



Original article

Short-term outcomes from drug-coated balloon for coronary *de novo* lesions in large vessels

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ABSTRACT

Background: A drug-coated balloon (DCB) has been designed as a new device for the treatment of coronary artery disease. The data regarding DCB-treated lesions in large coronary artery are limited. The purpose of our study was to explore the effectiveness and safety of DCB in large coronary artery.

Methods: We prospectively analyzed all patients treated with DCB in *de novo* lesions consistent with inclusion criteria between May 2015 and April 2017. The observed outcomes included target lesion revascularization (TLR), myocardial infarction, cardiac death and non-cardiac death, and major adverse cardiac events (MACE).

Results: There were 92 patients including 94 coronary *de novo* lesions treated in all. The most often utilized DCB diameters were 3.0 mm (41.5%) and 3.5 mm (39.4%). Two acute closures occurred in hospital. Six bailout drug-eluting stents were used in the percutaneous coronary interventions (6.4%). Quantitative coronary angiography measurement at follow-up showed late lumen loss was -0.02 ± 0.49 mm. The TLR rate and overall MACE rates were 4.3% and 4.3% during the follow-up period in the whole patient population, respectively.

Conclusions: Our study showed that the “DCB only” strategy is safe and efficient in large vessel lesions of patients whose predilation achieved an acceptable result.

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Introduction

The advent of drug-eluting stents (DES), which is a landmark event in the history of percutaneous coronary intervention, greatly improved the prognosis of patients with coronary artery disease in daily clinical practice [1]. Currently, interventional cardiologists tend to consider these devices as the standard revascularization treatment for *de novo* coronary lesions [2]. However, the use of metal scaffolding and polymer, which are partially attributed to the risk of late and very late stent thrombosis [3], failed to achieve a reduction in mortality or recurrent myocardial infarction [4]. And anti-proliferation drugs released by DES could simultaneously inhibit the proliferation of smooth muscle cells and endothelial cells for a long time, resulting in delayed and incomplete endothelialization.

A drug-coated balloon (DCB) has been designed as a new device for the treatment of coronary artery disease and peripheral vascular disease in recent years [5,6], ameliorating some limitations of DES. Apart from the mechanical treatment of underlying disease after balloon inflation, it also allows the local delivery of anti-proliferative drug without leaving a polymer or metal scaffold, which may increase inflammation and damage the coronary vasomotor response [7]. Compared to DES, DCB requires only short term dual antiplatelet therapy (DAPT) (usually 1–3 months) which is beneficial in patients having a bleeding risk. And positive remodeling of the treated vessel has been demonstrated after DCB treatment [8]. To date, there is an established indication for the use of DCB in the treatment of in-stent restenosis [9], and the effectiveness of DCB in the treatment of *de novo* lesions has been demonstrated in previous research [10]. However, most treated lesions are limited to small vessels, and the application value of DCB alone in large vessels needs further investigation. Consequently, the purpose of our study was to explore the effectiveness and safety of DCB in large coronary artery.

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Methods

Strategy for percutaneous coronary intervention procedure

All percutaneous coronary intervention (PCI) procedures were examined between May 2015 and April 2017 in a single center (The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China). As a part of this study, the consecutive patients with *de novo* lesions treated by DCB using iopromide as a carrier agent (paclitaxel at a dose of 3 $\mu\text{g}/\text{mm}^2$ balloon surface; SeQuent Please; B BraunMelsungen, Germany) were included. The reference lumen diameter (RVD) of lesions is over 2.75 mm for the definition of large coronary vessels. Patients with small vessel lesions and those with restenosis lesions were excluded. Patients were also excluded if their lesion had severe calcification and had produced chronic total occlusion.

All operations follow the standard PCI procedure. All patients were treated with aspirin (100 mg per day). Clopidogrel (loading dose 300 mg p.o.) followed by 75 mg per day or ticagrelor (loading dose 180 mg p.o.) followed by 90 mg bid per day was used as an ADP blocker. Use of glycoprotein IIb/IIIa inhibitors and additional boluses of heparin were left to operator discretion. The radial artery is used as the primary access site for PCI in our center. As a first step, predilatation with a semi-compliant balloon was routine, followed by dilatation of the lesion using a NSE balloon (Lacrosse[®] non-slip element balloon, Goodman Co., Ltd., Nagoya, Japan) or cutting balloon (Flextome Cutting Balloon, Boston Scientific, Natick, MA, USA) at the operator's discretion to achieve an optimal lumen diameter.

Before choosing the length and diameter of DCB for treatment, 100–200 μg nitroglycerine (NTG) was administered to the coronary lesion to alleviate coronarospasm. Subsequently, the DCB treatment was performed according to the German consensus statement [11]. It should be noted that the dominant aim of DCB is to transport antiproliferative drug to lesion, rather than dilating blood vessel. Specifically, a paclitaxel-coated balloon (SeQuent Please), with a balloon-vessel diameter ratio was 0.8–1.0 and the length of the DCB is two millimeters longer than the treated lesion at each end. DCB was kept inflated at nominal pressure for 30–60 s.

Additional stenting was determined by the treating physician, mainly in cases of a flow-limiting dissection (C–F) [12] or severe residual stenosis (>30%). For bailout stenting, second-generation drug-eluting stent (DES) (sirolimus-eluting stent) was considered and placed using the spot stenting strategy. The DAPT regimen at discharge consisted of aspirin (100 mg daily) recommended indefinitely, in association with clopidogrel or ticagrelor for at least six months [13]. If stent therapy is performed simultaneously, the DAPT duration should be in accordance with stent required.

Sample size

The primary outcomes for the current study is target lesion revascularization (TLR). The sample size was calculated according to the following equation:

$$N = \left(\frac{Z\alpha + Z\beta}{\delta} \right)^2 \times \pi_0 \times (1 - \pi_0)$$

where π is incident rate of TLR of DES in PCI, π_0 is incident rate of DCB in *de novo* lesions, $\delta = |\pi - \pi_0|$. Based on previous registry studies, the incident rate of TLR is 7.4% [14] in DES treatment and 2.9% [15] in DCB treatment, respectively. Hence 86 patients were required for a power of 0.8 with $\alpha = 0.05$.

Data collection and endpoints

Coronary angiography follow-up at 9 months was scheduled in consecutive patients after PCI. At 1, 3, 6, and 12 months after enrolment, patients were interviewed by clinical visit or telephone contact to obtain information on angina status, medication regimen, and concerned cardiovascular events. The observed outcomes during this long-term follow-up included restenosis, TLR, myocardial infarction (MI), cardiac death and non-cardiac death, and major adverse cardiac events (MACE). Only when obvious non-cardiac causes could be confirmed, death will be considered cardiac in origin. MI related to PCI was defined by elevation of troponin C (cTn) values (>5 times the upper limit of normal) in patients or a rise of cTn values >20% if the baseline values are elevated [16]. Occurrence of MACE, defined as the composite of cardiac death, MI, and TLR, was studied at 9 months from the index procedure.

Restenosis was defined as proposed by Holmes et al. [17] as an increase of at least 30% from immediate post-percutaneous transluminal coronary angioplasty (PTCA) stenosis to follow-up angiogram, an immediate post-PTCA stenosis of less than 50% that increased to 70% at follow-up, or a loss of at least 50% of the gain achieved at PTCA. Restenosis was evaluated by quantitative coronary angiography (QCA) analysis. In case of disagreement results were discussed by the team.

Angiographic and statistical analysis

The criteria for the success of interventional therapy is without a major dissection (>type B), significant residual stenosis, and limited flow [$<$ thrombolysis in myocardial infarction (TIMI) 3] after DCB treatment. QCA was used to assess the coronary lesions by a computer-based QCA-CMS system (Pie Medical Imaging Systems, Maastricht, Netherlands). The quantitative measurements included minimal lumen diameter, diameter stenosis, and reference vessel diameter of the treated segment at baseline and after device inflation, and also at the time of follow-up. Late lumen loss (LLL) was defined as the difference between the minimum lumen diameter immediately post-procedure and follow-up.

Statistical analyses were carried out using SPSS for Windows, version 22.0 (SPSS, Inc., Chicago, IL, USA). Data were expressed as numbers with percentage, mean \pm standard deviation. The study protocol was approved by the hospital ethics committee for clinical research.

Results

Patient characteristics

The patient characteristics are shown in Table 1. The mean age was 52.3 ± 10.7 years, 72 were male, and 18 were diabetic. Moreover, 30 had suffered prior MI, 33 had hyperlipidemia, and no patients had severe renal failure. All patients were markedly symptomatic before PCI; 40 had CCS (Canadian Cardiovascular Society) 3–4 symptoms and 47 presented with an acute coronary syndrome (ACS).

Procedure characteristics

There were 92 patients including 94 coronary *de novo* lesions treated in all. Finally, most PCIs could be performed according to the planned DCB only strategy without additional stenting ($n = 88$). Fig. 1 presents a flowchart of the study. The most often used DCB sizes were 3.0–3.5 mm. Thus, large coronary branches were treated in this study. Left anterior descending artery (LAD) was the most common target vessel (69.1%). Cutting balloon and NSE balloon

Table 1
Baseline characteristics of patients.

Variable	N or mean/%
Age, years	52.3 ± 10.7
Male	72/78.3
Risk factors	
Diabetes mellitus	18/19.6
Hypertension	32/34.8
Hypercholesterolemia (chol. >5.18 mmol/L or LDL >2.37 mmol/L or tri. >1.7 mmol/L)	33/35.9
Stable angina	45/48.9
NSTE-ACS	42/45.7
STE-ACS	5/5.4
Current smoker	16/17.4
Ex-smoker	23/25.0
Family history of CAD	19.1/19.6
Previous MI	30/32.6
Previous PCI	6/6.5
Previous CABG	1/1.1
Previous angina	88/95.7
CCS class	
CCS 1	1/1.1
CCS 2	51/55.4
CCS 3	26/28.3
CCS 4	14/15.2
Creatinine (μmol/L)	69.4 ± 19.6
Ejection fractions (%)	62.6 ± 3.5
Number of diseased arteries	
1	32/34.8
2	26/26.3
3	34/37.0

Values are expressed as mean ± SD or n. Chol, total cholesterol; LDL, low-density lipoprotein cholesterol; tri, triglycerides; NSTE-ACS, non-ST elevation myocardial infarction; STE-ACS, ST elevation myocardial infarction; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; CCS, Canadian Cardiovascular Society.

Table 2
Baseline characteristics of procedure.

	N/%
No. of patients	92
No. of lesions	94
Location of lesion DCB treated	
LAD	65/69.1
LCX	7/7.5
RCA	19/20.2
LM-bifurcation	3/3.2
Predilatation	
Semi-compliant balloon diameter, mm	2.5 ± 0.6
Semi-compliant balloon length, mm	14.2 ± 3.5
Cutting balloon (% of all lesions)	65/69.1
NSE balloon (% of all lesions)	19/20.2
Dissection after predilatation (>type B)	6/6.4
Dissection after DCB	17/18.1
Type A	2
Type B	7
Type C	7
Type D	1
Type E or F	0
Bailout DES	6/6.4
DCB only	88/93.6
DCB diameter, mm	3.4 ± 0.4
DCB length, mm	19.8 ± 4.5
Inflation time DCB, s	59.2 ± 8.5
Inflation pressure DCB, atm	8.6 ± 1.2
Medication, %	
DAPT	92/100
Stains	92/100
Glycoprotein IIB/IIIA inhibitor	73/79.3

Values are expressed as mean ± SD or n. DCB, drug-coated balloon; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; LM, left main coronary artery; NSE balloon, non-slip element balloon; DES, drug-eluting stent; DAPT, dual antiplatelet therapy.

were used in 65 lesions and 19 lesions to achieve adequate result after predilatation, respectively. The incidence of dissection after DCB dilation was 18.1% (17 lesions), including 7 in type C and 1 in type D according to the US National Heart, Lung, and Blood Institute classification. Acute closure occurred in two treated right coronary artery vessels and bailout DES was used at a second operation. Also, the other 4 additional stentings were performed for dissection of grade C and D. Table 2 presents the details of procedure characteristics.

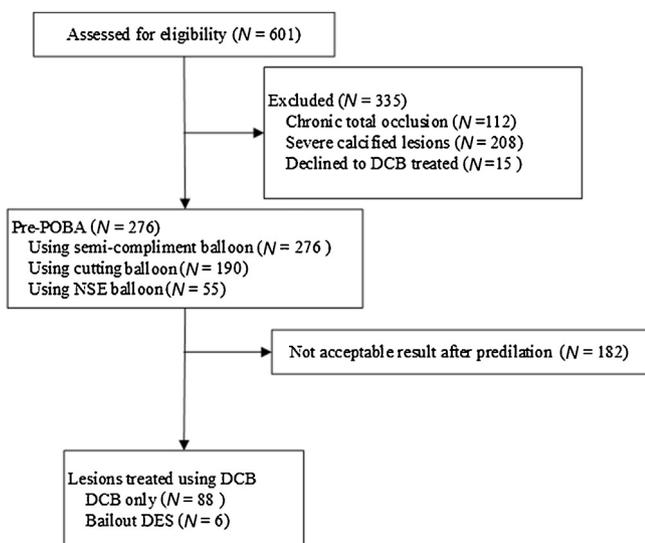


Fig. 1. Flowchart of the study. DCB, drug-coated balloon; POBA, plain old balloon angioplasty; DES, drug-eluting stent.

QCA data and clinical follow-up

A total of 78 lesions were evaluated after DCB intervention and at an angiographic follow-up at 8.3 ± 1.6 months; of which, 78 available QCA records were achieved. At follow-up, QCA analysis showed the data of LLL was -0.02 ± 0.49 mm. The details of QCA measurements are shown in Table 3.

Clinical follow-up data were obtained in all patients. In 5 out of 94 interventions, follow-up angiogram showed restenosis representing a rate of 5.3% (n = 5). Overall TLR was performed in 4 out of

Table 3
Quantitative coronary angiography measurements.

	N/% or mean ± SD	N/% or mean ± SD ^a
No. of patients, %	78/84.8	
Angiography follow-up, month	8.3 ± 1.6	
Before PCI		
Lesion length, mm	12.28 ± 3.48	12.46 ± 3.57
Reference vessel diameter, mm	3.32 ± 0.46	3.31 ± 0.44
Minimal lumen diameter, mm	0.97 ± 0.43	0.94 ± 0.43
Diameter stenosis, %	70.64 ± 12.71	71.49 ± 12.63
Immediately after PCI		
Reference vessel diameter, mm	3.31 ± 0.44	3.31 ± 0.42
Minimal lumen diameter, mm	2.54 ± 0.47	2.53 ± 0.45
Diameter stenosis, %	23.23 ± 10.15	23.47 ± 9.98
Follow-up data		
Reference vessel diameter, mm	3.28 ± 0.43	3.29 ± 0.40
Minimal lumen diameter, mm	2.56 ± 0.54	2.56 ± 0.51
Diameter stenosis, %	21.72 ± 14.43	22.15 ± 13.84
Late lumen loss, mm	-0.02 ± 0.49	-0.03 ± 0.51

Values are expressed as mean ± SD or N%. PCI, percutaneous coronary intervention. ^a Intention to treat.

Table 4
Clinical outcomes at follow-up.

	N/% or mean \pm SD
No. of patients	92/100
No. of lesions	94/100
Clinical follow-up, month	11.4 \pm 1.6
In-hospital events	
Acute closure	2/2.1
Death	0
Follow-up events	
Restenosis	5/5.3
TLR	4/4.3
MI	0
Death	0
MACE	4/4.3

Values are expressed as mean \pm SD or n.
TLR, target lesion revascularization; MI, myocardial infarction; MACE, major adverse cardiovascular events.

92 patients. Of them, 3 TLRs due to restenosis were performed in DCB-treated lesions, and in one due to additional in-stent restenosis (ISR) was in a separate lesion. During the follow-up period after DCB intervention, no patient died, suffered MI or stroke. Without other adverse events that occurred, the overall MACE rate was 4.3% in the whole patient population. Table 4 shows clinical outcomes of follow-up.

Discussion

DCB offers many theoretical advantages over stenting, evidence of DCB applied to large vessels comes mainly from the strategy of DCB in combination with bare metal stents (BMS). PEPCAD III compared a BMS mounted on a DCB to the Cypher DES (Cordis, Johnson & Johnson, New Jersey, USA) in the largest population-based randomized clinical trial (RCT) to date. The results showed that the DCB+BMS device did not meet the non-inferiority criteria versus the sirolimus DES presenting with exceptionally favorable results [18]. Similarly, our meta-analysis, which included 11 RCTs, did not favor the DCB+BMS strategy as an alternative therapeutic method to DES implantation for *de novo* coronary artery lesions [19]. In order to achieve satisfactory results with DCB, it is necessary to achieve sufficient predilation. In our study, semi-compliant balloon and non-compliant balloon were successively used in the sequence, if the results were still insufficient, particularly, NSE balloon or cutting balloon was selected for use (89.4%, $n = 84$). Predilation increased the acute gain of lumen diameter and improved the application of DCB. The most important is, for DCB, the creation of microdissections caused by predilation could improve drug uptake by the vessel wall, thus facilitating penetration of drugs in the intima and media, particularly for calcified lesions [10].

In our study, TLR rate was low, which corroborates the previous registry-based studies using DCB in *de novo* lesions [20,21], and was non-inferior to the rate in small vessels [15]. ALL 3 TLRs related to DCB treatment were due to severe residual stenosis rather than dissection. The low clinical TLR rate is likely to be explained in part by treated lesions in larger vessels (RVD, 3.31 ± 0.44 mm) and shorter lesion length (12.28 ± 3.48 mm). The overall MACE rate (4.3%) was similar as compared to published studies using DES [22]. However, the incidence of MACE could increase after DES implantation with time, which was mainly explained by increased TLR rate [23]. LLL is a significant follow-up outcome for DCB treatment in *de novo* lesions, the value of LLL in this study is -0.02 ± 0.49 mm. Similarly, Kleber et al. reported that local application of paclitaxel by DCB angioplasty to native coronary arteries after pre-dilatation without major dissection and recoil

leads to late lumen increase (1.75 ± 0.55 mm vs. 1.91 ± 0.55 mm, $p < 0.001$, follow-up of 4 months), which contributes to reduce the rate of TLR [8]. Interestingly, QCA data obtained in our study showed that 61.5% ($n = 48$) of patients showed luminal enlargement, which means the phenomenon of “late lumen enlargement” after DCB dilatation may occur in large vessels.

Two acute closures of the treated vessel occurred, and it was higher than the acute vessel closure rate after DCB treatment in *de novo* lesions that has been previously reported, ranging between 0% and 0.5% [20,24]. The patients had acute chest pain and electrocardiogram showed new ST segment change over the abnormal inferior wall lead, within 2 h after operation. Later, intravascular ultrasound (IVUS) was used to confirm the formation of lumen hematoma and severe lumen stenosis in treated locations due to type C dissection without affecting blood flow of the coronary artery. The cases indicated patients with lumen hematoma may have high risk of acute ischemic events, especially in large vessels. Hence, it may be necessary to use imaging techniques such as optical coherence tomography or IVUS to direct the operation and improve the clinical outcomes.

In general, the incidence of dissection in our study was similar to that previously reported in small vessels. It is worthwhile pointing out that the type C dissections that did not cause events in hospital were all healed at the time of follow-up. Even leaving some dissections alone is not absolutely contraindicated. As demonstrated in recent work, instead of bailout stent, most dissections (Type A–C) with no significant impact on blood flow heal after DCB treatment without clinical sequelae [24,25]. Thus, minor or moderate dissections are not harmful but, instead, may facilitate better drug penetration and later positive enlargement of the vessel.

Meanwhile, based on adequate assessment of angiographic images after DCB treatment, it is essential that stenting is limited to bailout situations [flow-limiting dissection (TIMI flow < 3) or significant recoil $> 30\%$] to achieve a low rate of restenosis [11]. It is particularly important to ensure safety for large lesions. It is noteworthy that bailout BMS after DCB treatment was not the most acceptable, due to strongly increasing the risk of restenosis. On the other hand, bailout DES is also a potential choice [26], an observational study using DES instead of BMS as a bailout after suboptimal DCB results shows that the procedure is safe and effective at 1 year [15]. Similar results are reported in one animal test combination of a drug-coated balloon with an everolimus-eluting stent in the same lesion [27]. In our study, in all 6 cases with bailout DES the occurrence of ISR or aneurysm during follow-up were not observed.

There are some important limitations in this prospective observational study. Firstly, as a study in a single center, the number of patients is relatively low. Secondly, since selection was based on clinical criteria and lesion type, this study is applicable to a select group of patients whose predilatation achieved an acceptable result. Finally, we have only reported data on the treatment of lesions in large vessels with DCB, and without comparing DCB with other treatment modalities (second-generation DES or surgery). A multicenter RCT is required to further evaluate the effectiveness of DCB in comparison to second-generation DES in these suitable lesions.

Conclusions

Our study showed that the “DCB only” strategy is safe and efficient in large vessels lesions of patients whose predilation achieved an acceptable result.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

- [1] Kastrati A, Mehilli J, Pache J, Kaiser C, Valgimigli M, Kelbaek H, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356(10):1030–9.
- [2] Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits PC, et al. Long-term safety of drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 2015;65(23):2496–507.
- [3] Hassan AK, Bergheanu SC, Stijnen T, van der Hoeven BL, Snoep JD, Plevier JW, et al. Late stent malapposition risk is higher after drug-eluting stent compared with bare-metal stent implantation and associates with late stent thrombosis. *Eur Heart J* 2010;31(10):1172–80.
- [4] De Luca G, Suryapranata H, Stone GW, Antoniucci D, Biondi-Zoccai G, Kastrati A, et al. Coronary stenting versus balloon angioplasty for acute myocardial infarction: a meta-regression analysis of randomized trials. *Int J Cardiol* 2008;126(1):37–44.
- [5] Mehrotra S, Paramasivam G, Mishra S. Paclitaxel-coated balloon for femoropopliteal artery disease. *Curr Cardiol Rep* 2017;19(2):10.
- [6] Jackson D, Tong D, Layland J. A review of the coronary applications of the drug coated balloon. *Int J Cardiol* 2017;226:77–86.
- [7] Nakazawa G, Finn AV, Joner M, Ladich E, Kutys R, Mont EK, et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: an autopsy study. *Circulation* 2008;118(11):1138–45.
- [8] Kleber FX, Schulz A, Waliszewski M, Hauschild T, Bohm M, Dietz U, et al. Local paclitaxel induces late lumen enlargement in coronary arteries after balloon angioplasty. *Clin Res Cardiol* 2015;104(3):217–25.
- [9] Unverdorben M, Vallbracht C, Cremers B, Heuer H, Hengstenberg C, Maikowski C, et al. Paclitaxel-coated balloon catheter versus paclitaxel-coated stent for the treatment of coronary in-stent restenosis: the three-year results of the PEPCAD II ISR study. *EuroIntervention* 2015;11(8):926–34.
- [10] Belkacemi A, Agostoni P, Nathoe HM, Voskuil M, Shao C, Van Belle E, et al. First results of the DEB-AMI (drug eluting balloon in acute ST-segment elevation myocardial infarction) trial: a multicenter randomized comparison of drug-eluting balloon plus bare-metal stent versus bare-metal stent versus drug-eluting stent in primary percutaneous coronary intervention with 6-month angiographic, intravascular, functional, and clinical outcomes. *J Am Coll Cardiol* 2012;59(25):2327–37.
- [11] Kleber FX, Rittger H, Bonaventura K, Zeymer U, Wohrle J, Jeger R, et al. Drug-coated balloons for treatment of coronary artery disease: updated recommendations from a consensus group. *Clin Res Cardiol* 2013;102(11):785–97.
- [12] Huber MS, Mooney JF, Madison J, Mooney MR. Use of a morphologic classification to predict clinical outcome after dissection from coronary angioplasty. *Am J Cardiol* 1991;68(5):467–71.
- [13] Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2018;39(3):213–60.
- [14] Tu JV, Bowen J, Chiu M, Ko DT, Austin PC, He Y, et al. Effectiveness and safety of drug-eluting stents in Ontario. *N Engl J Med* 2007;357(14):1393–402.
- [15] Vaquerizo B, Miranda-Guardiola F, Fernandez E, Rumoroso JR, Gomez-Hospital JA, Bossa F, et al. Treatment of small vessel disease with the paclitaxel drug-eluting balloon: 6-month angiographic and 1-year clinical outcomes of the Spanish Multicenter Registry. *J Interv Cardiol* 2015;28(5):430–8.
- [16] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012;60(16):1581–98.
- [17] Holmes Jr DR, Vlietstra RE, Smith HC, Vetrovec GW, Kent KM, Cowley MJ, et al. Restenosis after percutaneous transluminal coronary angioplasty (PTCA): a report from the PTCA Registry of the National Heart, Lung, and Blood Institute. *Am J Cardiol* 1984;53(12):77c–81c.
- [18] Christian H, Bodo WC, Helge M, Sven MW, Uwe Z, Matthias V, et al. PEPCAD III: a randomised trial comparing a paclitaxel-coated balloon/stent system with a sirolimus eluting stent. *Circulation* 2009;120(21):2157.
- [19] Lu W, Zhu Y, Han Z, Wang X, Wang X, Qiu C. Drug-coated balloon in combination with bare metal stent strategy for de novo coronary artery disease: a PRISMA-compliant meta-analysis of randomized clinical trials. *Medicine* 2017;96(12):e6397.
- [20] Wohrle J, Zadura M, Mobius-Winkler S, Leschke M, Opitz C, Ahmed W, et al. SeQuentPlease World Wide Registry: clinical results of SeQuent please paclitaxel-coated balloon angioplasty in a large-scale, prospective registry study. *J Am Coll Cardiol* 2012;60(18):1733–8.
- [21] Herdeg C, Oberhoff M, Baumbach A, Blattner A, Axel DI, Schroder S, et al. Local paclitaxel delivery for the prevention of restenosis: biological effects and efficacy in vivo. *J Am Coll Cardiol* 2000;35(7):1969–76.
- [22] Jensen LO, Thayssen P, Christiansen EH, Maeng M, Ravkilde J, Hansen KN, et al. Safety and efficacy of everolimus- versus sirolimus-eluting stents: 5-year results from SORT OUT IV. *J Am Coll Cardiol* 2016;67(7):751–62.
- [23] Bona KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, et al. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med* 2016;375(13):1242–52.
- [24] Cortese B, Silva Orrego P, Agostoni P, Buccheri D, Piraino D, Andolina G, et al. Effect of drug-coated balloons in native coronary artery disease left with a dissection. *JACC Cardiovasc Interv* 2015;8(15):2003–9.
- [25] Belkacemi A, Stella PR, Chunlai S, Uiterwijk M, Ali D, Agostoni P. Angiographic fate of side branch dissections in bifurcation lesions treated with a provisional single stenting strategy: a post-hoc analysis of the international multicenter randomized DEBIUT study. *Catheter Cardiovasc Interv* 2014;83(4):539–44.
- [26] Costopoulos C, Latib A, Naganuma T, Sticchi A, Figini F, Basavarajiah S, et al. The role of drug-eluting balloons alone or in combination with drug-eluting stents in the treatment of de novo diffuse coronary disease. *JACC Cardiovasc Interv* 2013;6(11):1153–9.
- [27] Ong PJ, Kubo T, Watson TJ, Seah AS, Wong PE, Akasaka T. Angiographic, optical coherence tomography and histology findings from combination of a drug-coated balloon with an everolimus-eluting stent in a porcine model. *Int J Cardiol* 2016;223:665–8.