Should We Still Do Plain Old Balloon Angioplasty following Rotational Atherectomy in Drug-Eluting Stent Era?

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Abstract

Background

Drug-eluting stent (DES) is well known effective in severely calcified lesion after rotational atherectomy (ROTA). However, there are still some situations when metal stents should be avoided and plain old balloon angioplasty (POBA) emerges as the preferred option. The aim of present study is to explore that whether POBA is comparably effective to DES in large and calcified coronary pretreated by ROTA in clinical outcomes.

Methods

A retrospective analysis of consecutive patients treated for severely calcified lesions in large (≥ 3 mm) coronary using ROTA + DES or ROTA + POBA was performed. Major adverse cardiac events (MACE) including all cause/cardiac death and target lesion revascularization (TLR) at 1- and 2-year post-treatment, were compared between groups, with Cox regression analyses to identify independent predictors of TLR and MACE.

Results

The analysis included 285 cases in the ROTA + DES and 47 in the ROTA + POBA group, while no relevant between-group differences in clinical baseline characteristics were found. Of note, lesion length was greater in the ROTA + DES group (37.2 mm *versus* 19.3 mm, $p < 0.001$), with 8.4% lesions being chronic total occlusion in this group, but none in the ROTA + POBA group. The in-hospital/30-day mortality rate (5.3%, DES, and 6.4%, POBA), as well as the 12- and 24-month all-cause/cardiac mortality rate (9.3% and 7.7%, respectively) were not significantly different between groups. TLR rates were not significantly different between groups at 12-month (4.6%, DES, and 4.3%, POBA) and 24-month (5.3%, DES and 6.4%, POBA) respectively.

Conclusions

Outcomes were comparable for ROTA + DES and + POBA in severely calcified large coronary arteries intervention, with respect to mid-term death or TLR rate, especially for short lesion < 20 mm.

Introduction

Epidemiological data have shown a worsening of coronary calcification with aging, with a prevalence of coronary calcification up to 50% among individuals 40–49 years of age, increasing to 80% among those 60–69 years of age [1]. Coronary calcification is a strong and independent predictor of adverse coronary events, even after a percutaneous coronary intervention (PCI) [2, 3]. Rotation atherectomy (ROTA), used to remove plaque and, thus, reduce the severity of calcification, can be effective in facilitating balloon dilation in modern cardiac catheterization settings [4]. In agreement with previously published findings [5], we have previously reported on the effectiveness of combining ROTA with drug-eluting stents (ROTA + DES) for the treatment of calcified lesions [6]. However, there are still some situations as adverse bleeding effects, medication nonadherence or large side branch ostial lesion, which may lead physicians to choose stent-less strategy and POBA emerges as the preferred option. By comparison, extremely poor outcomes have been reported for treatment of such lesions using the classic stent-less plain old balloon angioplasty (POBA) alone due to limited expansion of the lesion and risk of marked dissection. Meanwhile, it has been suggested that, with preparation of the vessel by ROTA, POBA could provide a stent-less alternative to ROTA + DES for the treatment of calcified lesions, which would reduce the risk associated with the long-term use of antiplatelet agents necessary after DES implantation [7].

Although several studies have evaluated the effectiveness of different ROTA-facilitated PCI strategies for the treatment of calcified lesions, the evidence remains limited by the relatively small number of cases reported (about 203), the relatively small size of vessels treated(≤ 3 mm), and use of casual follow-up methods, such as telephone interview or office visit at 9 months after implantation [5, 8–11]. Specifically with regard to ROTA + POBA, one study has reported on the safety and workability of this strategy for the management of complex cases, with a target lesion revascularization (TLR) rate of 22–31% in relatively small vessels with an average diameter of 2.6 mm [7], compared to a rate of 11–13% for the ROTA + DES strategy in vessels 3.1 mm in diameter, on average [5]. However, there is a paucity of data regarding outcomes of using ROTA + POBA for the treatment of large calcified coronary arteries, with evidence for the ROTA + DES strategy for these cases similarly being limited. In fact, the BASKET-PROVE study [12] reported a comparable rate of mortality or myocardial infarction for DES and bare metal stents (BMS), when used for the treatment of non-selected lesions in large vessel (≥ 3 mm). This raises the important issue of a potential effect of vessel diameter on PCI outcomes.

We do know that stent implantation in large vessels provides only a small clinical benefit, as the early advantage of a decrease in rate of restenosis is out-weighed by the rate of late stent thrombosis-related problems. Based on this information, we hypothesized that ROTA + POBA may not be inferior to ROTA + DES for the treatment of lesions in large calcified coronary arteries, with regards to the risk of a cardiac event.

To our knowledge, there is no available data comparing the safety, effectiveness and clinical prognosis of ROTA + DES or + POBA for the treatment of de novo lesions in large calcified coronary arteries. As such, the aim of our study was to compare the outcome of using ROTA + DES and + POBA for large vessel angioplasty on the occurrence of major adverse cardiac events (MACE) and clinically driven TLR, in a relatively large sample of patients, evaluated at a midterm follow-up after treatment.

Methods

Study population

This is a retrospective cohort study of consecutive patients who underwent treatment for de novo severe calcified lesions using ROTA facilitated PCI (either POBA or DES) at Sapporo Cardio Vascular Clinic, between January 2013 and November 2015. A large coronary artery was defined by a reference diameter ≥3.0 mm, measured using quantitative coronary angiography (QCA), or visually determined if QCA was not applicable [12]. Severe calcification was defined by a linear calcium density, visible on both sides of the target lesion under detailed fluoroscopic imaging [13].Patients with the following factors were excluded: in-stent restenosis (ISR); treated using ROTA plus a drug-coated balloon, bare metal stent, or cover stent; and lesions with visible thrombus. Patients lost to follow up were also excluded (Figure 1). The decision to perform ROTA+POBA or +DES was left to the doctor's discretion. Follow up was done regularly and routinely, at least twice within two years, with patients interviewed by the doctors in the clinic. Coronary computed tomography angiography (CTA) or interventional coronary angiography (CAG) examination were performed in cases of suspected ISR, or to investigate clinically-driven concerns (such as, new-onset symptoms, evidence of cardiac ischemia, or high index of clinical suspicion for significant coronary disease). The study was approved by the hospital ethic committee and all subjects were given informed consent.

Procedure

Coronary angiography was performed according to conventional methods. Dual antiplatelet therapy, using aspirin and thienopyridine (ticlopidine, 100 mg, twice daily; or clopidogrel, 75 mg, once daily), was prescribed for at least 12 months after ROTA+DES, and 3 months after ROTA+POBA treatment. Aspirin, 100 mg daily, was prescribed for life.

ROTA was performed using a Rotablator^{TM} (Boston Scientific, Natick, MA, USA). In accordance with Japanese insurance policy, a maximum of two burrs were used, when required. A modified ROTA technique was used in all cases, as per the clinical guidelines at our institution, previously described [6]. The standard of a stent/lumen ratio 1:1-1:1.02 for DES implantation was used, with the target lesion pretreated using sufficient rotablation and balloon dilatation. Angiographic success of ROTA+DES was defined as successful stent delivery and expansion, with an in-stent residual stenosis of ≤20% and a TIMI (Thrombolysis in Myocardial Infarction) flow grade of 3 [5].The ROTA+POBA strategy included a maximum burr/artery ratio ≦0.70, followed by routine balloon angioplasty, with very low pressure (1-4 atm) [7]. Angiographic success of ROTA+POBA was defined as a residual stenosis of <50%, with a TIMI flow grade of 3, determined by QCA, and no major dissections visible on the final angiogram of the index artery, after the last balloon inflation. In case of a residual stenosis ≥ 50%, a higher balloon inflation pressure or DES was used. DES would also be used in cases with severe dissection (type D-F) after POBA, with these cases included in the ROTA+DES group for analysis. The strategy of ROTA followed by DES or POBA was based on the doctor's clinical judgment. All clinical decisions, such as site of vascular access and burr size/speed/motion, were left to the doctor's discretion.

Quantitative coronary angiography

QCA was performed according to standard methods and definitions, using the quantitative angiographic analysis system CAAS (version 5.9.1; Pie Medical Imaging, Maastricht, the Netherlands) [14]. The images with the least amount of foreshortening and the highest degree of stenosis were selected for analysis.

Endpoints

MACE was defined as an acute occlusion or unscheduled emergent revascularization in hospitalization, all-cause or cardiac death, hospitalization due to heart failure, definite stent thrombosis, and TLR. Death from cardiac cause was defined as any death without a clear no cardiac cause. TLR was defined as a repeat intervention within 5 mm, proximal or distal, of the target lesion previously treated in the index procedure, or a coronary artery bypass graft surgery (CABG) of a lesion in the same epicardial vessel treated in the index procedure [15].

Statistical Analyses

Data were analyzed using SAS (Version 9.4; SAS Institute Inc, Cary, NC). Patients were divided into the ROTA+DES and +POBA groups for comparisons. Continuous variables with a non-normal distribution were presented as median (interquartile range, IQR), and analyzed using the Wilcoxon-Mann-Whitney U test. Categorical variables were presented as proportions (%) and analyzed using Pearson'schi-squared ($\chi 2$) test or Fisher's exact test, as appropriate for the data type. Collinearity was evaluated using Spearman's correlation and Belsley's criterion. Clinical event rates were calculated using Kaplan–Meier analysis, with between-group comparisons using the log-rank test. Hazard ratios (HR), and their 95% confidence interval (CI), were calculated using the Cox proportional hazards model, with assumptions of proportional hazards confirmed based on Schoenfeld residuals. All P-values are two-sided, with value <0.05 were regarded as significant.

Results

Baseline characteristics of the patients

During the 3-year period of the study, 1374 patients underwent ROTA-based PCI treatment and 332 of these patients presenting with 380 de novo lesions meeting our inclusion criteria (Figure 1). Relevant characteristics of the study group are summarized in Table 1. The median age was 76 years, with 38% of patients having diabetes and 86.7% hypertension. Of note, 47% had undergone a previous PCI, and 11.1% a CABG. The +DES:+POBA distribution was 6:1, with +DES 285 cases and +POBA 47 cases. The clinical baseline characteristics were comparable between the two groups, with the exception of a higher rate of previous PCI in the +DES (43.9%) than +POBA (66.0%; P=0.005) and rate of dual antiplatelet treatment (93.7% and 72.4%, respectively; P<0.001).

Baseline angiographic characteristics

Angiographic characteristics are reported in Table 2. The main target vessel was the left anterior descending artery in both groups. The reference vessel diameter was 3.3 (3.1, 3.6) mm and 3.3 (3.2, 3.7) mm in the +DES and +POBA group, respectively (P=0.271). The rate of American Heart Association/American College of Cardiology (AHA/ACC) type B2/C lesions was >97% in both groups. However, lesion median length was much greater in the +DES (37.2 mm) than +POBA (19.3 mm) group, with a higher rate of chronic total occlusion (CTO) lesions (8.4% *versus* 0%, respectively), while the +POBA group had a greater prevalence of ostial and bifurcation lesion.

PCI procedure data and QCA comparison

The angiographic success of both ROTA strategies was >97.9%. As shown in Table 3, more than half of the patients (57.4%) in the +POBA group required two burrs, a rate which was significantly higher than for the +DES group (27%). To achieve sufficient ablation, the maximum burr size was significantly larger in the +POBA (2.0 mm) than +DES (1.75 mm) group, resulting in a higher maximum burr/artery ratio (0.56 *versus* 0.52, respectively). The maximum balloon size, however, did not differ between the groups, although the maximum balloon pressure in the +DES strategy (24 atm)was much higher than that in +POBA (1 atm; P<0.001), for different ballooning purposes of full stent expansion and plaque redistribution respectively. As a result, the acute gain (2.1mm *versus* 1.3mm) and minimum lumen diameter (MLD) after PCI (3.3mm *versus* 2.5mm) were significantly greater in the +DES than +POBA group.

In-hospital and follow-up outcome

The 12- and 24-month follow-up rate was 100% and 57.5%, respectively, with a median follow-up of 15.3 months (IQR, 10.0-24 months). The in-hospital/30-days mortality rate was <1% in the +DES group, but no death in the +POBA group (Table 4). There were no significant between-group differences in the rate of all-cause or cardiac death at 12- and 24-months. Only one definite stent thrombosis was identified in the +DES group. The Kaplan-Meier curves indicated a TLR rate of 4.6% and 4.3%, respectively, for the +DES and +POBA groups, at 12-months, and 5.3% and 6.4%, respectively, at 24-months (P=0.398, Figure 2).The rate of MACE was 11.9% and 8.5% in the +DES and +POBA group, respectively, at 12-months; and 14.7% and 12.8% at 24 months, respectively (P=0.632, Figure 2).

Predictors of TLR and MACE in large calcified coronary

As shown in Table 5, current smoker [adjusted HR (aHR 95%CI): 1.81(1.11-2.94)] and hemodialysis [adjusted HR (aHR 95%CI): 8.33(3.20-21.68)] were associated with TLR. Meanwhile, impaired left ventricular ejection fraction [aHR (95%CI): 0.97(0.94-0.99)] and hemodialysis were significantly related to the occurrence of MACE. Of note, the choice of ROTA+DES or +POBA nor the maximum burr-to-artery ratio had no significant influence on prognosis.

Discussion

To the best of our knowledge, this is the first study to compare the effects of ROTA followed by DES or POBA for the treatment of de novo lesions in large calcified coronary arteries. The major findings of our study are as following. First, ROTA + POBA was also safe and feasible in severely calcified large coronary intervention. Second, ROTA + POBA was not inferior to ROTA + DES on the midterm rate of freedom of cardiac death or TLR in large and short-length calcified coronary lesions. Third, hemodialysis was an independent risk factor for TLR and MACE.

DES is widely used to treat patients with coronary artery disease, improving vessel patency after PCI due to its capability of preventing elastic recoil, residual arterial dissection and ISR [16]. However, compared to small coronary lesions, the benefit of DES (*versus* BMS) is relatively small in patients treated for larger coronary lesions. Specifically, the early advantage of DES in decreasing the rate of restenosis is out-weighted by the longer term risk for adverse cardiac events due to late stent thrombosis which may be greater for DES than for BMS [12, 17–20]. The necessity of using DES in large coronary lesions, therefore, is challenged by the emerging clinical practice. Although second-generation DES have been shown to significantly reduce the rate of target-vessel revascularization in large coronary arteries, the BASKET-PROVE study did not, however, identify a significant difference between in the rate of death or myocardial infarction between DES and BMS [12]. Of note, while the efficacy and safety of DES has been demonstrated in small-diameter vessels with heavily calcified lesions, following ROTA [12, 21], our study further demonstrates an angiographic success rate > 99% for the ROTA + DES strategy in heavily calcified large vessels, with the rate of TLR also be acceptably low at 5.3%. Furthermore, regarding hemorrhagic tendency or medication non-adherence may lead physicians to choose a stent-less strategy, since DES requires a longer duration of dual antiplatelet therapy. In the meantime, metal stents should be avoided or unessential for some specific lesions as ostial side branch alone or short length, ect.

On the other hand, POBA as a classic stent-less technique, might offer an alternative choice for the large coronary intervention [22, 23]. The utility of POBA for the treatment of heavily calcified coronary lesions has been associated with lower angiographic success and a higher rate of complications, because of the undilatable calcified ring and severe dissection or vessel perforation after high pressure ballooning [24]. However, the physical removal of plaque and reduction in plaque rigidity by ROTA has increased the feasibility of using the POBA strategy for the treatment of large calcified coronary lesions [11, 25]. It is important to note, as well, that the patients in our + POBA group had significantly greater complex health issues than patients included in a previous study [11], which further underlines the possible clinical utility of the ROTA + POBA strategy. Comorbid health conditions in the + POBA group included older age (median, 74 years), diabetes (42.6%), hemodialysis (8.5%), previous PCI (66%) and CABG (4.3%), and a high prevalence rate of AHA/ACC type B2/C lesions (99.4%). Fortunately, the high procedural success rate (97.9%) of the ROTA + POBA strategy, with a low rate of early MACE, compares favorably to the clinical outcomes reported in previous studies [26, 27]. Importantly, no perforation or other complication, with the exception of one burr getting stuck, and no abrupt vessel closure or 30-day MACE occurred in the + POBA group. As well, there was no occurrence of acute occlusion, nor of major complication associated with the ROTA + POBA strategy, which was consistent with the previous report [7], indicative of the safety of leaving a large coronary vessel without a stent after ROTA.

The overall clinical outcome of ROTA + POBA was comparable to that of ROTA + DES in our study, which may be explained as follows. First, the STRATAS study implicated a greater effect of surgical technique, than burr size, of the rate of acute complications and restenosis after ROTA [7]. In our study, all ROTA procedures were performed by skilled and experienced doctors to guarantee stable technique performance. Moreover, in the ROTA + POBA strategy, only a pressure of 1–4 atm was used to avoid intimal damage after ROTA. As well, an important component of POBA was to debulk and stabilize the lesion by redistributing the plaque, a strategy known as MTRA (minimal traumatic ROTA) in our institution. Although a previous study did not identify a benefit of MTRA for small diameter vessels [7], the technique may be of specific benefit in large vessels. Second, as the reference diameter of vessels treated in our study was large, aggressive ROTA would yield a large acute gain in lumen diameter, with the relatively high blood flow achieved offering some protection against acute restenosis. Third, almost all patients adhered to our strict follow-up protocol, including good medical adherence. Lastly, there was a higher prevalence of CTO and aorto-ostial lesions in the + DES than + POBA group, with the lesions also being of greater length in this group. Consequently, the heavy calcification would increase the risk of incomplete stent expansion and, thus, of a higher rate of restenosis. Follow-up coronary angiogram was clinically driven, which might have led to an underestimation of the rate of restenosis and TLR, especially in the + DES group.

Despite the lack of a difference in clinical outcomes between the two groups, we consider that there still must be some underlying difference which would distinguish the optimal strategy for specific cases. Although the prevalence of AHA/ACC type B2/C lesions was not different between the + DES and + POBA group, there was a greater prevalence of aorto-ostial and CTO lesions, as well as lesions of greater length in the + DES than + POBA group, all of which are strong risk factors for restenosis. After high pressure ballooning and provisional support to the vessel wall by the metal struts, MLD after PCI and the acute gain were significantly greater in the + DES than + POBA group. Therefore, the ROTA + DES strategy was deemed to provide excellent performance for the treatment of these specific types of lesion. By comparison, the ROTA + POBA strategy was used in our study for patients with shorter and bifurcation lesions, especially for left circumflex artery (LCX) ostial bifurcation lesions. Accurate stenting of a bifurcation lesion (such as an LCX ostial lesion) is normally considered to be challenging as the lesion cannot be fully covered by the stent, as well as the possibility of having the plaque shift to main branch (e.g. left main truck/ left anterior descending coronary) during implantation, which would lead to an even more complex situation. In this study, all LCX ostial lesions were successfully treated using the ROTA + POBA strategy. Therefore, the ROTA + POBA strategy can provide an alternative method to DES implantation for the treatment of such challenging lesions. Because of the noted differences in the characteristics of the lesions between the two groups, the detailed procedure of ROTA and ballooning likely differed between the two groups. Specifically, a more aggressive ablation strategy was adopted in ROTA + POBA group, with more burrs used, larger burr size and higher burr/artery ratio, and a lower rotational speed. The “low” ablation speed would further lead to a larger and smoother lumen as a result of burr deflection motion. This could potentially explain the predominant concept of “debulking” in the POBA strategy, to achieve a greater lumen diameter, compared to the strategy of “facilitated expansion” with DES. The maximum balloon-to-artery ratio did not differ, however, the balloon pressure was significantly lower in ROTA + POBA providing a sufficiently large lumen and plaque redistribution, without severe dissection as a conservative approach. Of note, a previous report that aggressive ROTA with adjunctive balloon inflation of < 1 atm did not provide an advantage over more routine burr sizing plus routine angioplasty was based on an analysis of small vessels only, with a reference diameter of only about 2.6 mm and a lumen diameter < 2.0 mm after PCI [7]. In our study, vessel diameters were ≥ 3 mm, with a lumen diameter after POBA of about 2.5 mm, much larger than previously reported. The favorable prognosis obtained in our case series is indicative of the feasibility of using an aggressive ROTA strategy, with controlled large ballooning, in large calcified arteries. We also believe it is important to emphasize the difference between plaque “debulking”, in POBA, from plaque “modification”, in DES, which would differentially guide the doctor’s ROTA performance.

To our knowledge, this is the first and largest retrospective study to have compared the early and midterm safety and effectiveness of ROTA + POBA and ROTA + DES for de novo lesions in large calcified coronary arteries.

Limitation

The limitations of our study should be acknowledged here. The major concern is that the selection of the ROTA + DES or ROTA + POBA in each case was at the doctor’s discretion, and not randomized, despite baseline characteristics being comparable between the two groups. Most frequently in this study, patients treated with POBA were at high risk of bleeding from DAPT or had recently undergone another surgical procedure recently. Therefore, we consider that our study provides pilot information on the ROTA practice for this subgroup of patients.

Conclusions

We did not identify a significant difference in the rate of early and midterm all-causes or cardiac death and TLR between ROTA + DES or + POBA for heavily calcified lesion in large coronary arteries. For calcified coronary > 3 mm in diameter and < 20 mm in length, ROTA + POBA provides a clinically acceptable alternative to DES implantation.

Abbreviations

DES: Drug-eluting stent; ROTA: rotational atherectomy; MTRA: Minimal traumatic ROTA; POBA: plain old balloon angioplasty; MACE: Major adverse cardiac events; BMS: bare metal stents; PCI: percutaneous coronary intervention; TLR: target lesion revascularization; CABG: Coronary artery bypass graft surgery; LCX: Left circumflex artery; CTO: chronic total occlusion.

Declarations

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Authors' contributions

Haojian Dong , Daisuke Hachinohe conceptualized the study outline, drafted and revised the manuscript; Zhiqiang Nie, Yutaka Tadano, Umihiko Kaneko drafted manuscript and performed statistics analysis; Yoshifumi Kashima, Takuya Haraguchi, Hidemasa Shitan, Tomohiko Watanabe, Takuro Sugie, Ken Kobayashi ,Daitaro Kanno, MorioEnomoto, Katsuhiko Sato collected data and drafted manuscript; Tsutomu Fujita, Jianfang Luo initiated the registry, conceptualized the study outline and drafted the manuscript. All authors have read and approved the final manuscript

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Availability of data and materials

The datasets used and/or analyzed during the current study are de-identified and available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The study was approved by the ethic committee of Sapporo Cardio Vascular Clinic and all subjects were given informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that there is no conflict of interest.

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Tables

Table 1. Baseline characteristics of participants

Characteristics	Overall	ROTA+DES (n=285)	ROTA+POBA (n=47)	P-value
Age (years)	76 (68,81)	76(69,82)	74(65,79)	0.067
BMI kg/m^2	23.4 (20.8,26.4)	23.4 (20.8,26.4)	23.5 (21.7,27.0)	0.388
Men, n (%)	114 (34.3)	100 (35.1)	14 (29.8)	0.478
Current smoker, n (%)	62 (18.7)	54 (18.9)	8 (17.0)	0.844
Diabetes mellitus, n (%)	126 (38.0)	106 (37.2)	20 (42.6)	0.483
Hypertension, n (%)	288 (86.7)	246 (86.3)	42 (89.4)	0.568
Hyperlipidemia, n (%)	248 (74.7)	210 (73.7)	38 (80.9)	0.295
Clinical diagnosis, n (%)				0.414
Stable angina	320 (96.4)	276 (96.8)	44 (93.6)	
Non-STEMI	1 (0.3)	1 (0.4)	0 (0.0)	
STEMI	11 (3.3)	8 (2.8)	3 (6.4)	
Previous MI, n (%)	67 (20.2)	58 (20.4)	9 (19.1)	0.849
Previous PCI, n (%)	156 (47.0)	125 (43.9)	31 (66.0)	0.005
Previous CABG, n (%)	37 (11.1)	35 (12.3)	2 (4.3)	0.105
Hemodialysis, n (%)	35 (10.5)	31 (10.9)	4 (8.5)	0.624
eGFR	50.5 (39.0,63.0)	51 (39,62)	50 (42,64)	0.641
LVEF	66.0 (61.0,69.0)	65.7 (61.0,69.0)	66.0 (61.3,68.9)	0.858
Dual antiplatelet, n (%)	301 (90.6)	267 (93.7)	34 (72.4)	<0.001
ACEI/ARB, n (%)	175 (52.7)	156 (54.7)	19 (40.4)	0.069
Statin, n (%)	181 (54.5)	151 (53.0)	30 (63.8)	0.166

Data are presented as medians (interquartile range) or absolute numbers (percentages). The Wilcoxon-Mann-Whitney U-test, Pearson $\chi 2$ test or Fisher exact test were used for between-group comparisons, as appropriate.

BMI, body mass index; STEMI, ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

Table 2. Baseline characteristics of involved lesions

Characteristics	Overall	ROTA+DES (n=285)	ROTA+POBA (n=47)	P-value
Treated vessel, n (%)				
Left main	20 (6.0)	15 (5.3)	5 (10.6)	0.151
LAD	168 (50.6)	138 (48.4)	30 (63.8)	0.05
LCX	44 (13.3)	28 (9.8)	16 (34.0)	<0.001
RCA	114 (34.3)	113 (39.6)	1 (2.1)	<0.001
Reference diameter, (mm)	3.3 (3.1,3.6)	3.3 (3.1,3.6)	3.3 (3.2,3.7)	0.271
Angulation >45°, n (%)	176 (53.0)	152 (53.4)	24 (51.1)	0.079
Lesion type, n (%)				0.263
A/B1	2 (0.6)	1 (0.4)	1 (2.1)	
B2/C	330 (99.4)	284 (99.6)	46 (97.9)	
Lesion length(mm)	31.0 (23.5,40.8)	37.2 (25.6,41.8)	19.3 (15.0,25.1)	<0.001
CTO	24 (7.2)	24 (8.4)	0 (0.0)	0.033
Ostial, n (%)	144 (43.4)	109 (38.2)	35 (74.5)	<0.001
Aortoostial n (%)	30 (20.8)	30 (27.5)	0 (0)	0.012
Non aortoostial n (%)	114 (79.2)	79 (72.5)	35 (100)	<0.001
Bifurcation, n (%)	176 (53.0)	144 (50.5)	32 (68.1)	0.025

Data are presented as medians (interquartile range) or absolute numbers (percentages). The Wilcoxon-Mann-Whitney U-test, Pearson χ2 test or Fisher exact test were used for between-group comparisons, as appropriate.

LAD, left anterior descending coronary; LCX, left circumflex artery; RCA, right coronary artery; CTO, chronic total occlusion.

Table 3. Comparison of percutaneous coronary intervention procedure and quantitative coronary angiography between the two strategies

Characteristics	Overall	ROTA+DES (n=285)	ROTA+POBA (n=47)	P-value
Procedure				
Maximum stent size (mm)	3.50 (3.00,3.50)	3.50 (3.00,3.50)	-	NA
Maximum burr size, (mm)	1.75 (1.75,1.75)	1.75(1.50,1.75)	2.00 (1.75,2.15)	<0.001
Maximum balloon size(mm)	3.5 (3.0,3.5)	3.5 (3.0,3.8)	3.5 (3.0,4.0)	0.582
Maximum balloon pressure	23 (18,24)	24 (20,24)	1 (1,14)	<0.001
Maximum burr-to-artery ratio	0.53 (0.47,0.57)	0.52 (0.47,0.56)	0.56 (0.53,0.61)	<0.001
Maximum balloon-to-artery ratio	1.00 (0.93,1.09)	1.00 (0.93,1.09)	1.01 (0.94,1.12)	0.976
Maximum stent-to-artery ratio	0.94 (0.83,1.00)	0.97 (0.89,1.01)	-	NA
Minimum rotational speed	140000 (113000,160000)	140000 (115500,160000)	120000 (100000,140000)	0.009
Total stents length	38 (24,38)	38 (24,38)	-	NA
Number of burrs used (≥2), n (%)	104 (31.3)	77 (27.0)	27 (57.4)	<0.001
Number of stents used	1 (1,1)	1 (1,1)	-	NA
Angiographic success n, (%)	325 (97.9)	279 (97.9)	46 (97.9)	>0.999
Immediate QCA				
MLD before PCI, (mm)	1.24 (0.94,1.45)	1.24 (0.95,1.45)	1.26 (0.92,1.44)	0.894
% stenosis before PCI	63 (57,72)	63 (57,72)	63 (57,74)	0.490
MLD after PCI (mm)	3.3 (2.9,3.5)	3.3 (3.0,3.6)	2.5 (2.1,2.8)	<0.001
% stenosis after PCI	4.0 (-4.0,14.8)	2.0 (-5.0,10.0)	28.0 (18.0,40.5)	<0.001
Acute gain(mm)	1.99 (1.63,2.33)	2.1 (1.7,2.4)	1.3 (0.9,1.5)	<0.001
PCI complication n, (%)	7 (2.1)	6 (1.8)	1 (0.3)	>0.999
Residual dissection type (≥C)	0 (0.0)	0 (0.0)	0 (0.0)	>0.999
Slow/no flow	2 (0.6)	2 (0.7)	0 (0.0)	>0.999
Perforation	4 (1.2)	4 (1.4)	0 (0.0)	>0.999
Burr stuck	1 (0.3)	0 (0.0)	1 (2.1)	0.141

Data are presented as medians (interquartile range) or absolute numbers (percentages). The Wilcoxon-Mann-Whitney U-test, Pearson $\chi2$ test or Fisher exact test were used for between-group comparisons, as appropriate.

QCA, quantitative coronary angiography; MLD, minimum lumen diameter; PCI, percutaneous coronary intervention.

Table 4. Clinical outcomes at 12- and 24-months between the two strategies

Characteristics	Overall	ROTA+DES (n=285)	ROTA+POBA (n=47)	P-value
In-hospital/ 30-days outcomes, n (%)				
TLR	0 (0.0)	0 (0.0)	0 (0.0)	>0.999
In-hospital death	2 (0.6)	2 (0.7)	0 (0.0)	>0.999
30-days death	2 (0.6)	2 (0.7)	0 (0.0)	>0.999
12-month follow-up, n (%)				
MACE	38 (11.4)	34 (11.9)	4 (8.5)	0.495
All-cause death	18 (5.4)	16 (5.6)	2 (4.3)	>0.999
Cardiac death	9 (2.7)	7 (2.5)	2 (4.3)	0.482
Stent thrombosis (definite)	0 (0.0)	0 (0.0)	0 (0.0)	>0.999
HF	10 (3.0)	8 (2.8)	2 (4.3)	0.638
TLR	15 (4.5)	13 (4.6)	2 (4.3)	>0.999
24-month follow-up, n (%)				
MACE	48 (14.5)	42 (14.7)	6 (12.8)	0.722
All-cause death	21 (6.3)	18 (6.3)	3 (6.4)	>0.999
Cardiac death	9 (2.7)	7 (2.5)	2 (4.3)	0.482
Stent thrombosis (definite)	1 (0.3)	1 (0.4)	0 (0.0)	>0.999
HF	15 (4.5)	13 (4.6)	2 (4.3)	>0.999
TLR	18 (5.4)	15 (5.3)	3 (6.4)	0.728

Data are presented as absolute numbers (percentages).

The Pearson's $\chi 2$ test or Fisher's exact test was used, as appropriate.

ROTA, rotational atherectomy; DES, drug-eluting stent; POBA, plain old balloon angioplasty; TLR, target lesion revascularization. MACE, major adverse cardiac events.

Table 5. Predictors of TLR in large calcified coronary arteries

variables	Univariate analysis HR (95% CI)	P-value	Multivariable analysis HR (95% CI)	P-value
LVEF	1.00 (0.94-1.05)	0.871		
Current smoker	1.67 (1.03-2.70)	0.037	1.81 (1.11-2.94)	0.017
Diabetes	3.00 (0.40-22.44)	0.284		
Hyperlipidemia	2.01 (0.59-6.86)	0.265		
Hemodialysis	7.37 (2.86-19.03)	<0.001	8.33 (3.20-21.68)	<0.001
ROTA+DES vs POBA	1.60 (0.53-4.83)	0.403		
Reference diameter	1.64 (0.66-4.05)	0.288		
Lesion length	1.01 (0.99-1.03)	0.605		
MLD after PCI	1.09 (0.39-3.04)	0.863		
%DS after PCI	1.08 (0.97-1.04)	0.637		
Maximum burr-to-artery ratio	0.09 (0.00-28.03)	0.420		
Statin	2.55 (0.93-7.04)	0.070		

TLR, target lesion revascularization; LVEF, left ventricular ejection fraction; ROTA, rotational atherectomy; DES, drug-eluting stent; POBA, plain old balloon angioplasty; MLD, minimum lumen diameter; DS, diameter stenosis.

Table 6. Predictors of MACE in large calcified coronary arteries

variables	Univariate analysis HR (95% CI)	P-value	Multivariable analysis HR (95% CI)	P-value
LVEF	0.96 (0.93-0.98)	0.001	0.97 (0.94-0.99)	0.008
Current smoker	0.87 (0.61-1.23)	0.429		
Diabetes	2.02 (0.73-5.58)	0.177		
Hyperlipidemia	1.02 (0.56-1.88)	0.940		
Hemodialysis	6.49 (3.65-11.55)	<0.001	6.15 (3.30-11.46)	<0.001
ROTA+DES vs POBA	1.19 (0.58-2.44)	0.633		
Reference diameter	0.90 (0.45-1.79)	0.769		
Lesion length	1.00 (0.99-1.02)	0.739		
MLD after PCI	0.97 (0.53-1.78)	0.923		
%DS after PCI	1.00 (00.98-1.02)	0.961		
Maximum burr-to-artery ratio	0.60 (0.20-18.85)	0.768		
Statin	1.11 (0.65-1.90)	0.700		

MACE, major adverse cardiac events; LVEF, left ventricular ejection fraction; ROTA, rotational atherectomy; DES, drug-eluting stent; POBA, plain old balloon angioplasty; MLD, minimum lumen diameter; DS, diameter stenosis.

Figures

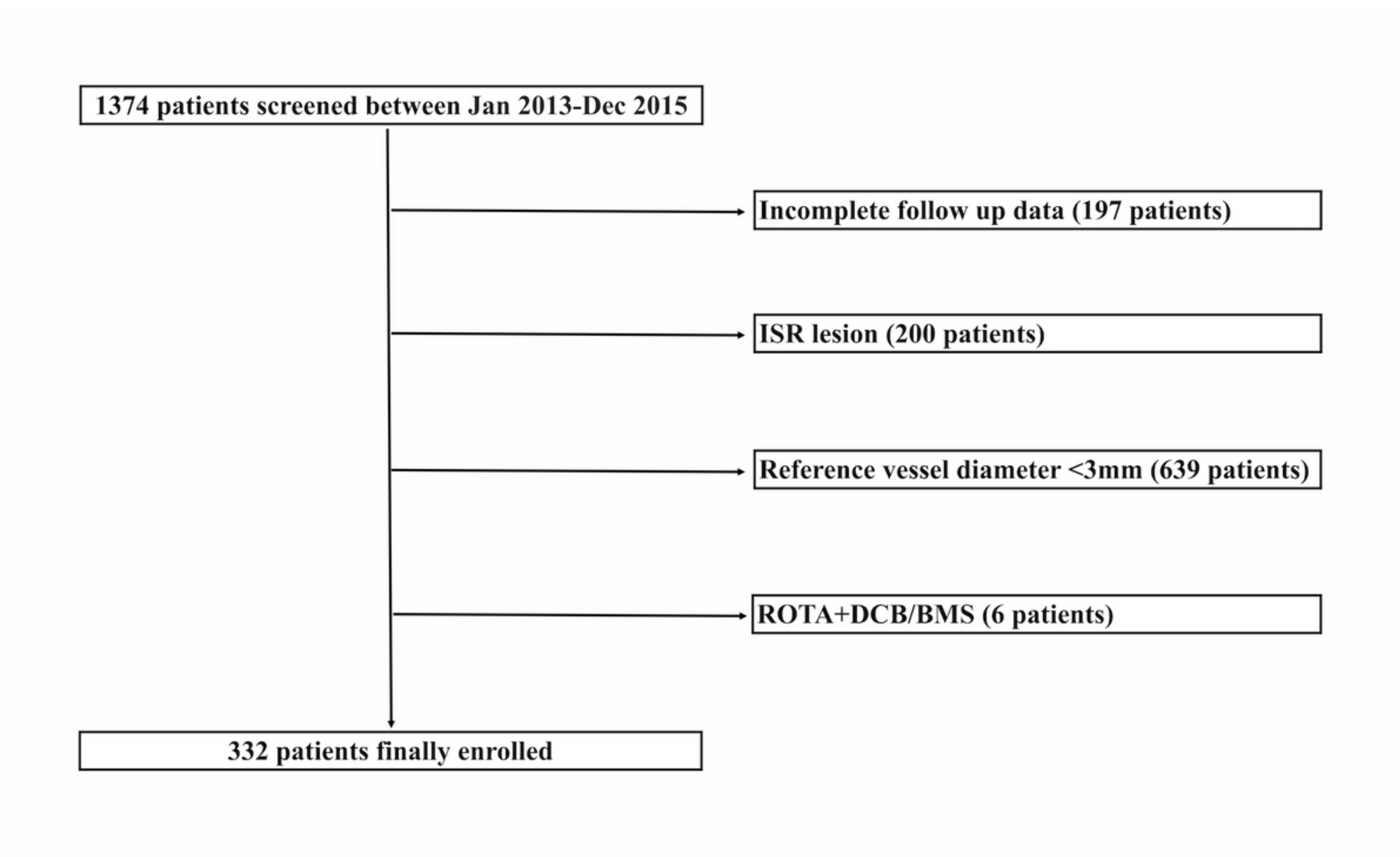
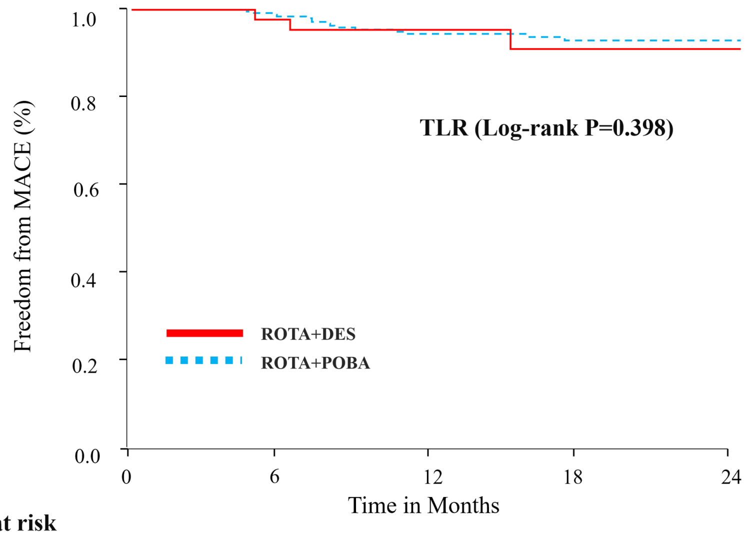


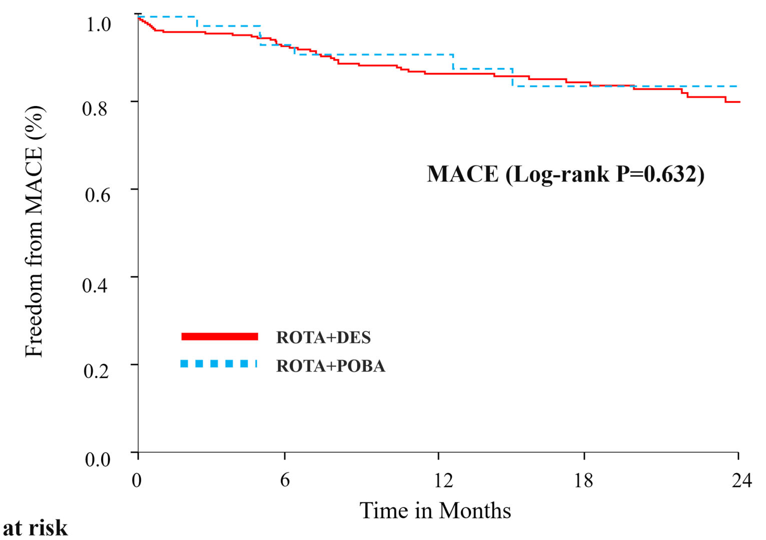
Figure 1

Screening procedure to identify the study population from our patient database. BMS, bare metal stent; DCB, drug-coated balloon; ISR, in-stent restenosis; ROTA, rotational atherectomy.



NO. at risk					
ROTA+DES	285	249	179	114	64
ROTA +POBA	47	43	31	18	13

Event rate(%)				
ROTA +DES	1.4	4.6	5.3	5.3
ROTA +POBA	2.1	4.3	6.4	6.4



NO. at risk					
ROTA+DES	285	247	175	112	63
ROTA +POBA	47	43	31	18	13

Event rate(%)				
ROTA +DES	6.7	11.9	13.0	14.7
ROTA +POBA	6.4	8.5	12.8	12.8

Figure 2

Comparison of target lesion revascularization (TLR) and major adverse cardiac event (MACE) among different PCI strategies. DES, drug-eluting stent; POBA, plain old balloon angioplasty; ROTA, rotational atherectomy.