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RESEARCH ARTICLE

Yan et al: 2-year DCB outcomes in TASC C/D IPADs

Drug-coated balloon treatment for tasc c/d infrapopliteal disease: Two-year matched cohort outcomes

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ABSTRACT

As the most common form of peripheral arterial disease, lower extremity arterial disease—caused by atherosclerotic stenosis or occlusion—has led to widespread concern due to the high risk of postoperative restenosis. This study aimed to evaluate the effectiveness of drug-coated balloon (DCB) angioplasty in treating severe infrapopliteal artery (IPA) lesions. Plain

old balloon (POB) angioplasty served as the control. Patients who underwent procedures at our center for Trans-Atlantic Inter-Society Consensus (TASC) C/D IPA lesions between June 2020 and June 2022 and met the inclusion criteria were enrolled in this retrospective cohort study, which used the propensity score matching (PSM) method. The primary outcomes were the 2-year cumulative rates and survival trends of primary patency (PP) and target lesion revascularization (TLR), based on the treated lesions. Secondary outcomes included limb-based major amputation (MA) and patient-based all-cause death (ACD). A total of 278 target lesions were initially included, with significant differences ($p < 0.05$) observed in some non-outcome variables. After PSM, analyses were conducted on 240 target lesions, 221 limbs, and 195 patients. The PSM models satisfied both the common support and parallel trend assumptions. In terms of PP, the 2-year cumulative rate in the DCB group was significantly higher than in the POB group (48.0% vs. 22.9%, $p < 0.001$). The log-rank test yielded a p-value of < 0.001, and the adjusted hazard ratio (HR) from Cox regression analysis was 2.303 [95% confidence interval (CI): 1.518–3.495]. However, there was no statistically significant difference in TLR between the two groups: the 2-year cumulative rates were 25.0% vs. 27.1% ($p = 0.767$), the log-rank test p-value was 0.563, and the adjusted HR was 0.956 (95% CI: 0.523–1.747). Similarly, no significant differences were found between groups in MA or ACD ($p > 0.05$). Based on these findings, the study concludes that for severe IPA lesions such as TASC C/D, DCB angioplasty is superior to POB angioplasty in maintaining primary patency over a 2-year period, without any inferiority in other clinical outcomes.

Keywords: infrapopliteal arterial disease; drug coated balloon; primary patency; target lesion revascularization.

INTRODUCTION

Infrapopliteal arterial disease (IPAD), with or without femoropopliteal inflow disease, is the primary cause of critical limb ischemia (CLI) [[1], [2]]. Femoropopliteal-to-distal bypass surgery is considered the traditional treatment option for revascularization in IPADs [[3]-[5]]. In the past few decades, percutaneous transluminal angioplasty (PTA) [i.e., plain old balloon angioplasty (POBA) alone], which is more minimally invasive, has been widely used, especially for patients whose physical conditions make it difficult to withstand open surgery or who do not have suitable distal arteries for bypass [[6]-[10]]. However, although this modality has a satisfactory technical success rate, it still has a significantly high risk of

clinical failure caused by lesion restenosis even in the short term [**Error! Reference source not found.**-[13]].

The superiority of drug coated balloon (DCB) angioplasty for femoropopliteal artery lesions over POBA has been demonstrated [[14]-**Error! Reference source not found.**] in recent years. However, the exploration path for the superiority of DCBs in the treatment of infrapopliteal artery (IPA) lesions is relatively tortuous. Compared with POBA alone, significantly lower cumulative rates of target lesion restenosis and revascularization at the 1st year after drug coated balloon angioplasty (DCBA) have been reported by Schmidt et al. and Liistro et al., respectively [[17] [18]]. However, in the later IN.PACT Deep trial [[19]], which included 358 patients, the cumulative rate of target lesion revascularization (TLR) at the 1st postoperative year was not significantly different between the groups (11.9% vs. 13.5%, p =0.682). Moreover, in the BIOLUX P-II trial [[20]], there were no statistically significant differences in the cumulative rates of the following outcomes during the same follow-up period (p >0.05): TLR (30.1% vs. 30.6%), patency loss (50.8% vs. 45.6%), and major amputation (MA, 3.3% vs. 5.6%). However, the conclusion of the AcoArt II-BTK trial from China published in 2021 favored DCB [[21]]. This study included 79% chronic total occlusion (CTO) lesions and reported better results for the DCB group with 6-month primary patency (PP, 75.0% vs. 28.3%, p <0.001) and 1-year TLR (8.5% vs. 23.2%, p =0.028). The Lutonix BTK trial [[22]], which involved a single arm and included 69.3% of Trans-Atlantic Inter-Society Consensus (TASC) C/D IPA lesions [5] (Figure S1), reported satisfactory DCBA results. However, there are no published controlled studies including only TASC C/D lesions. Thus, this study was conducted in accordance with the STROBE reporting checklist to determine the superiority of DCBs in these severe lesions.

MATERIALS AND METHODS

Study design and setting

This was a single center retrospective cohort study. The institution was a comprehensive tertiary hospital in Beijing, China. We searched the hospital's electronic medical record management system for patients who underwent endovascular therapies in lower extremity arteries from June 2020 to June 2022. All patients who had undergone DCBA or alone POBA for TASC C/D IPA lesions and did not meet the following exclusion criteria were included in the study: (1) planned amputation before intervention and (2) absence of follow-up data

because of loss to follow-up or other reasons. The DCB was defined as any balloon for dilatation that was coated with antiproliferative drugs (paclitaxel, sirolimus, everolimus, etc.) on the outer surface. The included records were divided into two independent groups according to the above two intervention modalities, namely, the DCB group and the plain old balloon (POB) group (control). The same patient could not be included into both groups simultaneously, and inclusion in the DCB group was preferable. Data extraction and analyses were subsequently performed. Case screening was performed by YY and HT separately and independently. Any disagreements would be decided by ML after discussion.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional ethics committee (No. 2024-03-01). The need to obtain individual consent for this retrospective analysis was waived.

General treatment procedure

In this retrospective study, although we did not require the process experienced by the included cases to be consistent with our established general treatment procedure, this procedure has been widely followed. The main criteria included the following: (1) the patient received antiplatelet therapy preoperatively for more than 1 month (otherwise he or she received a loading dose of the drug (aspirin or clopidogrel, 300 mg) on the operating day); (2) he or she received antiplatelet therapy for at least 6 months postoperatively; (3) skin puncture points for endovascular operation could be located on the ipsilateral or contralateral side; (4) intraoperatively, a guide wire system through the target lesion was established in the true lumen, and a balloon was placed along the guide wire to perform a dilatation; (5) the diameter of the balloon did not exceed 120% of the diameter of the reference vessel; (6) after DCBA, POBAs at the same location were no longer performed; (7) he or she was asked to visit the clinic for follow-up visits at the 1st, 3rd, 6th, 12th, 18th, and 24th months postoperatively unless he or she came on his or her own because of complaints; and (8) at each follow-up, condition inquiry, physical and ankle-brachial index (ABI) examination, and imaging studies [i.e., Doppler ultrasound (DUS), computed tomography angiography (CTA), or quantitative vascular angiography (QVA)] were carried out, followed by the evaluation for the outcomes of interest and Rutherford's classification (RC).

In addition, once the restenosis of the lumen diameter of a treated lesion is found to reach 50% after operation, early intensive drug intervention will be initiated regardless of whether the symptom of lower limb ischemia reappears. Drug intervention should include at least the following: increasing the dosage of antiplatelet drugs and/or adding anticoagulant drugs, increasing vasodilators such as prostaglandins, and instructing patients to strengthen lower limb exercise represented by brisk walking. Regardless of whether the restenosis is alleviated after the aforementioned drug intervention with unlimited course of treatment, TLR will only be considered if the symptom reappears and reaches at least RC-3. Notably, some patients refused to undergo revascularization.

Variables and data

When data were extracted, all observations were based on the target lesion, which was defined as an IPA lesion of TASC C/D that had undergone the intervention modality (i.e., DCBA or POBA) corresponding to its group. An arterial site with a stenosis less than 30% of the diameter of the reference artery nearby was considered a "normal site". The lesions that were separated by a normal site with a length of less than 20 mm or had undergone the same balloon dilatation simultaneously, were considered as the same target lesion in total length; otherwise, they were considered separate and distinct target lesions. The variables were broadly divided into 5 categories by period: preoperative demography, angiography findings before intervention during the operation, intraoperative intervention, short-term postoperative medication and complications, and follow-up. All variables that may have different definitions (such as calcification and dissection classification [23]) were evaluated according to unified criteria set in advance. The inclusion period for postoperative follow-up data for all patients was 2 years (690-750 days). To avoid bias due to abnormalities [25], if the preoperative ABI of an affected limb was ≥1.4, the postoperative ABI was recorded as a missing value.

We considered the PP and the TLR (both based on the target lesion) as primary outcomes, and the MA (based on the limb) and all-cause death (ACD, based on the patient) as secondary outcomes. The PP was defined as freedom from restenosis (<50% residual lumen diameter under CTA/QVA, or peak systolic velocity ratio ≥2.4 under DUS) without TLR. All DUS examinations were performed by experienced vascular ultrasound professionals. TLR was defined as repeat percutaneous or surgical intervention because of angiographic evidence of >50% restenosis with recurrence of pain in the foot and/or the presence of a nonhealing

limb ulcer/gangrene. MA was defined as amputation above the ankle. The outcome measures were the cumulative rates of the above outcomes at the follow-up end point, and the hazard ratios (HRs, DCBs vs. POBs) with their 95% confidence intervals (CIs).

After data extraction, dataset No. 0 was obtained. The data were based on the units (i.e., target lesion, limb, or patient) corresponding to their original meanings separately. To unify the units on which the data in each analysis were based, data merging was performed. The concrete methods included: taking the most severe value (such as the Rutherford classification), taking the mean value (such as the length of the target lesion), and taking the missing value (such as the location of the target lesion). The following datasets according to the original units for each outcome of interest were subsequently obtained: No. 1, which was based on the target lesion (PP and TLR); No. 2, which was based on the limb (MA); and No. 3, which was based on the patient (ACD).

Error control

The propensity score matching (PSM) method was used to filter all included observations to reduce selection bias [26]. To examine statistical power, the PSM derived sample size was compared with that estimated.

Statistical analysis

The data distribution for a numerical variable was represented as the "mean ± standard deviation", and that for a categorical variable was represented as the "number (percentage)". Stata (Stata Corp., College Station, Texas, United States) version 16.0 was used for all the statistical analyses. All hypothesis tests were two-sided with a significance level set at 0.05. Univariate analyses for variables other than the outcomes of interest between groups were performed on the 4 datasets separately via Student's t test [[27]] or Fisher's exact test [[28]]. All variables that were significantly different and not affected by the intervention measures were not used. Including the above selected variables, 1:1 nearest neighbor PSMs (logit regression) using calipers with widths of 0.01 allowing replacements of the POB group's observations, were performed for datasets No. 1, No.2, and No. 3. Cohorts formed after matching were incorporated separately into their respective datasets. The kernel density plots before and after matching were plotted and compared to determine whether the regression model met the common support assumption. After matching, univariate analyses were performed again on each dataset. The results were evaluated for compliance with the parallel

test assumption by observing the changes in the intergroup differences of each variable derived from univariate analyses before and after matching. Then, on the basis of the corresponding matched datasets, the outcomes of interest were measured using the following methods: comparison of cumulative rates between groups, plotting of the Kaplan-Meier (K-M) survival curve with the log-rank test [[29]], and multivariate Cox regression analysis [[30]]. In the regression analyses, the preoperative ABI values exceeding 1.4 were replaced with missing values. Additionally, sample size estimation was performed using PASS (NCSS Corp., Kaysville, Utah, United States) version 15.0 under the settings of equal numbers between groups. The 2-year cumulative PP values of the two groups in this study were substituted into the above calculation to estimate the minimum sample size with qualified statistical power.

RESULTS

Data before matching

A total of 221 patients who met the selection criteria with 253 affected limbs and 278 target lesions were included. They were all Han Chinese, were mostly male (61.1%), and ranged from 52 to 90 years in age. All DCBs used were Litos®/Tulip® (Acotec Scientific Corp., Beijing, China). This type of balloon is suitable for 0.014/0.018-inch wire guide system, whose surface is coated with 3 μg/mm² paclitaxel. Except for those of body mass index, hypertension, dyslipidemia, auricular fibrillation, current smoking, and postoperative statin use, the data of all the nonoutcome variables were not significantly different between the groups ($p > 0.05$). The details are shown in Tables S1 and S2.

Primary outcomes

In the dataset No. 1 in which all variables were based on the target lesion, no other variables with significant data differences between groups were found except for the above 6 variables before matching. After these 6 variables were included in the PSM model, a new database No. 1 was obtained. Only a small number of observations were dropped (7/107 and 31/171), which met the common support assumption well. In the kernel density plot, the values of the two groups largely overlapped, which also demonstrated the compliance of the model with the assumption (Figure 1). After matching, the data of the nonoutcome variables were all not

significantly different between the groups (p >0.05), which was in accordance with the parallel test assumption. The details are shown in Tables 1 and 2.

A comparison of the matched data revealed that the 2-year cumulative PP rate in the DCB group was significantly greater than that in the POB group (48.0% vs. 22.9%, p <0.001; Table 3). The results of the K-M survival analysis with the log-rank test were similar (Figure 2). The HR value obtained by adjusted Cox regression analysis was 2.303 (95% CI: 1.518-3.495). However, the difference in TLR between the two groups was not statistically significant: the 2-year cumulative rate was 25.0% vs. 27.1% (p =0.767, Table 3), the survival curve was approximate (Figure 3), and the adjusted HR was 0.956 (95% CI: 0.523-1.747). The sample size estimated with PASS software was 85 cases per group. And we obtained a size exceeding this value (100 cases in DCB group and 140 cases in POB group), representing the eligible statistical power of the study.

Secondary outcomes

After matching, a new dataset No. 2 that met the common support assumption and parallel test assumption was obtained (Tables S3 and S4 and Figure S2). There were no significant differences in MA between the groups (Table 3 and Figure S3). Only after 3 variables (complete IPA before intervention, postoperative statin use, and postoperative antiplatelet use) were removed could multivariate Cox regression converge successfully. After a satisfactory dataset No. 3 was obtained, there were also no significant differences in ACD between the groups (Tables S5, S6, and 3 and Figures S4 and S5), without variable removal in the Cox regression analysis. In addition, there were no significant differences in the RCs at the end of follow-up between the groups (p =0.292), but the ABI at the end of follow-up in the DCB group was significantly greater (mean 0.50 vs. 0.43, p =0.005) (Table 3).

DISCUSSION

This presented study retrospectively compared the 2-year outcomes of TASC C/D IPAD patients underwent DCB and POB treatment. The results showed that compared with the traditional POB, the application of DCB could better maintain the PP in the lesions in the mid-term postoperative period (HR =2.303, 95% CI: 1.518-3.495).

The results of other studies in which DCBs were applied to IPA lesions are less consistent [[17]-[22]]. We believe that this may be related to the inclusion of more severe cases in

studies reporting results in favor of DCBs [[21], [22]]. In 2015, the TASC Steering Committee issued the latest classification criteria for the severity of IPA lesions [5], which are widely followed. We used this standard to screen for more severe patients with IPAD, and retrospectively analyzed the superiority of DCBs over POBs. With the help of the PSM method, selection bias was effectively reduced, making the analysis more convincing.

The recognized disadvantage of POBA is a high rate of restenosis and the concomitant need for TLR. Unlike coronaries with similar diameters, IPA lesions involve longer segments, often at multiple levels with decreased flow rates, leading to restenosis even when the immediate angiographic results are excellent [[31]]. The proliferation of smooth muscle cells (SMCs) is a significant cause of neo-intimal hyperplasia, which ultimately causes restenosis [[32]]. The anti- proliferative mechanism of drugs such as paclitaxel and sirolimus is beneficial for antagonizing the proliferation of SMCs and reducing the restenosis rate. This is the theoretical basis for the widespread application of DCBs.

The first study on DCBs for IPAD was published in 2011 [[17]]. It was a prospective single arm study with all DCBs used from IN.PACT™ (Medtronic Corp., Minneapolis, Minnesota, United States), and the study reported a cumulative MA rate of 3.8% and a cumulative ACD rate of 16.3% at the 12th month. Since then, various related studies have been published. Most of them reported early to mid-term results at the 6th or 12th month; a randomized controlled trial (RCT) -IN.PACT DEEP [[33]] and a retrospective cohort study [[34]] reported results at the 5th year; and only 1 study, which was a prospective single arm study named BIOLUX P-III [[35]], reported 2-year results, like the present study. Moreover, only 1 study specifically included only TASC C/D IPAD patients [[36]], as we did, but reported results only at the 6th month.

Previous studies have reported 1-year cumulative PP rates of 59%-73% after DCBA for IPADs [[18], [33], [37]]. The present study, which included only severe lesions, had a 2-year cumulative rate of 48%, which is an exciting result. The 1-year cumulative TLR rate after DCBA was previously reported to be 8%-30% [[18], [20], [21], [33], [37], [38]]. The 2-year cumulative TLR rate for severe lesions of 25% that we obtained seems acceptable. In addition, the previously reported 1-year postoperative MA rates and ACD rates were 0%-16% and 2%-16%, respectively [[17], [18], [20], [21], [33], [37]-[39]], with scopes containing the 2-year rates we reported. In the BIOLUX P-III study, better rates of PP (83%) and TLR (9%) than ours were reported; however, the opposite was true for MA (26%) and

ACD (21%). The loss to follow-up rate in this study reached 17% at just the 6th month postoperatively, due in part to a high mortality (7%). We believe that this may be one of the reasons why good PP and TLR rates were reported.

The results of the present study revealed that for TASC C/D IPA lesions, the postoperative PP rate ($p < 0.001$) in the DCB group was better than that in the POB group. This finding is consistent with the 6-month results ($p < 0.001$) reported by two sub-studies [[21], [38]] from different countries in the AcoArt BTK trial, which used the same brand of DCBs as our study did. This reflects the superiority of DCBs and indicates that severe restenosis of the target lesions can begin 6 months or even earlier after the operation. However, we did not conclude that the postoperative TLR risk was significantly lower in the DCB group ($p > 0.05$). We believe that this is because many non-PP target lesions had not yet caused clinical manifestations of CLI and therefore had not undergone revascularisation. This finding is supported by the significant difference in the ABI between the groups at the end of follow-up ($p = 0.005$) and the equivalence of the RCs ($p = 0.292$) in the present study. This result is consistent with the 1-year results reported by some RCTs [[20], [33]]. In addition, there was no difference ($p > 0.05$) in the secondary outcomes, i.e., MA and ACD, between the groups. This is consistent with the results reported by most RCTs [[18], [20], [21], [33], [38]]. Notably, the 95% CI of the HR value of DCB for MA was particularly broad (0.3 to 6144.4), which we attribute to a very low incidence (event count) of MA. In addition to PP, there are some unmeasurable factors that may also affect the above clinical outcomes, such as wound management measures and nursing experience. Their distributions may differ, leading to bias to some extent. Notably, the IN.PACT trial reported 5-year results that were consistent with those of the present study [[33]]. This may indicate that restenosis of the target lesion tends to stabilize 1-2 years after balloon dilation angioplasty. In summary, we believe that DCBs have advantages over traditional POBs for TASC C/D lesions, especially in maintaining postoperative PP. PP is the most direct indicator that reflects the severity of restenosis, which is considered a historical conundrum. Although there were no significant differences in other clinically relevant outcomes, the milder the restenosis was, the better the outcomes.

The present study had several limitations. First, this was a retrospective study. Although the PSM method was used, there is possible selection bias. Second, this was a single center study, and only one type of DCB was used. This weakens the generalizability of the study to the overall population. Third, we used the TASC standard, to screen for severe IPA lesions,

which primarily evaluates severity on basis of the lesion length rather than the degree of calcification, to screen for severe IPA lesions. The efficacy of DCBs is negatively correlated with the degree of calcification at the target lesion [[40], [41]]. We look forward to international, multicenter RCTs that include multiple types of DCBs and severe lesions on multiple views.

CONCLUSION

For severe IPA lesions such as of TASC C/D, DCBs are superior to POBs in maintaining PP for 2 years postoperatively, with no inferiorities in other clinical outcomes such as avoiding TLR, MA or ACD. Therefore, DCB is a reliable device.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Preoperative data based on target lesion in the analyses of primary patency and target lesio revascularization

Variable	Before propensity score matching			After propensity score matching		
	DCB group (n=107)	POB group (n=171)	p value	DCB group (n=100)	POB group (n=140)	p value
Duplicate patient	25 (23.4)	32 (18.7)	0.363	23 (23.0)	24 (17.1)	0.322
Duplicate limb	13 (12.2)	12 (7.0)	0.195	12 (12.0)	11 (7.9)	0.374
Duplicate artery	4 (3.7)	3 (1.8)	0.435	4 (4.0)	3 (2.1)	0.455
Restenosis	20 (18.7)	31 (18.1)	1.000	20 (20.0)	26 (18.6)	0.868
Previous revascularization	27 (25.2)	37 (21.6)	0.558	26 (26.0)	30 (21.4)	0.441
Left side	58 (54.2)	93 (54.4)	1.000	52 (52.0)	81 (57.9)	0.430
Preoperative RC			0.574			0.896
3	5 (4.7)	3 (1.8)		3 (3.0)	3 (2.1)	
4	33 (30.8)	52 (30.4)		32 (32.0)	41 (29.3)	
5	45 (42.1)	77 (45.0)		44 (44.0)	63 (45.0)	
6	24 (22.4)	39 (22.8)		21 (21.0)	33 (23.6)	
Preoperative ABI†	0.40±0.13	0.37±0.14	0.078	0.40±0.13	0.37±0.14	0.099
Preoperative ABI exceeding 1.4	8 (7.5)	6 (3.5)	0.164	8 (8.0)	5 (3.6)	0.156
Age (year)	73.3±7.8	71.8±7.6	0.113	73.4±7.8	72.4±7.4	0.337
Male	70 (65.4)	104 (60.8)	0.448	65 (65.0)	88 (62.9)	0.786
Body mass index	25.3±2.0	24.4±2.1	0.002*	25.1±2.0	24.6±2.1	0.071
Hypertension	95 (88.8)	123 (71.9)	0.001*	88 (88.0)	109 (77.9)	0.060
Diabetes mellitus	93 (86.9)	159 (93.0)	0.137	88 (88.0)	130 (92.9)	0.257
Dyslipidemia	59 (55.1)	67 (39.2)	0.013*	52 (52.0)	60 (42.9)	0.190
Coronary heart disease	63 (58.9)	107 (62.6)	0.613	57 (57.0)	97 (69.3)	0.057
Auricular fibrillation	19 (17.8)	55 (32.2)	0.008*	19 (19.0)	37 (26.4)	0.216
Chronic kidney disease	24 (22.4)	44 (25.7)	0.569	22 (22.0)	28 (27.1)	0.450
Chronic lung disease	14 (13.1)	32 (18.7)	0.248	12 (12.0)	26 (18.6)	0.210
Anaemia	50 (46.7)	76 (44.4)	0.712	49 (49.0)	61 (43.6)	0.432
Previous cerebral infarction	40 (37.4)	46 (26.9)	0.083	36 (36.0)	44 (31.4)	0.489
Previous myocardial infarction	18 (16.8)	36 (21.0)	0.438	18 (18.0)	30 (21.4)	0.624
Current smoking	49 (45.8)	55 (32.2)	0.030*	46 (46.0)	49 (35.0)	0.108
Previous smoking	79 (73.8)	109 (63.7)	0.088	72 (72.0)	91 (65.0)	0.265
Preoperative statin‡	53 (49.5)	68 (39.8)	0.136	51 (51.0)	63 (45.0)	0.363
Preoperative antiplatelet‡	58 (54.2)	83 (48.5)	0.389	54 (54.0)	73 (52.1)	0.794

Observations are presented as "n (%)" or "x,¯ ± standard deviation". RC: Rutherford classification; ABI: ankle brachial index; DCB: drug coated balloon; POB: plain old balloon. †99/165 and 92/135 observations respectively; ‡lasted at least 6 months; *significant statistical difference due to a p value of less than 0.05.

Table 2. Intra- and postoperative data based on target lesion in the analyses of primary patency and target lesion revascularization

Variable	Before propensity score matching				After propensity score matching		
	DCB group (n=107)	POB group (n=171)	p value		DCB group (n=100)	POB group (n=140)	p value
Arterial location			0.481				0.661
Anterior tibial	38 (35.5)	61 (35.7)			34 (34.0)	46 (32.9)	
Peroneal	6 (5.6)	12 (7.0)			6 (6.0)	12 (8.6)	
Posterior tibial	34 (31.8)	50 (29.2)			31 (31.0)	42 (30.0)	
Tibiofibular trunk - peroneal	15 (14.0)	15 (8.8)			15 (15.0)	14 (10.0)	
Tibiofibular trunk - posterior tibial	14 (13.1)	33 (19.3)			14 (14.0)	26 (18.6)	
TASC classification[5]			0.324				0.511
C	63 (58.9)	90 (52.6)			58 (58.0)	74 (52.9)	
D	44 (41.1)	81 (47.4)			42 (42.0)	66 (47.1)	
Complete IPA before intervention†			0.704				0.684
0	65 (60.8)	108 (63.2)			61 (61.0)	90 (64.3)	
1	42 (39.2)	63 (36.8)			39 (39.0)	50 (35.7)	
Calcification classification			0.607				0.590
0 (no visible calcium)	4 (3.7)	5 (2.9)			4 (4.0)	3 (2.1)	
1 (unilateral calcification <5cm)	9 (8.4)	13 (7.6)			8 (8.0)	12 (8.6)	
2 (unilateral calcification ≥5cm)	29 (27.1)	62 (36.3)			27 (27.0)	50 (35.7)	
3 (bilateral calcification <5cm)	46 (43.0)	66 (38.6)			44 (44.0)	56 (40.0)	
4 (bilateral calcification ≥5cm)	19 (17.8)	25 (14.6)			17 (17.0)	19 (13.6)	
Chronic total occlusion	53 (49.5)	99 (57.9)	0.176		51 (51.0)	82 (58.6)	0.292
Length (mm)	154.2±37.2	158.1±32.3	0.374		154.2±38.3	157.6±33.7	0.466
Reference vessel diameter (mm)	2.54±0.11	2.53±0.12	0.648		2.54±0.11	2.53±0.12	0.642
Intervention to SPAs	16 (15.0)	22 (12.9)	0.720		15 (15.0)	17 (12.1)	0.566
Maximum balloon diameter (mm)	2.98±0.24	2.94±0.28	0.178		3.00±0.24	2.93±0.27	0.064
Maximum dilatation pressure (atm)	13.20±0.85	13.34±0.70	0.141		13.18±0.87	13.36±0.68	0.067
No. of dilatation	2.79±0.71	2.91±0.62	0.166		2.80±0.71	2.91±0.62	0.186
Dilatation duration (sec)	493.8±131.3	510.0±110.0	0.271		495.1±131.4	511.2±110.5	0.303
Subintimal angioplasty	22 (20.6)	46 (26.9)	0.254		21 (21.0)	40 (28.6)	0.229
Retrograde angioplasty	12 (11.2)	28 (16.4)	0.293		11 (11.0)	25 (17.9)	0.199
Crossover	8 (7.5)	21 (12.3)	0.231		7 (7.0)	18 (12.9)	0.198
Stent implantation	1 (0.9)	0 (0)	0.385		1 (1.0)	0 (0)	0.417
Dissection			0.815				0.618
A (minor radiolucent areas)	12 (11.2)	18 (10.5)			11 (11.0)	13 (9.3)	
B (linear dissection)	8 (7.5)	9 (5.3)			8 (8.0)	9 (6.4)	

C (contrast outside lumen)	4 (3.7)	4 (2.3)			4 (4.0)	3 (2.1)	
D (spiral dissection)	1 (0.9)	1 (0.6)			1 (1.0)	0 (0)	
Complete IPA after intervention†			0.339				0.555
1	8 (7.5)	12 (7.0)			8 (8.0)	10 (7.1)	
2	65 (60.8)	90 (52.6)			59 (59.0)	74 (52.9)	
3	34 (31.8)	69 (40.4)			33 (33.0)	56 (40.0)	
Device success	107 (100)	171 (100)	1.000		100 (100.0)	140 (100.0)	1.000
Technical success	105 (98.1)	166 (97.1)	0.711		98 (98.0)	137 (97.9)	1.000
Postoperative statin‡	97 (90.6)	141 (82.5)	0.078*		90 (90.0)	120 (85.7)	0.429
Postoperative antiplatelet‡	100 (93.4)	152 (88.9)	0.290		95 (95.0)	128 (91.4)	0.321
Serious complications	1 (0.9)	1 (0.6)	1.000		1 (1.0)	1 (0.7)	1.000
Minor complication: AKI	9 (8.4)	15 (8.8)	1.000		9 (9.0)	14 (10.0)	0.828
Minor complication: MB	5 (4.7)	3 (1.8)	0.267		3 (3.0)	1 (0.7)	0.311
Minor complication: PRP	3 (2.8)	6 (3.5)	1.000		3 (3.0)	4 (2.9)	1.000

Observations are presented as "n (%)" or "$\bar{x}$ ± standard deviation". TASC: Trans-Atlantic Inter-Society Consensus; IPA: infrapopliteal artery; SPA: suprapopliteal artery; AKI: acute kidney injury; MB. minor bleeding; PRP: puncture related problem; DCB: drug coated balloon; POB: plain old balloon. †infrapopliteal artery directly reaching foot without stenosis of more than 30%; ‡lasted at least 6 months; *the p value in the comparison of observations based on patient was 0.042.

Table 3. Outcome data after propensity score matching

Outcome	DCB group	N	POB group	N	p-value	Hazard ratio with 95% confidence interval[†]
PP (based on target lesion)	48 (48.0)	100	32 (22.9)	140	<0.001[*]	2.303 (1.518-3.495)
TLR (based on target lesion)	25 (25.0)	100	38 (27.1)	140	0.767	0.956 (0.523-1.747)
MA (based on limb)	5 (5.6)	89	5 (3.8)	132	0.529	43.284 (0.305-6144.367)
ACD (based on patient)	11 (14.5)	76	17 (14.3)	119	1.000	0.932 (0.293-2.962)
RC (based on limb)		77		115	0.292	-
0-3	30 (39.0)		33 (28.7)			
4	28 (36.4)		58 (50.4)			
5	10 (13.0)		13 (11.3)			
6	9 (11.7)		11 (9.6)			
ABI (based on limb)	0.50±0.18	72	0.43±0.16	110	0.005[*]	-

Observations are presented as "n (%)" or "x,$^{-}$ ± standard deviation". PP: primary patency; TLR: target lesion revascularization; MA: major amputation; ACD: all-cause death; RC: Rutherford classification; ABI: ankle brachial index; DCB: drug coated balloon; POB: plain old balloon. [*]significant statistical difference due to a p-value of less than 0.05; [†]the value of hazard ratio (DCB vs. POB) of maintaining PP or avoiding the other 3 outcomes.

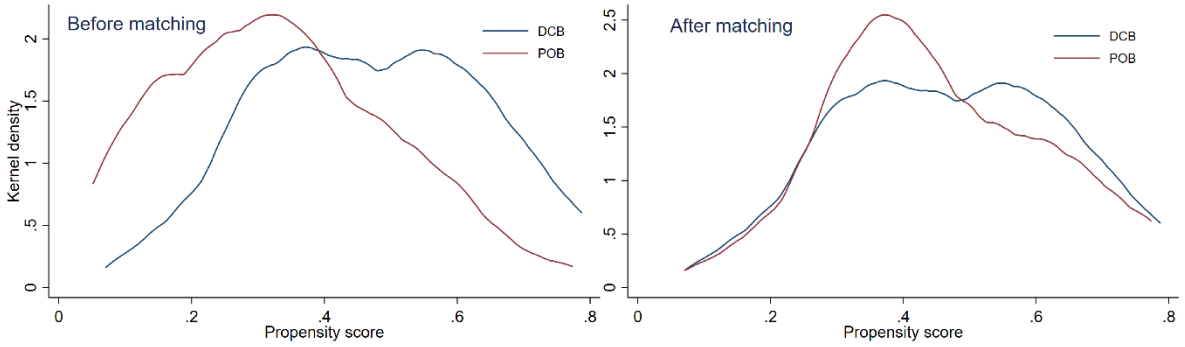


Figure 1. Comparison of the kernel density distribution before and after propensity score matching for the data based on target lesion. DCB: drug coated balloon; POB: plain old balloon.

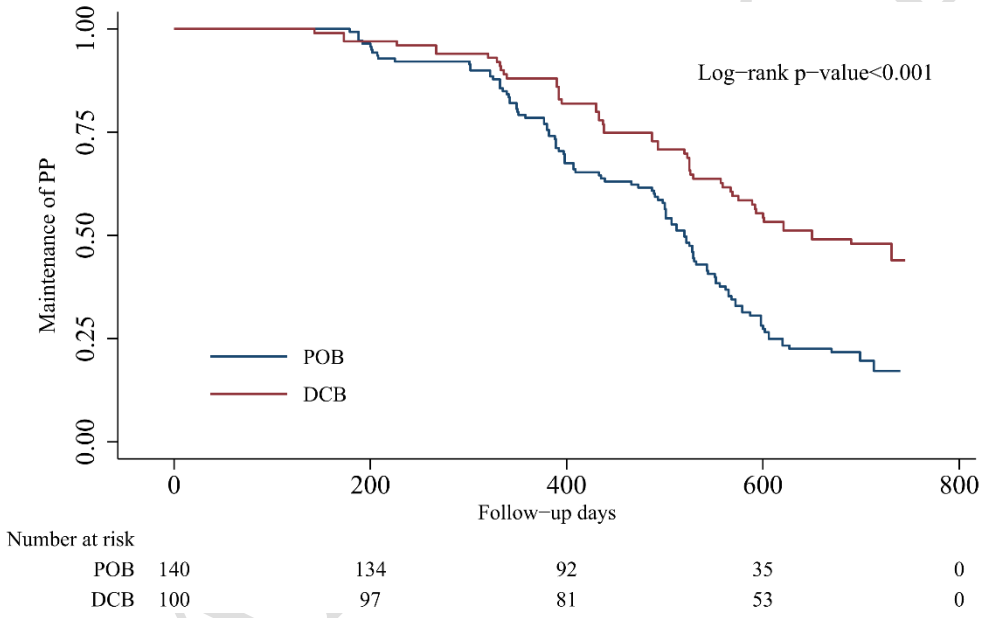


Figure 2. Kaplan-Meier survival of primary patency. POB: plain old balloon; DCB: drug coated balloon.

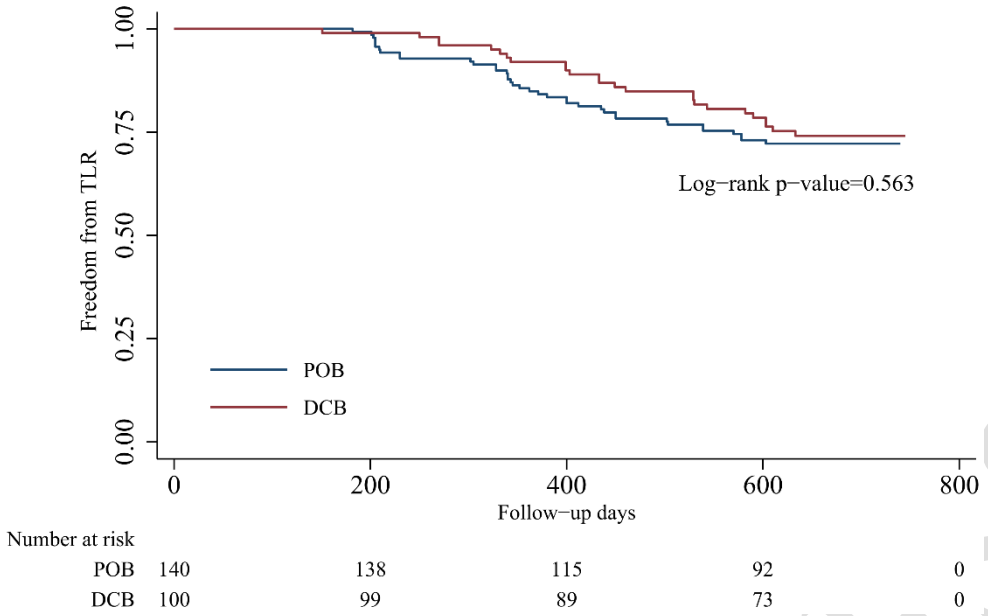
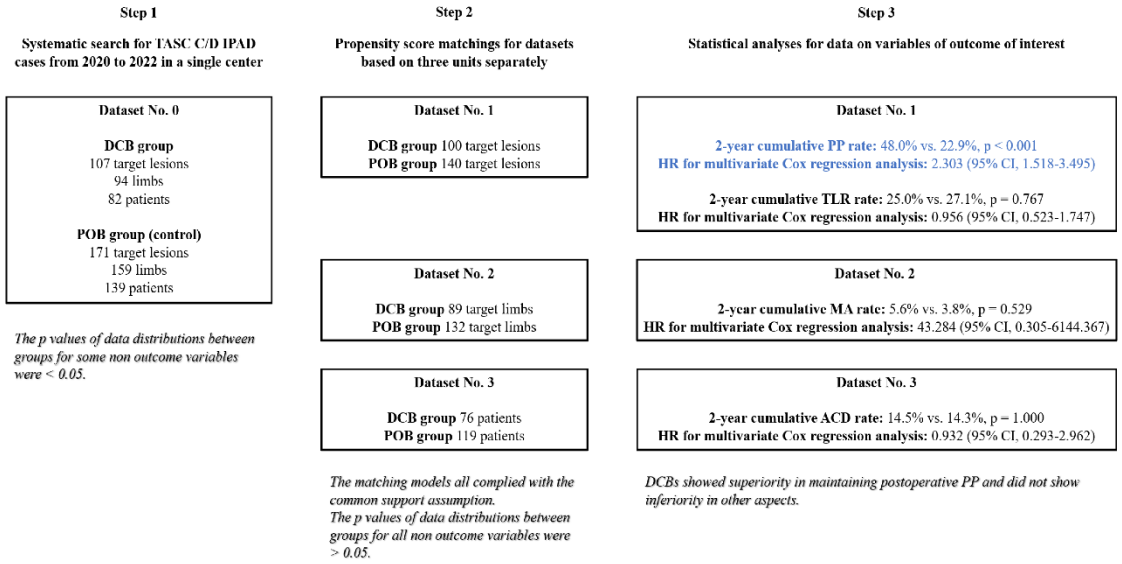


Figure 3. Kaplan-Meier survival of freedom from target lesion revascularization. POB: plain old balloon; DCB: drug coated balloon.

SUPPLEMENTAL DATA

Additional figure: graphical abstract



TASC: Trans-Atlantic Inter-Society Consensus; IPAD: infrapopliteal artery disease; DCB: drug coated balloon; POB: plain old balloon; PP: primary patency; TLR: target lesion revascularization; MA: major amputation; ACD: all-cause death; HR: hazard ratio; CI: confidence interval.

Supplemental data are available at the following link:

https://www.bjbms.org/ojs/index.php/bjbms/article/view/12157/3924