BMJ Open

Rationale and design for comparison of non-compliant balloon with drug-coating balloon angioplasty for side branch after provisional stenting for patients with true coronary bifurcation lesions: a prospective, multicentre and randomised DCB-BIF trial

Xiao-Fei Gao ,[1] Zhen Ge,[1] Jing Kan ,[1] Xiang-Quan Kong,[1] Yan Wang,[2] Chun-Guang Qiu,[3] Damras Tresukosol,[4] Yu-Quan He,[5] Qiang Wu,[6] Ji-Fu Li,[7] Hai-Tao Yuan,[8] Chengxing Shen,[9] Xiang Chen,[2] Muhammad Munawar,[10] Bashir Hanif,[11] Teguh Santoso,[12] Eun-Seok Shin ,[13] Imad Sheiban,[14] Fei Ye,[1] Jun-Jie Zhang,[1] Shao-Liang Chen,[1] On behalf of the DCB-BIF investigators

To cite: Gao X-F, Ge Z, Kan J, *et al*. Rationale and design for comparison of non-compliant balloon with drug-coating balloon angioplasty for side branch after provisional stenting for patients with true coronary bifurcation lesions: a prospective, multicentre and randomised DCB-BIF trial. *BMJ Open* 2022;**12**:e052788. doi:10.1136/bmjopen-2021-052788

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-052788).

X-FG, ZG and JK are joint first authors.

Received 25 April 2021
Accepted 17 November 2021

For numbered affiliations see end of article.

Correspondence to
Dr Shao-Liang Chen; chmengx@126.com and Dr Jun-Jie Zhang; jameszll@163.com

ABSTRACT

Introduction Provisional stenting using drug-eluting stent is effective for simple coronary bifurcation lesions. Kissing balloon inflation using conventional non-compliant balloon is the primary treatment of side branch (SB) after main vessel (MV) stenting. Drug-coating balloon (DCB) is reported to be associated with less frequent clinical events in in-stent restenosis and small vessel disease. The importance of DCB in bifurcation treatment is understudied. Accordingly, this trial is designed to investigate the superiority of DCB to non-compliant balloon angioplasty for SB after provisional stenting in patients with true coronary bifurcation lesions.

Methods and analysis The DCB-BIF trial is a prospective, multicentre, randomised, superiority trial including 784 patients with true coronary bifurcation lesions. Patients will be randomised in a 1:1 fashion to receive either DCB or non-compliant balloon angioplasty if SB diameter stenosis >70% after MV stenting. The primary endpoint is the composite of major adverse cardiac event at the 1-year follow-up, including cardiac death, myocardial infarction (MI) or clinically driven target lesion revascularisation. The major secondary endpoints include all-cause death, periprocedural MI, spontaneous MI, clinically driven target vessel revascularisation, in-stent restenosis, stroke and individual component of the primary endpoint. The safety endpoint is the risk of stent thrombosis.

Ethics and dissemination The study protocol and informed consent have been reviewed and approved by the Institutional Review Board of all participating centres. The written informed consent for participation in the trial will be obtained from all participants. The results of this study will be published in a peer-reviewed journal and disseminated at conferences.

Trial registration number NCT04242134.

Strengths and limitations of this study

- This is the first randomised trial to investigate the superiority of drug-coating balloon for side branch (SB) after provisional stenting in patients with true coronary bifurcation lesions.
- We plan to enrol a total of 784 patients in at least 15 sites in 6 countries.
- Primary endpoint is clinical event ('hard' endpoint).
- This study will provide high-level evidence to help to create an algorithm for provisional stenting technique in coronary bifurcation lesions.
- True coronary bifurcation lesions with SB length less than 10 mm are included, which may not be reflective of complex bifurcation lesions.

BACKGROUND

Coronary bifurcation lesions are encountered in about 15%–20% of daily percutaneous coronary intervention (PCI) procedures, but with technical complexity and poor long-term outcomes.[1] The systematic two-stent technique (mostly DK-CRUSH) has been demonstrated to improve the clinical outcomes for DEFINITION criteria-defined complex bifurcation lesions,[2 3] while provisional stenting (PS) technique is regarded as the default strategy for simple bifurcation lesions.[4 5] Routine side branch (SB) dilation with kissing balloon inflation (KBI) could not provide clinical benefits in PS, and SB ostium dilation is recommended only when severe

ostial SB stenosis is present.[1] Currently, non-compliant (NC) balloon is widely used in SB ostium dilation after stenting main vessel (MV) to restore normal blood flow in the SB, but it still yields more frequent restenosis and repeat revascularisation at the ostium of SB. Drug-coated balloon (DCB) is developed to deliver the antiproliferative agents into the vessel wall via a semicompliant balloon, which would suppress the proliferation of vascular smooth muscle cells (VSMCs) and reduce the restenosis by leaving no metal behind.[6] Sufficient data have proven good efficacy and safety in treating in-stent restenosis (ISR)[7 8] and de novo small vessel disease.[9 10] The combined use of PS technique and DCB to treat the true bifurcation lesions is very attractive, which might improve the clinical outcomes. Previous studies[11–13] showed that the combination of a stent in the MV and a DCB in the SB for the treatment of a bifurcation lesion could result in the lower late lumen loss (LLL) and less frequent SB ostium restenosis. However, those studies unlikely provide the benefits of clinical outcomes after SB dilation using a DCB in bifurcation lesions, mainly because of bare-metal stent (BMS) usage,[12] small sample size (only 52,[11] 35[12] or 28 patients[13]), surrogate endpoint (LLL)[11–13] and short follow-up duration (6[11] or 9 months[12 13]). Therefore, we designed this prospective, multicentre, randomised trial to investigate the superiority of DCB to NC balloon angioplasty for SB after PS in patients with true coronary bifurcation lesions.

STUDY DESIGN AND METHODS

Study hypothesis

This study is designed to test the hypothesis that DCB dilation will lead to a fewer rate of major adverse cardiac event (MACE), including cardiac death, myocardial infarction (MI) or clinically driven target lesion revascularisation (TLR), compared with conventional balloon angioplasty for SB after PS in patients with true coronary bifurcation lesions at 12-month follow-up.

Study design

The present study is a prospective, multicentre, randomised, superiority trial in at least 15 sites in 6 countries to enrol 784 patients with true coronary bifurcation lesions. The overall study flow chart is summarised in figure 1. This study has been registered at ClinicalTrials.gov, according to the statement of the International Committee of Medical Journal Editors. The study protocol and informed consent have been reviewed and approved by the Institutional Review Board at each participating centre. The written informed consent for participation in the trial will be obtained from all enrolled patients.

Study population and randomisation

A total of 784 patients with true coronary bifurcation lesions (Medina 1,1,1 or 0,1,1 or 1,0,1) suitable for drug-eluting stent implantation are randomised in a 1:1 fashion to DCB or NC balloon angioplasty for SB after stenting main vessel. The detailed inclusion and exclusion criteria are presented in box 1.

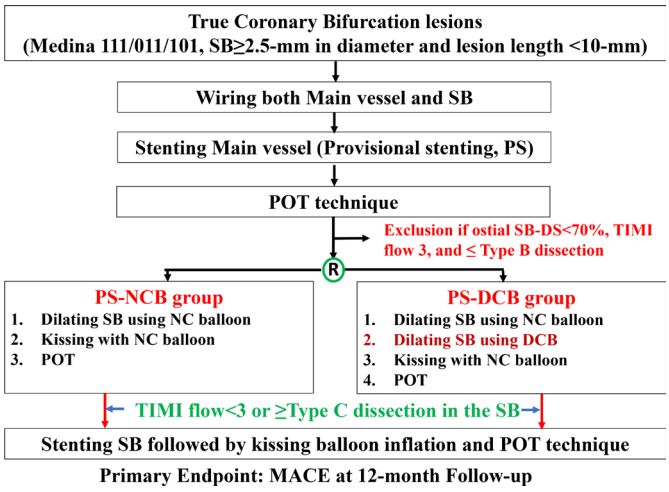

Figure 1 Study flow chart. DCB, drug-coated balloon; DS, diameter stenosis; MACE, major adverse cardiac event; NC, non-compliant; NCB: non-compliant balloon; POT, proximal optimisation technique; SB, side branch; TIMI, thrombolysis and thrombin inhibition in myocardial infarction.

Study intervention and medication

All patients in this study will receive PS technique for true coronary bifurcation lesions.

PS technique

PS technique has been described in detail previously.[1] Briefly, a stent (a ratio of stent diameter to distal MV diameter at 1:1) is implanted in the MV across the SB ostium, with a jailed wire or a jailed balloon in the SB. Predilatation in severe SB stenosis before MV stent implantation is at the discretion of the interventional cardiologists. The proximal optimisation technique (POT) with a short NC balloon (a ratio of balloon diameter to proximal MV diameter) is performed. Randomisation is initialised if diameter stenosis of ostial SB ≥70% after POT, SB rewiring crossing the distal stent struts closest to carina is recommended, following KBI using short NC balloons with a diameter adapted to both distal branches. An additional SB stent is required if SB thrombolysis and thrombin inhibition in myocardial infarction (TIMI) flow <3 or ≥type C dissection. POT-SB-rePOT is recommended for all procedures.

PS-DCB group

The beginning steps of PS-DCB procedures are the same as PS techniques. After randomisation, SB dilation using NC balloon (1:1 ratio of diameters) is performed, followed by second dilation using a paclitaxel-coating balloon. Specifically, the DCB, which has to be 2–3 mm proximal or distal to injured segments by NC balloon, is inflated

Gao X-F, *et al*. *BMJ Open* 2022;**12**:e052788. doi:10.1136/bmjopen-2021-052788

Box 1 Inclusion and exclusion criteria

Inclusion criteria:

1. Subject must be aged ≥18 years.
2. Subject has silent ischaemia, or stable/unstable angina, or acute MI (>7 days from the onset of chest pain to admission).
3. Subject (or legal guardian) understands the trial design and treatment procedures and provides written informal consent before any trial-specific tests or procedures are performed.
4. Subject is willing to comply with all protocol-required follow-up evaluations.
5. Target lesion must be a true bifurcation lesion on coronary angiography (defined as Medina 0,1,1, Medina 1,0,1, or Medina 1,1,1 coronary bifurcation lesions) and is eligible for PCI.
6. Target lesion reference vessel diameter (both main vessel and side branch) ≥2.5 mm by visual estimation.
7. Target lesion must have visually estimated stenosis ≥50%.
8. Target lesion length of side branch must be <10 mm by visual estimation.
9. Ostium side branch must have visually estimated stenosis ≥70% after proximal optimisation technique for the main vessel stenting.

Exclusion criteria:

1. Pregnant and breastfeeding mothers.
2. Comorbidity with an estimated life expectancy of <50% at 12 months.
3. Scheduled major surgery in the next 12 months.
4. Inability to follow the protocol and comply with follow-up requirements or any other reason that the investigator feels would place the patient at increased risk.
5. Previous enrolment in this study or treatment with an investigational drug or device under another study protocol in the past 30 days.
6. Known allergy against ticagrelor, or against clopidogrel, or aspirin history of major haemorrhage (intracranial, gastrointestinal, etc).
7. Chronic total occlusion lesion in either LAD, or LCX or RCA not recanalised.
8. Severe calcification needing rotational atherectomy.

LAD, left anterior descending artery; LCX, left circumflex coronary artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

at nominal pressure for 60 s. The ratio of the DCB diameter to the nominal diameter of the SB is recommended to be between 0.8 and 1.0. DCB should be delivered to the lesion within 2 min after entering human body. After DCB angioplasty, further kissing inflation using two NC balloons is performed. RePOT and SB stenting are in line with previous description in PS technique.

PS-NC balloon group

All procedures are consistent with technical requirements in the PS technique.

Intracoronary imaging and study stents

Intracoronary imaging tools (intravascular ultrasound or optical coherence tomography) are at the discretion of the interventional cardiologists. Stents for all implanted lesions are limus-eluting stents, including BuMA stent (Sino Medical, Tianjin, China); Firebird2 or Firehawk (Microport Co, Shanghai, China); EXCEL (Jiwei Co, Shandong, China); GuReater, Partner or Nano (Lepu Med, Beijing, China); Endeavor Resolute or Resolute Integrity (Medtronic, Minneapolis, Minnesota, USA); and Xience or Xience Prime (Abbott Vascular, Santa Clara, California, USA).

Medications

All patients in this trial are treated according to contemporary guidelines and local practice. A loading dose of aspirin (300 mg) and clopidogrel (300 mg, or ticagrelor 180 mg) is recommended at least 6 hours before PCI procedure. Heparin or an alternative antithrombotic (such as bivalirudin) must be used during the interventional portion of the procedure to maintain the activated clotting time >250 s throughout the interventional portion of the procedure. After procedure, lifelong aspirin in a dose of 100 mg/day will be prescribed. Duration of clopidogrel treatment with 75 mg/day (or ticagrelor with 90 mg two times per day) is at least 6 months for stable patients or at least 12 months for patients with acute coronary syndrome.

Biomarker assessment

Total creatine kinase (CK), CK-myocardial band isoenzyme (MB) and troponin T/I are dynamically measured before the procedure and until 48 hours after procedure.

Study endpoints

The primary endpoint is MACE at 12 months after the indexed procedure, defined by the composite of cardiac death, MI and clinically driven TLR. The major secondary endpoints include all-cause death, periprocedural MI, spontaneous MI, clinically driven target vessel revascularisation, ISR, stroke and each individual component of the primary endpoint. The safety endpoint is the risk of Academic Research Consortium-defined stent thrombosis. Other endpoints are listed in box 2. The detailed definitions of study endpoints are described in the online supplemental appendix 1.

Box 2 Study endpoints

Primary endpoint:

- Major adverse cardiac events at 12 months, composite of cardiac death, myocardial infarction (MI) or clinically driven target lesion revascularisation (TLR).

Secondary endpoints:

- All-cause death: cardiac death, non-cardiac death.
- MI: periprocedural MI, spontaneous MI or target vessel MI.
- Revascularisation: TLR, target vessel revascularisation.
- In-stent restenosis.
- Periprocedural endpoints: angiographic success rate; clinical procedural success rate; crossover rate from single-stent technique to two-stent technique.

Safety endpoint:

- Stent thrombosis.

All endpoints are site reported in an electronic web-based capture system with additional submission of supporting medical documents. All clinical events will be assessed by an independent committee who was blinded to the patient's allocation.

Follow-up

After hospital discharge, clinical follow-up is performed with visits (preferred) or telephone contact at 1, 6 and 12 months. Follow-up will be continued to 3 years after procedure annually. Angiographic follow-up at 13 months is optional for all patients.

Quantitative coronary analysis

Quantitative coronary angiographic analysis at baseline, post-procedure and follow-up will be performed off-site by the Core lab (Rodebern Research Institute, Nanjing, China) using Cardiovascular Angiographic Analysis System II software V.5.0 (Pie Medical Imaging, Maastricht, the Netherlands). Basic angiography for all lesions should include at least two injections after intracoronary injection of 100–200 µg nitroglycerin. There should be an angulation difference (at least 30°) between the two-baseline angiography. The diagnostic/guiding catheter and the index lesions should be well visible without foreshorting, near the centre of the angiogram. All balloon inflations and stent implantations from the preprocedure and post-procedure should be recorded by short cine runs. The images are analysed by two experienced technicians who are blinded to the study design, with the interobserver and intraobserver variability under 5% (kappa test).

Statistical analysis

All statistical analyses will be performed in the intention-to-treat population, regardless of the treatment actually received. We hypothesised that the rate of a 1-year MACE would be 10% in PS-DCB group and 17% in the PS-NC balloon group based on the previous studies.[3 11–16] A total sample size of 746 is needed to detect a power of 0.8 (type II error=0.2–0.05, two tailed). Because of the considerable uncertainty, the enrolment is extended to 784 patients with 5% increment.

The distribution of continuous variables will be assessed by the Kolmogrov-Smirnov test. Continuous variables are expressed as mean±SD or median, and compared by Student's t-test (for normal data) and Mann-Whitney U test (for non-normally distributed variables). Categorical variables are summarised as frequencies or percentages, and compared by X^2 or Fisher's exact test. Survival curves with time-to-event data are generated by the Kaplan-Meier method and compared by the log-rank test. Comparison between two groups will be performed using the Cox proportional hazard model with reporting HR and 95% CI. A p value of <0.05 is considered statistically significant. All analyses are performed with the use of the statistical program SPSS V.24.0 (SPSS Institute).

The extensive subgroup analysis will be performed to assess the variation of treatment effects, as well as a test of interaction with treatment for each subgroup variable. The substudies of clinical factors include age (age ≥75 years old), sex, diabetes mellitus, chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73 m^2), acute coronary syndrome, cardiac dysfunction, left main bifurcation lesion or non-left main bifurcation lesion, intracoronary images guidance and multivessel disease. Therefore, there are at least nine prespecified subgroup analyses to explore the consistency of effects of DCB treatment on primary endpoint for coronary bifurcation lesions.

ETHICS AND DISSEMINATION

This protocol is conducted following the Guidelines of Standard Protocol Items: Recommendations for Interventional Trials (online supplemental appendix 2). The study will be performed in compliance with the Declaration of Helsinki of the World Medical Association. The study protocol and informed consent have been reviewed and approved by the Institutional Review Board of Nanjing First Hospital (KY20200110-01) and all other participating centres (online supplemental appendix 3). The written informed consent for participation in the trial will be obtained from all participants. The results of this study will be published in a peer-reviewed journal and disseminated at conferences.

Trial organisation

The trial has been designed by the principal investigator and the executive committee. The executive committee members are also responsible for reporting the results and drafting the manuscripts. The executive committee, together with the steering committee, the data and safety monitoring board (DSMB) and the independent endpoints adjudication committee, are involved in the present trial. All data will be collected in paper-based case report form (CRF), and then entered into an electronic CRF. All data will also be carefully examined and verified by two trained investigators. Research assistants will regularly check adherence to the protocol and the accuracy of the data by on-site visits or remote monitoring. All severe adverse events will be recorded in detail and reported to the ethics committee. DSMB will review all adverse events regularly to evaluate the safety of DCB in treating the coronary bifurcation lesions.

Patient and public involvement

No patient involved in the development of the research question, study design, recruitment, outcome measures and conduct of the study.

DISCUSSION

The present study describes the methodology of a randomised trial on the effect of SB DCB treatment

after PS in patients with true coronary bifurcation lesion. Coronary bifurcation lesions account for 15%–20% of coronary lesions treated with PCI. PS technique has been considered as a default strategy for simple bifurcation lesions, due to no benefit of systematic two-stent approach but with higher procedure time, radiation exposure, contrast volume and cost.[17–19] Technically, active SB protection could reduce the risk of SB occlusion in high-risk bifurcation lesions with a V-RESOLVE score ≥12 points.[20] Routine KBI or SB dilation after main vessel stenting has failed to provide clinical benefits.[21 22] If inadequate results of SB are present (TIMI <3, severe ostial SB stenosis or Fractional Flow Reserve<0.8), guidewire should be inserted into the SB through the distal cell, and then KBI or SB dilation is performed (POT-KBI-rePOT, or POT-SB dilation-rePOT). SB stenting should be considered by the T-stenting, T-stenting and minimal protrusion (TAP), or Culotte technique if SB TIMI <3, major SB dissection, or severe ostial SB stenosis after KBI or SB dilation. When the guidewire is inserted in the SB through the distal cell, T-stenting could be done; when SB access is performed through a proximal strut, TAP or Culotte is necessary to cover the SB ostium.[23]

Although above-mentioned standard protocol of PS has been widely used in our daily clinical practice, the frequent restenosis at the SB ostium still remains an unsolved problem. In the DK-CRUSH V trial,[15 24] it reported that the rate of ISR at the ostium of left circumflex coronary artery reached up to 12.0% with PS for treating true distal left main bifurcation lesions. DCB is a semicompliant balloon coated with antiproliferative drugs, which could be released into the vessel wall after balloon inflation to inhibit the VSMC proliferation. The efficacy and safety of DCB have been fully investigated for ISR[7 8] and de novo small vessel disease,[9 10] meanwhile emerging studies have indicated promising results of DCB in treating bifurcation lesions, de novo large vessel disease and patients at risk of high bleeding.[6 11–13 16] Because MB stenting with provisional SB stenting has been recommended as a default strategy for most bifurcation lesions, a stent in MB first following a DCB in SB is more preferable to be accepted for bifurcation lesions. BIOLUX-I[13] and DEBSIDE[11] Studies enrolled 35 patients and 52 patients, respectively, showing that the combination of a DCB in MB and a DCB in SB appeared to be a safe and effective treatment for bifurcation lesions with a very low LLL. However, these studies[11–13] could not provide the enough power to establish the use of DCB in bifurcation lesions, due to the BMS usage,[12] small sample size,[11–13] surrogate endpoint[11–13] and short follow-up duration.[11–13] Currently, these data[11–13] combined with our daily clinical practice could confirm the safety of DCB usage in bifurcation lesions, and our protocol also recommends that an additional SB stent will be implanted if SB TIMI flow <3 or ≥type C dissection after DCB dilation in SB. Besides, DSMB will review all adverse events regularly to evaluate the safety of DCB in treating the coronary bifurcation lesions.

This study is the first prospective, randomised, active-controlled multicentre trial to assess the hypothesis that using DCB is more efficient than NC balloon angioplasty for SB after PS for patients with true coronary bifurcation lesion. Of note, true coronary bifurcation lesions with SB length less than 10 mm are included, which may not be reflective of complex bifurcation lesions. This well-designed, adequately powered randomised controlled trial with hard endpoint will provide high-level evidence to help to create an algorithm for PS technique in coronary bifurcation lesions.

Author affiliations
[1]Department of Cardiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, Jiangsu, China
[2]Department of Cardiology, Xiamen Cardiovascular Hospital, Xiamen University, Xiamen, Fujian, China
[3]Cardiology, Zhengzhou University First Affiliated Hospital, Zhengzhou, Henan, China
[4]Department of Cardiology, Medicine Siriraj Hospital, Bangkok, Thailand
[5]Department of Cardiology, China-Japan Union Hospital of Jilin University, Changchun, Jilin, China
[6]Department of Cardiology, Xuzhou Central Hospital, Xuzhou, Jiangsu, China
[7]Department of Cardiology, Qilu Hospital, Jinan, Shandong, China
[8]Department of Cardiology, Shandong Provincial Hospital, Jinan, Shandong, China
[9]Department of Cardiology, Shanghai Sixth People's Hospital, Shanghai, Shanghai, China
[10]Department of Cardiology, Binawaluya Heart Hospital, Jakarta, Indonesia
[11]Department of Cardiology, Tabba Heart Institute, Karachi, Pakistan
[12]Department of Cardiology, Medistra Hospital, Jakarta, Indonesia
[13]Department of Cardiology, Ulsan Medical Center, Ulsan, Korea (the Republic of)
[14]Interventional Cardiology, Casa di Cura Dottor Pederzoli SpA, Peschiera del Garda, Italy

Acknowledgements The authors appreciate the contributions of Ling Lin, Hai-Mei Xu and Ying-Ying Zhao to data collection.

Contributors S-LC and JZ made substantial contributions to study conception and design, and to critical revision of the manuscript. XG, ZG and JK wrote the first draft. X-QK, YW and C-GQ provided data management and statistical expertise. DT, Y-QH, QW, J-FL, H-TY, CS, XC, MM, BH, TS, E-SS, IS and FY provided comments and suggestions in critical revision of the article. All authors approved the final version of the article.

Funding This study was funded by Social Development Project of Jiangsu Province (BE2019615 and BE2019616).

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Xiao-Fei Gao http://orcid.org/0000-0001-7428-119X
Jing Kan http://orcid.org/0000-0002-6268-2954

Eun-Seok Shin http://orcid.org/0000-0002-9169-6968

REFERENCES

1 Burzotta F, Lassen JF, Louvard Y, *et al*. European bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. *Catheter Cardiovasc Interv* 2020;96:1067–79.
2 Zhang J-J, Ye F, Xu K, *et al*. Multicentre, randomized comparison of two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: the definition II trial. *Eur Heart J* 2020;41:2523–36.
3 Chen S-L, Sheiban I, Xu B, *et al*. Impact of the complexity of biFurcation lesIons treated with drug-eluting steNts: the definition study (definitions and impact of complEx biFurcation lesIons on clinical outcomes after percutaNeous coronary intervention using drug-eluting steNts). *JACC Cardiovasc Interv* 2014;7:1266–76.
4 Loh PH, Lassen JF, Jepson N, *et al*. Asia Pacific consensus document on coronary bifurcation interventions. *EuroIntervention* 2020;16:e706–14.
5 Neumann F-J, Sousa-Uva M, Ahlsson A, *et al*. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J* 2019;40:87–165.
6 Yerasi C, Case BC, Forrestal BJ, *et al*. Drug-Coated Balloon for De Novo Coronary Artery Disease: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;75:1061–73.
7 Chen Y, Gao L, Qin Q, *et al*. Comparison of 2 different Drug-Coated balloons in in-stent restenosis: the restore ISR China randomized trial. *JACC Cardiovasc Interv* 2018;11:2368–77.
8 Giacoppo D, Alfonso F, Xu B, *et al*. Paclitaxel-Coated balloon angioplasty vs. drug-eluting stenting for the treatment of coronary in-stent restenosis: a comprehensive, collaborative, individual patient data meta-analysis of 10 randomized clinical trials (Daedalus study). *Eur Heart J* 2020;41:3715–28.
9 Tang Y, Qiao S, Su X, *et al*. Drug-Coated balloon versus drug-eluting stent for small-vessel disease: the restore SVD China randomized trial. *JACC Cardiovasc Interv* 2018;11:2381–92.
10 Jeger RV, Farah A, Ohlow M-A, *et al*. Long-Term efficacy and safety of drug-coated balloons versus drug-eluting stents for small coronary artery disease (BASKET-SMALL 2): 3-year follow-up of a randomised, non-inferiority trial. *Lancet* 2020;396:1504–10.
11 Berland J, Lefèvre T, Brenot P, *et al*. DANUBIO - a new drug-eluting balloon for the treatment of side branches in bifurcation lesions: six-month angiographic follow-up results of the DEBSIDE trial. *EuroIntervention* 2015;11:868–76.
12 Mathey DG, Wendig I, Boxberger M, *et al*. Treatment of bifurcation lesions with a drug-eluting balloon: the PEPCAD V (paclitaxel Eluting PTCA balloon in coronary artery disease) trial. *EuroIntervention* 2011;7 Suppl K:K61–5.
13 Worthley S, Hendriks R, Worthley M, *et al*. Paclitaxel-Eluting balloon and everolimus-eluting stent for provisional stenting of coronary bifurcations: 12-month results of the multicenter BIOLUX-I study. *Cardiovasc Revasc Med* 2015;16:413–7.
14 Chen S-L, Santoso T, Zhang J-J, *et al*. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (double kissing crush versus provisional stenting technique for treatment of coronary bifurcation lesions) trial. *J Am Coll Cardiol* 2011;57:914–20.
15 Chen S-L, Zhang J-J, Han Y, *et al*. Double Kissing Crush Versus Provisional Stenting for Left Main Distal Bifurcation Lesions: DKCRUSH-V Randomized Trial. *J Am Coll Cardiol* 2017;70:2605–17.
16 Jing Q-M, Zhao X, Han Y-L, *et al*. A drug-eluting balloon for the trEatment of coronarY bifurcatiON lesions in the side branch: a prospective multicenter ranDomized (beyond) clinical trial in China. *Chin Med J* 2020;133:899–908.
17 Colombo A, Bramucci E, Saccà S, *et al*. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: the cactus (coronary bifurcations: application of the crushing technique using sirolimus-eluting stents) study. *Circulation* 2009;119:71–8.
18 Hildick-Smith D, de Belder AJ, Cooter N, *et al*. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British bifurcation coronary study: old, new, and evolving strategies. *Circulation* 2010;121:1235–43.
19 Steigen TK, Maeng M, Wiseth R, *et al*. Randomized study on simple versus complex stenting of coronary artery bifurcation lesions: the Nordic bifurcation study. *Circulation* 2006;114:1955–61.
20 Dou K, Zhang D, Pan H, *et al*. Active SB-P Versus Conventional Approach to the Protection of High-Risk Side Branches: The CIT-RESOLVE Trial. *JACC Cardiovasc Interv* 2020;13:1112–22.
21 Niemelä M, Kervinen K, Erglis A, *et al*. Randomized comparison of final kissing balloon dilatation versus no final kissing balloon dilatation in patients with coronary bifurcation lesions treated with main vessel stenting: the Nordic-Baltic bifurcation study III. *Circulation* 2011;123:79–86.
22 Pan M, Medina A, Suárez de Lezo J, *et al*. Coronary bifurcation lesions treated with simple approach (from the Cordoba & Las Palmas [CORPAL] Kiss Trial). *Am J Cardiol* 2011;107:1460–5.
23 Sawaya FJ, Lefèvre T, Chevalier B, *et al*. Contemporary Approach to Coronary Bifurcation Lesion Treatment. *JACC Cardiovasc Interv* 2016;9:1861–78.
24 Chen X, Li X, Zhang J-J, *et al*. 3-Year outcomes of the DKCRUSH-V trial comparing DK crush with provisional stenting for left main bifurcation lesions. *JACC Cardiovasc Interv* 2019;12:1927–37.