of DCB-only angioplasty compared with 2nd generation DES for pPCI showing no difference in all-cause mortality between DCB and DES for STEMI and no difference in the propensity score-matched analysis. Furthermore, there was no difference in any of the net adverse cardiac events including unplanned TLR. pPCI has significantly improved the outcomes including survival of patients presenting with STEMI [17 18]. Even though pPCI with 2nd generation DES has emerged as the standard of care, stent related events have persisted despite great advances in stent technology [8 19 20]. DCB-only angioplasty, an emerging treatment strategy providing local drug delivery to prevent restenosis without the placement of a permanent stent, has not been fully evaluated compared to 2nd generation DES. The recent REVELATION trial demonstrated safety and efficacy of DCB compared to DES for STEMI in terms of fractional flow reserve [21]. In addition, there are only few, small studies that have assessed safety of DCB compared to 2nd generation DES,

demonstrating that DCB-only strategy is feasible in STEMI [12 13 22]. This is the largest analysis reporting on the most relevant, hard endpoint of all-cause mortality and also all net adverse cardiac events including unplanned TLR.

We have demonstrated that DCB-only angioplasty is safe in patients with STEMI and de novo disease compared to 2nd generation DES. In our institution, over the last six years a comparable number of patients with first presentation of STEMI due to de novo coronary artery disease were treated with DCB-only strategy and DES-only strategy, while at the same time, the number of patients treated with both DCB and DES remained low. In the short term, DCB-only angioplasty appears safe with no difference in in-hospital outcomes and reassuringly no cases of acute vessel closure. Furthermore, there was no difference in mortality or any of the net adverse cardiac events including unplanned TLR, after >3 years (median) follow up. These results were similar following propensity score matched analysis and consistent with previous smaller studies [12 13 22]. Subgroup analysis demonstrated consistent results in both small or large vessels and in bifurcation disease. Further studies will need to verify these results in such subgroups. Given the equipoise of our results, it is important to note that in the context of STEMI, a DCB-only strategy may provide an advantage in cases of a) uncertain vessel size resulting in inadequate stent apposition b) uncertainty about antiplatelet compliance or bleeding risk and c) may simplify treatment of complex bifurcation lesions [5]. In our institution, all interventional cardiologists have become very experienced in DCB-only angioplasty and use it when they feel this will provide a very good result. Following optimal lesion preparation, DCB is considered if there is no more than type B dissection and no more than 30% vessel recoil [5].

We included a large number of consecutive patients with STEMI due to de novo disease and no restriction in vessel size. More than 80% of the culprit vessels in both groups had

diameter ≥ 3mm, indicating that the great majority of patients treated had large vessel disease. The median vessel diameter was 3.5mm in both groups. Furthermore, the groups were well balanced in terms of baseline patient characteristics. The only differences were that the DCB group had more patients with previous stroke while the DES group had more patients with history of smoking. In terms of angiographic characteristics, the DCB group had more patients with bifurcations and true bifurcations treated indicating that complex disease was treated, and possibly reflects operator bias towards a DCB-only approach in bifurcations.

Limitations

The retrospective, non-randomised nature of our cohort from a single centre is a possible source of bias. However, our institution provides cardiac intervention as a large tertiary centre to a population in excess of 1.5 million people for pPCI, and has one of the highest implantation of DCBs for coronary artery disease in the UK [23]. In addition, we included all consecutive patients fulfilling the inclusion criteria ameliorating referral bias. DCB-only angioplasty, as most interventional techniques, is accompanied by a learning curve; therefore, our results might not be generalizable to smaller institutions with less clinical experience in DCB-only strategy. The decision to use DCB or DES was at the discretion of the treating interventional cardiologists who used what they felt would provide best result for the patient. Therefore, as this was not a randomised study, it is a limitation.

Our data did not allow us to use the ARC-HBR criteria which were published a few years after the start of our cohort [24]. However, we have calculated and run the analysis using the 'Acuity' score. Finally, even though this study is retrospective and non-randomised, our clinical database was completed prospectively and the high-rate of DCB implantation in our institution resulted in groups well-balanced in terms or patient and angiographic characteristics. Lastly, despite our

efforts we were not able to review the follow up angiograms of 9 (1.9%) patients in the DCB group and 13(1.9%) patients in the DES group who have had re-PCI elsewhere.

CONCLUSIONS

In conclusion, this is the largest cohort analysis comparing DCB-only angioplasty to 2nd generation DES in STEMI reporting on all-cause mortality and all net adverse cardiac events including unplanned TLR. Using propensity matching, we have demonstrated that DCB-only angioplasty is safe with no difference in mortality or any of net adverse cardiac events including unplanned TLR, compared to DES in STEMI.

CLINICAL PERSPECTIVES

WHAT IS KNOWN?

pPCI has significantly improved the prognosis of patients with STEMI. DCB-only angioplasty for patients with STEMI has not been fully evaluated.

WHAT IS NEW?

In this analysis of 1139 patients with STEMI there was no difference in all-cause mortality after an average of 3 years, between DCB and 2nd generation DES. There was no difference in any of the net adverse cardiac events including unplanned TLR.

WHAT IS NEXT?

DCB-only angioplasty in STEMI appears safe and can be considered.

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FIGURE LEGENDS

Figure 1. Consort diagram

Consort diagram indicating how the final population included in the analysis was identified

STEMI: ST segment elevation myocardial infarction, DCB: drug coated balloon, DES: drug eluting stent, POBA: plain old balloon angioplasty, BMS: bare metal stent

Figure 2. Kaplan Meier estimator plot of all-cause mortality

Kaplan Meier estimator plot of all-cause mortality for DCB vs 2nd generation DES with numbers at risk shown below the graph. DCB: drug coated balloon, DES: drug eluting stent

Figure 3. Kaplan Meier estimator plot in propensity score matched groups

Kaplan Meier estimator plot in propensity score matched groups showing no difference in mortality between DCB and DES.

DCB: drug coated balloon, DES: drug eluting stent

Central illustration DCB versus DES in STEMI

DCB: drug coated balloon, DES: drug eluting stent, STEMI: ST elevation myocardial infarction, TLR: target lesion revascularisation

Table 1. Baseline patient characteristics

Characteristic	**Overall**, N = 1,139[1]	**DCB**, N = 452	**DES**, N = 687	**p-value**
Age, Mean (SD)	66 (12)	66 (13)	66 (11)	0.97[2]
Sex, n (%)				0.69[4]
Male	839 (74)	330 (73)	509 (74)	
Female	300 (26)	122 (27)	178 (26)	
Hypercholesterolaemia, n (%)	179 (16)	79 (17)	100 (15)	0.18[4]
Hypertension, n (%)	424 (37)	183 (40)	241 (35)	0.065[4]
Peripheral vascular disease, n (%)	14 (1.2)	7 (1.5)	7 (1.0)	0.43[4]
Stroke, n (%)	30 (2.6)	18 (4.0)	12 (1.7)	**0.021**[4]
Previous myocardial infarction, n (%)	65 (5.7)	30 (6.6)	35 (5.1)	0.27[4]
Previous percutaneous coronary intervention, n (%)	54 (4.7)	25 (5.5)	29 (4.2)	0.31[4]
Previous coronary artery bypass graft, n (%)	11 (1.0)	5 (1.1)	6 (0.9)	0.76[3]
Heart failure, n (%)	4 (0.4)	2 (0.4)	2 (0.3)	0.65[3]
Atrial fibrillation, n (%)	91 (8.0)	37 (8.2)	54 (7.9)	0.84[4]
Family history of IHD, n (%)	114 (10)	44 (9.7)	70 (10)	0.80[4]
Chronic obstructive pulmonary disease, n (%)	62 (5.4)	27 (6.0)	35 (5.1)	0.52[4]
Diabetes, n (%)	146 (13)	63 (14)	83 (12)	0.36[4]
Smoking (current / previous),	689 (63)	254 (58)	435 (67)	**0.006**[4]

Characteristic	**Overall**, N = 1,139[1]	**DCB**, N = 452	**DES**, N = 687	**p-value**
n (%)				
Estimated glomerular filtration rate, Mean (SD)	91 (26)	92 (27)	90 (25)	0.23[2]
Frailty Score, Median (IQR)	0.00 (0.00 – 0.70)	0.00 (0.00 – 0.80)	0.00 (0.00 – 0.50)	**0.034**[2]
Acuity score, Median (IQR)	17 (14 – 23)	17 (14 – 23)	18 (14 – 23)	0.87[2]
Discharge medications				
Aspirin, n (%)	1,100 (97.5)	421 (94.4)	679 (99.6)	**<0.001**[4]
Second antiplatelet, n (%)	1,125 (99.7)	446 (100)	679 (99.6)	0.16[4]
DAPT duration (Mean, SD)	347 (77)	348 (78)	346 (77)	0.73[2]
Anticoagulation	54 (4.8)	23 (5.2)	31 (4.5)	0.64[4]
Beta blocker, n (%)	1,051 (93.2)	414 (92.8)	637 (93.4)	0.71[4]
ACE inhibitor / ARB, n (%)	1,053 (93.4)	415 (93.0)	638 (93.5)	0.74[4]
Statin, n (%)	1,104 (97.9)	437 (98.0)	667 (97.8)	0.84[4]
Aldosterone antagonist, n (%)	155 (13.7)	60 (13.5)	95 (13.9)	0.82[4]

[1] Median (IQR); Range; n (%); Mean (SD)
[2] Wilcoxon rank sum test
[3] Fisher's exact test
[4] Pearson's Chi-squared test

Table 1. Baseline patient characteristics of patients treated with DCB or DES. Bold characters indicate significant result.

DCB: drug coated balloon, DES: drug eluting stent, eGFR: estimated glomerular filtration rate

Table 2. Angiographic characteristics of target vessels

Characteristic	**Overall**, N = 1,139[1]	**DCB**, N = 452	**DES**, N = 687	**p-value**
Vessel treated, n (%)				0.075[3]
LMS	7 (0.6)	2 (0.4)	5 (0.7)	
LAD	452 (40)	196 (43)	256 (37)	
LCx	181 (16)	78 (17)	103 (15)	
RCA	496 (44)	175 (39)	321 (47)	
Graft	3 (0.3)	1 (0.2)	2 (0.3)	
LMS treated, n (%)	7 (0.6)	2 (0.4)	5 (0.7)	0.71[3]
LMS/LAD treated, n (%)	459 (40)	198 (44)	261 (38)	0.050[4]
Multivessel PCI, n (%)	43 (3.8)	17 (3.8)	26 (3.8)	0.98[4]
Bifurcation, n (%)	386 (34)	188 (42)	198 (29)	**<0.001**[4]
True bifurcation, n (%)	88 (7.7)	50 (11)	38 (5.5)	**<0.001**[4]
Heavy calcification, n (%)	159 (14)	67 (15)	92 (13)	0.50[4]
Vessel diameter, Median (IQR)	3.50 (3.00 – 4.00)	3.50 (3.00 – 3.50)	3.50 (3.00 – 4.00)	**<0.001**[2]
Lesion length, Median (IQR)	25 (20 – 32)	25 (20 – 30)	24 (18 – 32)	0.93[2]
Culprit Vessel ≥3mm, n (%)	958 (85)	363 (81)	595 (87)	**0.008**[4]
TIMI flow pre-PCI, n (%)				0.28[4]
0/1	852 (75)	330 (73)	522 (76)	
2/3	286 (25)	121 (27)	165 (24)	
TIMI flow post-PCI, n (%)				0.75[3]

Characteristic	**Overall**, N = 1,139[1]	**DCB**, N = 452	**DES**, N = 687	**p-value**
0/1	9 (0.8)	4 (0.9)	5 (0.7)	
2/3	1,130 (99)	448 (99)	682 (99)	
Coronary Dissection, n (%)				>0.99[3]
No angiographic dissection	317 (70)	317 (70)	0 (NA)	
Type A	72 (16)	72 (16)	0 (NA)	
Type B	62 (14)	62 (14)	0 (NA)	
Bifurcation treatment strategy, n (%)				**<0.001**[3]
DCB MB Only	148 (38)	148 (79)	0 (0)	
DCB SB Only	20 (5.2)	20 (11)	0 (0)	
DCB MB & SB	17 (4.4)	17 (9.1)	0 (0)	
DCB MB & POBA SB	2 (0.5)	2 (1.1)	0 (0)	
DES MB	169 (44)	0 (0)	169 (85)	
DES MB & SB	8 (2.1)	0 (0)	8 (4.0)	
DES MB & POBA SB	6 (1.6)	0 (0)	6 (3.0)	
DES SB Only	15 (3.9)	0 (0)	15 (7.6)	

[1] Median (IQR); Range; n (%); Mean (SD)
[2] Wilcoxon rank sum test
[3] Fisher's exact test
[4] Pearson's Chi-squared test

Table 2. Angiographic characteristics of target vessels treated with DCB or DES.

DCB: drug coated balloon, DES: drug eluting stent, LMS: left main stem, LAD: left anterior descending, Cx: left circumflex, RCA: right coronary artery, TIMI: thrombolysis in myocardial infarction, bold characters indicate significant result

Table 3. Univariable Cox regression analysis

Mortality (Univariate)	**N**	**HR (95% CI)**[1]	**p-value**
DES		0.78 (0.53 to 1.13)	0.18
Age (per year)	1,139	1.09 (1.07 to 1.11)	**<0.001**
Female		1.29 (0.87 to 1.93)	0.21
Hypercholesterolaemia	1,139	0.75 (0.43 to 1.32)	0.32
Hypertension	1,139	1.50 (1.03 to 2.18)	**0.033**
Peripheral vascular disease	1,139	5.84 (2.56 to 13.3)	**<0.001**
Stroke	1,139	3.98 (2.01 to 7.88)	**<0.001**
Previous Myocardial infarction	1,139	2.49 (1.42 to 4.36)	**0.001**
PCI	1,139	1.40 (0.65 to 3.01)	0.39
CABG	1,139	4.95 (2.02 to 12.1)	**<0.001**
Heart failure	1,139	31.6 (11.4 to 87.4)	**<0.001**
Atrial fibrillation	1,139	2.46 (1.48 to 4.08)	**<0.001**
Family history	1,139	0.37 (0.15 to 0.90)	**0.029**
COPD	1,139	3.57 (2.13 to 5.98)	**<0.001**
Diabetes	1,139	2.13 (1.38 to 3.31)	**<0.001**
Current / ex-smoker	1,090	0.98 (0.66 to 1.45)	0.90
eGFR (per ml/min/1.73m^2)	1,138	0.97 (0.96 to 0.98)	**<0.001**
Frailty	1,139	1.24 (1.18 to 1.30)	**<0.001**
Acuity score	1,102	1.12 (1.09 to 1.15)	**<0.001**

Mortality (Univariate)	**N**	**HR (95% CI)**[7]	**p-value**
LMS treated	1,139	8.88 (3.62 to 21.8)	**<0.001**
Multivessel PCI	1,139	1.00 (0.37 to 2.73)	>0.99
Vessel diameter (per mm)	1,133	0.93 (0.68 to 1.27)	0.64
Lesion length (per mm)	1,133	1.01 (0.99 to 1.02)	0.38
Vessel ≥3mm	1,133	0.85 (0.52 to 1.39)	0.52
TIMI flow post-PCI	1,139	0.91 (0.13 to 6.55)	0.93
Bifurcation	1,139	1.39 (0.95 to 2.03)	0.088
True bifurcation	1,139	2.69 (1.64 to 4.42)	**<0.001**
Heavy calcification	1,135	2.50 (1.66 to 3.78)	**<0.001**

[7] HR = Hazard Ratio, CI = Confidence Interval

Table 3. Results of univariable Cox regression analysis for all-cause mortality.

PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, COPD: chronic obstructive pulmonary disease, eGFR: estimated glomerular filtration rate, TIMI: thrombolysis in myocardial infarction. Bold characters significant result

Table 4. Multivariable Cox regression analysis

All-Cause Mortality (Multivariate)	**N**	**HR (95% CI)**[7]	**p-value**
DCB/DES [DES]	1,138	0.90 (0.80 to 1.02)	0.11
Age (per year)	1,138	1.01 (1.00 to 1.01)	**0.020**

All-Cause Mortality (Multivariate)	N	HR (95% CI)[7]	p-value
History of stroke	1,138	1.36 (0.93 to 1.98)	0.11
History of Heart Failure	1,138	11.6 (4.29 to 31.5)	**<0.001**
Family History of Coronary Artery Disease	1,138	0.66 (0.53 to 0.80)	**<0.001**
Estimated glomerular filtration rate (per ml/min/1.73m^2)	1,138	1.00 (1.00 to 1.00)	0.13
Frailty Score	1,138	1.06 (1.02 to 1.10)	**0.001**

[7] HR = Hazard Ratio, CI = Confidence Interval

Table 4. Results of multivariable Cox regression analysis

DCB: drug coated balloon, DES: drug eluting stent, bold characters indicate significant result

Table 5. Multivariable Cox regression analysis for propensity matched population

All-Cause Mortality (Multivariate)	N	HR (95% CI)[1]	p-value
DCB/DES	878	0.89 (0.78 to 1.01)	0.080
History of Heart Failure	878	8.94 (3.28 to 24.4)	**<0.001**
Family History of Coronary Artery Disease	878	0.68 (0.53 to 0.86)	**0.002**
Bifurcations	878	1.14 (0.99 to 1.30)	0.067
Frailty Score	878	1.06 (1.02 to 1.10)	**<0.001**
Acuity Score	878	1.01 (1.00 to 1.02)	**0.031**

[1] HR = Hazard Ratio, CI = Confidence Interval

PVD: peripheral vascular disease, COPD: chronic obstructive pulmonary disease, DES: drug eluting stent * indicates significant result