Drug-Coated Balloons for Small Coronary Artery Disease: A Randomized Non-inferiority Trial

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Abstract

Background: Drug-coated balloons (DCB) are a novel therapeutic strategy for small native coronary artery disease. However, their safety and efficacy as compared to drug-eluting stents (DES) is poorly defined.

Methods: In a multicenter, open-label, randomized non-inferiority trial, 758 patients with de-novo lesions in coronary vessels <3mm and an indication for percutaneous coronary intervention were randomized 1:1 to angioplasty with DCB vs. implantation of a second-generation DES after successful predilatation via an interactive internet-based response system. The primary objective of this trial was to demonstrate non-inferiority of DCB vs. DES regarding major adverse cardiac events (MACE, i.e., cardiac death, non-fatal myocardial infarction, and target-vessel revascularization) after 12 months. The non-inferiority margin was set at an absolute rate difference of 4%. Dual antiplatelet therapy was given according to current guidelines.

Findings: There were 382 patients assigned to DCB and 376 to DES. Non-inferiority of DCB vs. DES was demonstrated since the 95% CI of the absolute difference in MACE in the per-protocol set was below the predefined margin (-3·83, 3·93%, p=0·0217). After 12 months, event proportions were similar in both groups of the full-analysis set (DCB vs. DES; MACE 7·5 vs. 7·3%; HR 0·97 [0·58, 1·64], p=0·9180) without any statistical difference for the single components of the primary endpoint (DCB vs. DES; cardiac death 3·1 vs. 1·3%, HR 2·33 [0·82, 6·61], p=0·1131; non-fatal myocardial infarction 1·6 vs. 3·5%, HR 0·46 [0·17, 1·2], p=0·1123; target vessel revascularization 3·4 vs. 4·5%, HR 0·75 [0·36, 1·55], p=0·4375). There was no statistical difference regarding stent thrombosis and major bleeding.

Interpretation: In small native coronary artery disease, DCB was non-inferior to DES regarding MACE up to 12 months, with similar event rates for both treatment groups.

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Second-generation drug-eluting stents (DES) are the preferred treatment strategy for percutaneous coronary intervention (PCI) in coronary artery disease (CAD).[1] However, the efficacy of stents is limited in small coronary arteries.[2] This limitation applies not only to bare metal stents (BMS),[3] but also to first- and second-generation DES.[4]

Drug-coated balloons (DCB) are a novel concept for the treatment of CAD and an established therapeutic option for restenosis of both BMS[5,6] and DES.[7,8] The technique is based on the fast delivery of highly lipophilic drugs to the vessel wall after single balloon inflation using a specific matrix.[9] To overcome the limitations of elastic recoil and flow-limiting dissections after balloon angioplasty, optimal lesion preparation is mandatory as outlined in current recommedations.[10] The feasibility of the technique in small-vessel CAD has been suggested in several pilot studies.[11-16]

However, a large pivotal randomized controlled trial comparing DCB with second-generation DES using clinical endpoints is lacking. Therefore, the objective of the Basel Kosten Effektivitäts Trial – Drug-Coated Balloons vs. Drug-eluting Stents in Small Vessel Interventions (BASKET-SMALL) 2 was to test the non-inferiority of DCB vs. second-generation DES in small vessel CAD using a 12-month composite clinical endpoint of major adverse cardiac events (MACE) consisting of cardiac death, non-fatal myocardial infarction, and target vessel revascularization (TVR) in a large all-comer population.

Methods

Trial Design. BASKET-SMALL 2 is an investigator-initiated, prospective, randomized, multicenter, open-label, non-inferiority trial.[17] The primary aim of this study is to demonstrate the non-inferiority of paclitaxel-coated balloons vs. second-generation DES regarding a composite of clinical endpoints in an all-comer population with native small-vessel CAD. The 14 participating centers are listed in the supplementary Appendix, in addition to the protocol and the statistical analysis plan.

Patients. All patients with an indication for PCI either due to acute coronary syndrome, chronic angina pectoris, or silent ischemia, and angiographic lesions in native coronary

arteries <3 mm in diameter were eligible for enrollment. However, randomization was only possible if predilatation of the lesion with an angioplasty balloon was successful, i.e., if an acceptable angiographic result was obtained (no higher-grade dissections NHLBI grade C-F,[18] no decreased blood flow TIMI ≤2, or no residual stenosis >30%) according to current consensus group recommendations.[10] Exclusion criteria were concomitant PCI of large lesions ≥3 mm in diameter in the same epicardial coronary artery, PCI of in-stent restenosis, life expectancy <12 months, pregnancy, enrollment in another randomized trial, or inability to give informed consent. The trial was performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines, and the protocol was approved by the ethics committees in all participating centers. All patients provided written informed consent prior to the intervention. In urgent cases where the intervention could not be postponed, oral consent was given prior to the intervention, which was documented by a second medical person not involved in the trial, and written informed consent was obtained after the intervention.

Randomization and treatment. Randomization was performed 1:1 to either the paclitaxel-coated balloon SeQuent Please® (B. Braun Melsungen AG, Germany) or one of two second-generation DES, i.e., the everolimus-eluting Xience® stent (Abbott Vascular, Santa Clara, CA) or the paclitaxel-eluting Taxus Element® stent (Boston Scientific, Natick, MA), via an interactive internet-based response system. The study was started with Taxus Element® as comparator to use devices with similar agents, but later had to be continued with Xience® because the initial stent became unavailable.[17] The sample size was consequently increased to conform to the different efficacy of the two DES. PCI was performed strictly according to current guidelines. Specifically, the DCB, which had to be 2-3 mm longer on each side than the predilatation balloon, was inflated at nominal pressure for a minimal time of 30 seconds.[10] In case of flow-limiting dissections or residual significant stenosis after DCB treatment, additional spot stenting avoiding geographic mismatch was allowed. PCI was performed under dual antiplatelet therapy with acetylsalicylic acid and either a thienopyridine or ticagrelor. After PCI, dual antiplatelet therapy was continued in stable patients for 4 weeks (DCB) or 6 months (DES) and in acute coronary syndrome patients for 12 months.[19] In

patients treated with a combination of DCB and BMS, dual antiplatelet therapy was given for 3 months, whereas it was given for 6 months in patients with DCB and DES. In patients on oral anticoagulation, current guidelines irrespective of DCB or DES treatment were followed.[1]

Endpoints and assessments. The primary objective of this trial was to demonstrate non-inferiority of DCB vs. DES regarding MACE after 12 months. MACE was defined as the composite of cardiac death, non-fatal myocardial infarction, and TVR. Cardiac death was defined as any death not clearly of extracardiac origin, and myocardial infarction according to current guidelines.[20] Secondary endpoints included the single components of the primary endpoint, probable or definite stent thrombosis according to the ARC definition,[21] major bleeding defined as BARC type 3 to 5 bleeding,[22] and net clinical benefit defined as the composite of MACE and major bleeding. All endpoints were adjudicated by an independent Critical Events Committee. Follow-up was done using structured clinical questionnaires or phone calls.

Statistical analysis. The required sample size to demonstrate non-inferiority of DCB vs. DES regarding MACE at 12 months was estimated to be 758 patients. This estimation was performed at the time when the Steering Committee decided to change comparator stents and based on an expected MACE rate of 7% for DCB[14] and 10% for DES[23] with non-inferiority being declared if the upper limit of the two-sided 95% confidence interval (CI) of the absolute risk difference was <4% (non-inferiority margin). Because the event rates of paclitaxel-eluting stents were expected to be higher than rates of everolimus-eluting stents,[24] sample size calculation was based on the DES with expected lower event rates. Sample size was calculated with a resampling procedure, i.e., samples were evaluated by sampling various sample sizes 9999 times from binomial distributions based on expected rates, and was set to ensure at least 90% power ($1-\beta=0.9$) at a significance level of $\alpha=5\%$. Considering an overall dropout rate of 5%, 758 patients were necessary to ensure 720 analyzable patients. After the enrollment of 75% of patients, a blinded sample size re-assessment was performed, which suggested that the trial could be continued without increase of sample size.[25] To test for non-inferiority, the analysis of the absolute MACE risk difference at 12

months between DCB and DES groups and the 2-sided 95% CI was performed on the per-protocol set (PPS) by applying a continuity corrected modification of Wilson's score method; a p-value for non-inferiority was calculated following the Z_{CU} method.[26] The analysis was repeated on the full-analysis set (FAS) for sensitivity. The FAS was defined as all patients matching inclusion criteria that provided informed consent and were assigned to a treatment arm. To form the PPS, patients from the FAS with major protocol violations (received neither DCB nor DES despite being randomized, unapproved procedures, received the opposite treatment than randomized due to complications) or patients lost to follow-up were excluded; patients in the PPS were analyzed as treated. Time-dependent occurrence of events was investigated with Cox proportional hazards models and Kaplan-Meier curves; hazard ratios (HR) are presented with 95% CI. For baseline characteristics, continuous variables are reported as mean and standard deviation, while categorical variables are reported as frequency and percent. CI presented for secondary endpoints are not adjusted for multiple testing and inferences drawn from these may be not reproducible. The primary analysis in the PPS had no missing values per-definition; in the sensitivity analyses using the FAS we assumed no event for patients lost to follow-up. All secondary analyses are performed on the FAS following the intention-to-treat principle with patients analyzed as randomized. All analyses were performed with the statistical software system R version 3.5.0.[27]

Role of the funding source. The study sponsors did not have any role in study design, collection, analysis, and interpretation of data or writing of the report, and did not participate in the decision to submit the manuscript for publication. The Principle Investigator (RJ) and NG had full access to all data. The corresponding author had final responsibility for the decision to submit for publication.

Results

Patients. Between 2012 and 2017, 883 patients were enrolled into the trial, of which 758 (86%) were randomized and 125 (14%) entered a separate registry. Randomization ended once the calculated sample size was reached. Of the randomized patients, 382 were

assigned to the DCB group and 376 to the DES group. Overall, 728 patients (96%) had full data for the primary endpoint (Fig. 1). The baseline demographic and clinical characteristics of the patients are shown in Table 1, while angiographic data are shown in Table 2. The two treatment groups were well balanced. However, the percentage of men in the DCB group was slightly higher than in the DES group (77 vs. 70%, p=0·0232).

Primary endpoint. The absolute risk difference of MACE between the two treatment groups was 0·0005 (95% CI -0·038 to 0·039) in the PPS (Fig. 2). Since the margin of the 95% CI did not cross the pre-defined value of 4% (p=0·0217), non-inferiority of DCB vs. DES could be demonstrated. A sensitivity analysis in the FAS gave similar results, with risk difference assessed at -0·0012 (95% CI -0·040 to 0·037). In the FAS, proportion of MACE events after 12 months was 7·3% in DCB and 7·5% in DES patients (HR 0·97, 95% CI 0·58 to 1·64; p=0·9180; Fig. 3).

Secondary endpoints. Rates of cardiac death (3·1 vs. 1·3%; HR 2·33, 95% CI 0·82 to 6·61; p=0·1131), non-fatal myocardial infarction (1·6 vs. 3·5%; HR 0·46, 95% CI 0·17 to 1·20; p=0·1123), and TVR (3·4 vs. 4·5%; HR 0·75, 95% CI 0·36 to 1·55; p=0·4375) did not differ between DCB and DES patients (Fig. 6-8 in the supplementary Appendix). Probable or definite stent thrombosis occurred in both treatment groups since stents were implanted in DCB patients as well, mostly in other territories of the coronary vasculature; however, rates were low and not statistically different between DCB and DES patients (0·79 vs. 1·60%; HR 0·73, 95% CI 0·16 to 3·26). Of note, there was no incidence of acute vessel closure in the DCB group. Rates of major bleeding were low and similar in DCB and DES patients (1·1 vs. 2·4%; HR 0·45, 95% CI 0·14 to 1·46). Rates of the net clinical benefit were similar in DCB vs. DES groups (7·9 vs. 9·6%; HR 0·81, 95% CI 0·50 to 1·32).

Prespecified subgroups. The effect of DCB vs. DES was assessed in specific pre-defined subgroups. None of the subgroups revealed support for strong differential effects between the treatment groups (Fig. 4; interaction tests).

Exploratory analyses. Regarding the slight imbalance of sexes between the treatment groups, MACE proportions after 12 months were generally higher in men than in women but

similar within both treatment groups (males, DCB vs. DES, 7·8 vs. 8·0%; HR 0·93, 95% CI 0·52 to 1·69; females, DCB vs. DES, 5·8 vs. 6·1%; HR 1·21, 95% CI 0·37 to 4·01). The interaction between sex and treatment was statistically not significant (interaction term 0·93; 95% CI 0·25 to 3·41; p=0·9127).

Within the two treatment groups, specific post-hoc analyses regarding the combination of DCB with stents (DCB group) and the different stent types (DES group) were performed (Fig. 5). In the DCB group, 20 (5%) patients were treated with a combination of DCB and stents in the index lesion (mostly DES). MACE rates for DCB and stents were numerically higher than for DCB only (DCB/stent vs. DCB only, 15·0 vs. 6·8%; HR 2·08, 95% CI 0·61 to 7·07; p=0·2404). In the DES group, 94 (25%) patients were treated with paclitaxel-eluting stents, which had numerically higher event rates than everolimus-eluting stents (12·8 vs. 5·7%, HR 2·04, 95% CI 0·88 to 4·76; p=0·0987). The specific HR for the comparison between DCB and everolimus-eluting stents was 1·21 (95% CI 0·63 to 2·32; p=0·5751) and for the comparison between DCB and paclitaxel-eluting stents 0·52 (95% CI 0·26 to 1·04; p=0·0649), respectively.

Discussion

Our trial demonstrates the non-inferiority of DCB vs. DES regarding clinical events in a large all-comer population undergoing PCI in native small-vessel CAD. After 12 months, MACE rates were low and similar for both treatment groups.

The DCB technique is based on the interaction of a highly lipophilic drug with a coating matrix and allows a fast and homogenous drug delivery into the vessel wall. While many devices exist on the market, balloons coated with paclitaxel and iopromide have shown favorable clinical results and currently are most widely used.[9] DCB are an established treatment option for the treatment of in-stent restenosis,[5-8] but in native small-vessel CAD the technique has been tested in smaller studies only.[15,16] Advantages of DCB are the potential for favorable vascular remodeling after angioplasty in the absence of a stent, the theoretical lack of any stent thrombosis, and the option of shortening dual antiplatelet therapy to only 4

weeks. Possible limitations go back to the early days of interventional cardiology where the method of plain balloon angioplasty – at that time in the absence of dual antiplatelet therapy – was limited by acute vessel closure due to elastic recoil and flow-limiting dissections.[28] Therefore, in our study rigorous lesion preparation according to established consensus group recommendations to achieve an acceptable angiographic result before DCB use was mandatory to avoid complications.[10]

So far, only two randomized controlled trials have been performed to assess the efficacy and safety of DCB vs. DES in native small-vessel CAD.[15,16] The PICCOLETO study tested the effect of a paclitaxel-eluting balloon (Dior®, Eurocor, Bonn, Germany), in which the drug adhered to the roughened surface without matrix, to a first-generation paclitaxel-eluting stent (Taxus Liberté®, Boston Scientific, Natick, MA) and was prematurely halted after 57 patients.[15] The study found an increased rate of the primary angiographic endpoint (% diameter stenosis) in DCB vs. DES patients after 6 months and also an increased rate of the combined clinical endpoint, which was mainly attributed to the lacking efficacy of the type of DCB and the fact that geographic mismatch was not prevented.[29] In contrast, the BELLO study tested the efficacy of a paclitaxel-eluting balloon using urea as matrix (IN.PACT Falcon®, Medtronic, Santa Rosa, CA) to a first-generation paclitaxel-eluting stent (Taxus Liberté®) and enrolled 182 patients.[16] In this study, the primary angiographic endpoint of non-inferiority regarding angiographic in-stent/-balloon late loss after 6 months was met, while the combined clinical endpoint showed similar event rates for both groups after 6 and 36 months.[30] While in BELLO more than 95% of lesions were treated with optimal lesion preparation, this was true for only 25% in PICCOLETO. Therefore, besides the use of a DCB with favorable clinical data, the prevention of geographic mismatch and an optimal lesion preparation might have been essential for the positive result of BASKET-SMALL 2. Regarding the statistically not significant differences between the two treatment arms seen in the single components of the primary endpoint, no conclusions can be drawn as the study was not powered to detect differences in them and none received strong statistical support of an effect. The potential long-term benefit of DCB over permanently implanted stents may not

be seen until after a few years.[30] Long-term follow-up data of the current study are still being collected and will be reported in due time.

Two distinct interventional treatment entities in our trial are of special interest. First, the MACE rate in patients receiving bailout stents after DCB treatment was numerically higher than in patients treated with DCB only. A higher event rate with the combination of DCB and stents might be explained by accidental angiographic mismatch and is in accordance with previous data where increased rates of restenosis were reported when DCB were combined with BMS.[14,15] Therefore, current guidelines on DCB therapy advocate the use of DES in case of unplanned stent implantation,[10] and current generation "limus"-DES should be preferred.[31] However, the combination of DCB with stents in the same lesion should be avoided whenever possible. Second, the MACE rates of DES patients receiving paclitaxel-eluting stents were numerically higher than of patients receiving everolimus-eluting stents. This is in accordance with prior non-randomized data.[23,24] However, a randomized controlled pilot study in small-vessel CAD found even a numerically lower event rate for paclitaxel-eluting vs. zotarolimus-eluting stents.[32] Based on the present data paclitaxel seems to be more efficient in the setting of the DCB than the DES technique.

Rates of major bleeding were numerically lower in DCB than DES patients since DCB require a shorter dual antiplatelet therapy than DES in stable patients, i.e., 4 weeks only instead of 6 months.[10,19] The shorter duration of dual antiplatelet therapy might be of additional benefit, which was not accounted for in the current non-inferiority trial.

Our study has some limitations. Specifically, the trial was initially designed with a second-generation paclitaxel-eluting stent as comparator to the paclitaxel-eluting balloon, in order to use the same drug and make comparisons possible. However, since the stent became unavailable during the study, the comparator was changed to an everolimus-eluting stent with an increase of sample size. Therefore, the trial was switched from a pure comparison of two different devices to a more comprehensive comparison of two interventional strategies. In addition, there was a certain imbalance regarding sex distribution among the randomized groups, with more male patients being randomized to the DCB group. However, a specific

analysis revealed that male patients had higher event rates than women underlining the efficacy of DCB, and that there was no significant interaction between sex and treatment. In addition, extrapolation of the study's results to other types of DCB may not be justified. Finally, there was no routine angiographic follow-up in the study; therefore, event rates could have been underestimated. Since this was a clinical trial, there was no routine core-lab analysis of the angiographies at trial entry and at follow-up.

In conclusion, this is the first large randomized controlled trial testing the efficacy of a paclitaxel-iopromide-coated DCB vs. second-generation DES in a large all-comer population regarding clinical endpoints. Our study showed that DCB are non-inferior to DES in lesions of small native coronary arteries regarding MACE up to 12 months, with similar event rates for both treatment groups. Therefore, small native CAD may safely be treated with DCB after successful predilatation.

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Authors' Contributions

RJ, NG, CK, BS: study design, data acquisition data interpretation, drafting of the manuscript, final approval of the version to be published. AF, MAO, NM, SMW, GL, DW, JW, SR, MS, FM, AL, FPS, CM, PR, SO: data acquisition critical revision of the work for important intellectual content, final approval of the version to be published. MC: study design, data analysis, final approval of the version to be published.

Declaration of Interest

RJ has received lecture honoraria and travel support from B.Braun. MAO has received proctoring honoraria and travel support from Biosensors and research support from Terumo. NM has received speaker´s honoraria from Edwards and Medtronic, and consultant honoraria from Biotronik. GL is a medical user advisory board member for REVA Medical and has relationships with drug and device companies including Terumo, Acrostak, Bionsensors, Boston Scientific, Abbott Vascular, Impuls Medical, and Orbus Neich. FM is supported by Deutsche Gesellschaft für Kardiologie, Deutsche Hochdruckliga, and Deutsche Forschungsgemeinschaft (SFB TRR 219), and has received grant support and personal fees from Medtronic and Recor Medical. AL has received speaker honoraria or served as a consultant for the following companies: Medtronic, St. Jude Medical, Claret Medical Inc., Boston Scientific, Edwards Lifesciences, Symetis, and Bard, and holds stock options from Claret Medical Inc., Emboline and Transverse Medical. In addition, he received grant support from Medtronic and Claret Medical Inc. and speaker honoraria from Novartis and Bayer. NG has received travel support from B.Braun. BS is shareholder of InnoRa GmbH, Berlin, and

was named as co-inventor on patent applications submitted by Charité university hospital, Berlin, Germany. The other authors declare no other conflict of interest.

Data Sharing Statement

As secondary analyses are ongoing, data collected for the study, including individual participant data and a data dictionary defining each field in the set, will not be made available to others.

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Figure legends

Fig. 1. Patient flow-chart according to CONSORT.

Fig. 2. Event numbers and MACE rates in the PPS and the FAS. The absolute difference in event rates between the DCB and the DES group is presented with the 95% confidence intervals. The p-value tests whether the absolute difference in rates is equal to the pre-defined non-inferiority margin, 0.04. PPS, per protocol set; FAS, full analysis set; MACE, major adverse cardiac events; DCB, drug-coated balloons; DES, drug-eluting stents.

Fig. 3. Cumulative incidence rates for MACE according to randomization: DCB (red), DES, (blue). MACE, major adverse cardiac events; DCB, drug-coated balloons; DES, drug-eluting stents.

Fig. 4. MACE rates and hazard ratios (95% confidence interval) of DCB over DES for all subgroup analyses. Cox proportional hazards models were fitted with time-to-MACE as outcome and with patients censored at last observation if experiencing no event. A p-value for the test of the study arm and subgroup is provided. All analyses were performed on the full analysis set with treatment arm as assigned to patients in randomization. MACE, major adverse cardiac events; DCB, drug-coated balloons; DES, drug-eluting stents.

Fig. 5. Cumulative incidence rates for MACE according to the actual treatment patients received: DCB (red), DCB and stent (orange), paclitaxel-eluting stent (light blue), everolimus-eluting stent (grey). MACE, major adverse cardiac events; DCB, drug-coated balloons.

Table 1: Baseline Characteristics

	DCB		DES	
n	382		376	
Age (mean, SD)	67·2	(10·3)	68·4	(10·3)
Sex Male (%)	295	(77·2)	262	(69·7)
BMI (mean, SD)	28·4	(4·5)	28·2	(4·6)
Smoking (%)				
Current smoker	82	(21·9)	72	(19·6)
Former smoker	144	(38·5)	123	(33·5)
No smoker	148	(39·6)	172	(46·9)
Hypercholesterolemia (%)	262	(68·8)	259	(70·0)
Arterial hypertension (%)	324	(84·8)	332	(88·8)
Family history of CAD (%)	150	(42·6)	128	(38·0)
Diabetes mellitus (%)				
IDDM	48	(12·6)	47	(12·6)
NIDDM	74	(19·4)	83	(22·3)
No diabetes	259	(68·0)	243	(65·1)
Previous MI (%)	160	(41·9)	133	(35·4)
Previous PCI (%)	235	(61·5)	241	(64·1)
Previous CABG (%)	37	(9·7)	34	(9·0)
Cerebrovascular insult (%)				
No	352	(92·4)	339	(90·2)
Stroke	16	(4·2)	23	(6·1)
TIA	13	(3·4)	14	(3·7)
PAOD (%)	27	(7·1)	26	(6·9)
COPD (%)	28	(7·3)	36	(9·6)
Renal failure (%)	54	(14·1)	59	(15·7)

	DCB		DES	
Presentation (%)				
STEMI	11	(2·9)	4	(1·1)
NSTEMI	53	(13·9)	56	(14·9)
Unstable angina	48	(12·6)	42	(11·2)
Stable angina	270	(70·7)	274	(72·9)
Oral anticoagulation (%)	33	(9·0)	31	(8·4)
LVEF (%, median, IQR)	60	[50,60]	60	[55, 65]

Continuous variables are reported as mean and standard deviation, while categorical variables are reported as frequency and %.

DCB, drug coated balloon; DES, drug eluting stent; SD, standard deviation; BMI, body mass index, CAD coronary artery disease; IDDM, insulin dependent diabetes mellitus; NIDDM, non insulin dependent diabetes mellitus; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; TIA, transient ischemic attack; PAOD, peripheral arterial occlusive disease; COPD, chronic obstructive pulmonary disease; ACS, acute coronary syndrome; LVEF, left ventricular ejection fraction; IQR, interquartile range.

Table 2: Angiographic data

	DCB		DES	
Target vessel				
Left anterior descending artery (%)	128	(33·5)	116	(30·9)
Left circumflex artery (%)	179	(46·9)	183	(48·7)
Right coronary artery (%)	75	(19·6)	77	(20·5)
Multi-vessel disease (%)	313	(81·9)	285	(75·8)
Bifurcation lesion (%)	22	(5·8)	29	(8·0)
Procedural success (%, mean, SD)	96	(19)	98	(13)
Number of DCB or DES (mean, SD)	1·68	(0·82)	1·26	(0·55)
Length of DCB or DES (mm; mean, SD)	23·93	(11·74)	23·18	(12·85)
Effective size of DCB or DES (mm; mean, SD)	2.75	(2.14)	2.57	(0.25)
Inflation pressure (atm; mean, SD)	11·06	(3·54)	13·58	(3·90)
Duration of inflation (sec; mean, SD)	48.45	(28.24)	23.36	(18.92)
Compliant balloon for predilatation (%)	282	(73·4)	276	(73·8)

Continuous variables are reported as mean and standard deviation, while categorical variables are reported as frequency and %.

DCB, drug coated balloon; DES, drug eluting stent; SD, standard deviation