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Rotational Atherectomy Combined with Drug Coated-Balloons for in-Stent Restenosis☆,☆☆

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ABSTRACT

Background: Refractory coronary in-stent restenosis remains a clinically relevant problem in interventional cardiology despite the use of drug coated balloon angioplasty and further drug eluting stent deployment. In this study, we investigated whether the novel approach of lesion debulking with rotational atherectomy prior to drug coated balloon angioplasty for challenging coronary in-stent restenosis is safe and effective.
Methods: Procedural and registry data was retrospectively analysed for 26 patients who underwent rotational atherectomy immediately followed by drug coated balloon angioplasty to 43 coronary in-stent restenosis lesions with mean follow up of 19 months.
Results: Lesion success was achieved in all cases with no major procedural complications. There were no instances of death or myocardial infarction in the follow up period. Target lesion revascularisation occurred in six patients and target vessel revascularisation occurred in eight patients. All target lesion revascularisation occurred in lesions that had already failed drug coated balloon angioplasty without debulking previously while four such lesions were free of lesion failure in the follow up period.
Conclusions: Lesion debulking with rotational atherectomy followed by drug coated balloon angioplasty is a feasible treatment option for selected cases of in-stent restenosis. Further study is needed to fully assess its efficacy in comparison to conventional treatment.

1. Introduction

Despite the introduction of drug eluting stents more than a decade ago, coronary in-stent restenosis (ISR) remains a clinically relevant and difficult management problem in interventional cardiology [1–3]. While there are many treatment options in this context, recent meta-analyses suggest that implantation of a further drug eluting stent (particularly everolimus eluting) or drug coated balloon (DCB) angioplasty have lower target lesion revascularisation rates than other methods of treatment [4,5]. Even with these treatments, trials comparing second generation drug eluting stents to DCBs for ISR still have target lesion revascularisation (TLR) rates between 3 and 16% [6,7].

Rotational atherectomy alone has been used for in-stent restenosis for several years with limited success. The theoretical basis of early attempts was to debulk lesions with or without plain balloon angioplasty to decrease target vessel revascularisation (TVR) and clinical events. These treatments have been shown to be inferior to drug eluting stents and drug coated balloons in various meta-analyses and one study showed clinical event rates at 6 months in the rotablation arm were 20.4% [4,5,8].

The combination of lesion debulking followed by DCBs is poorly studied. There are trials from more than a decade ago involving lesion debulking prior to brachytherapy for coronary ISR that may have some relevance in this context. One trial comparing debulking with brachytherapy to balloon angioplasty with brachytherapy showed a small improvement in minimal lumen diameter in follow up angiography in the debulking group but no significant benefit in TLR or clinical endpoints [9]. However, the most promising results have been seen in the setting of peripheral endovascular intervention combining excimer laser or rotational atherectomy with DCBs but no studies have considered this treatment in coronary arteries [10,11].

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Given the results in peripheral vascular disease, interventionists at our institution have used rotational atherectomy to debulk eccentric, calcified and long segments of ISR particularly in drug eluting stents prior to DCB angioplasty in cases where further drug eluting stent insertion was considered to be undesirable. This observational study reviews the procedural characteristics and outcomes of patients receiving this intervention.

2. Material and methods

2.1. Study design and population

This study is a retrospective cohort study where data from a registry of consecutive patients presenting to our institution between December 2010 and April 2016 were analysed. All patients receiving treatment for in-stent restenosis with rotational atherectomy followed by DCB inflation in the target lesion were included. Patients were selected based on lesion analysis by their treating physician with characteristics such as lesion calcification, long lesion length, proximal vessel tortuosity, large vessel calibre and recurrent ISR taken in to account. All patients provided written consent for the required follow up and ethics approval was obtained from the relevant authorities.

2.2. Objectives

The primary objectives assessed were mortality, myocardial infarction (MI), stroke, TLR and TVR.

2.3. Definitions

In-stent restenosis was defined as greater than or equal to 50% stenosis in a previously stented segment. ISR was classified in to four patterns as described by Mehran et al. [12]. Pattern I includes lesions less than or equal to 10 mm in length, pattern II includes lesions greater than 10 mm but still within the stent, pattern III includes lesions greater than 10 mm extending outside of the stent and pattern IV includes total occlusion due to ISR. TLR was defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. TVR was defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The Society for Cardiovascular Angiography and Interventions (*SCAI*) definition of MI was used [13].

2.4. Follow up

Follow up was achieved by a mailed questionnaire at 30 days and twelve months. If no response was received, patients were called and the questionnaire was administered by telephone. Further information was sought for adjudication from primary healthcare providers and hospital notes if patients were unreachable or unable to provide required information. TVR and TLR rates were calculated from records of repeat procedures performed at our facility and on questionnaire with patients.

3. Results

There were 26 patients who underwent rotational atherectomy with DCB angioplasty for ISR to 43 lesions. Baseline patient characteristics are detailed in Table 1. The mean age of studied patients was 68 and the population was predominantly male (21 males, 5 females). Twelve patients had undergone previous coronary artery bypass grafting (46%), eight were diabetic (31%) and most patients were on treatment for hypertension and hyperlipidaemia (85% and 92% respectively). Thirteen patients had a history of smoking (50%). All but one patient were on dual antiplatelet therapy with the other taking the combination of warfarin and clopidogrel.

Table 1
Baseline characteristics. PCI – percutaneous coronary intervention. CABG – coronary artery bypass grafting.

Patients	26
Procedures	31
Lesions	43
Mean age (range)	68 (51–76)
Sex	
Male (%)	21 (80)
Female (%)	5 (20)
Previous CABG (%)	12 (46)
Previous myocardial infarction (%)	8 (31)
Type 2 diabetes mellitus (%)	12 (46)
Chronic kidney disease (%)	5 (19)
Hypertension (%)	22 (85)
Hyperlipidaemia (%)	24 (92)
Smoking history (%)	13 (50)
Medications at time of PCI (%)	
Aspirin	25 (96)
Clopidogrel	25 (96)
Prasugrel	1 (4)
Warfarin	2 (8)
Statin	26 (100)
ACE inhibitor/Angiotension receptor blocker	22 (85)
Beta blocker	11 (42)
Oral hypoglycaemic agent	8 (31)
Insulin	4 (15)

Lesions characteristics are detailed in Table 2. Most patients had pattern I or pattern II in-stent restenosis (35% and 60% respectively). Two patients had pattern IV in-stent restenosis (5%). Quantitative coronary analysis (QCA) showed a mean proximal reference diameter of 3.0 mm and a mean distal reference diameter of 2.9 mm. The average minimum luminal diameter was 0.6 mm with an average stenosis by diameter of 79%. The circumflex artery was the most common target (48%) followed by the right coronary and left anterior descending arteries (21% and 14% respectively). Two of the lesions were in saphenous vein grafts. Most of the ISR was within drug eluting stents (29) with two lesions within bare metal stents. In 12 cases, the original stent type was not available. Ten of the lesions had already failed treatment with DCBs without lesion debulking prior to their procedure (23%).

Table 2
Lesion characteristics. ISR – in-stent restenosis. DCB – drug coated balloon. SD – standard deviation.

ISR classification	
I	15
II	26
III	0
IV	2
Quantitative coronary analysis	
Proximal reference mean (SD)	3.0 mm (0.6)
Distal reference mean (SD)	2.9 mm (0.6)
Minimum luminal diameter (SD)	0.6 mm (0.4)
Lesion length (SD)	11.7 mm (3.4)
Stenosis by diameter (SD)	79% (11)
Target vessel	
Left main (%)	1 (2)
Left anterior descending (%)	6 (14)
Circumflex (%)	21 (49)
Right coronary artery (%)	9 (21)
Saphenous vein graft (%)	2 (5)
Intermediate (%)	4 (9)
Original stent	
Drug eluting stent (%)	29 (67)
Bare metal stent (%)	2 (5)
Unknown (%)	12 (28)
Already failed DCB angioplasty (%)	10 (23)

Procedural outcomes are detailed in Table 3. Lesion success was achieved in all cases. Mean residual stenosis for all lesions was 11.2%. Mean burr size for rotational atherectomy was 1.7 mm ranging from 1.25 mm to 2.0 mm. All lesions were predilated to at least the diameter of the DCB after rotational atherectomy with compliant balloons in one lesion, unspecified balloons in 8 and non-compliant balloons in the remainder. A mean of 1.07 DCBs were used per lesion with a mean diameter and length of 2.8 mm and 21.8 mm respectively. There were no procedural myocardial infarctions, deaths or cerebrovascular events. There were no coronary perforations or use of stents for bail-out in the target lesions. A drug eluting stent was inserted in another lesion in the target vessel in two cases.

Patient outcomes are detailed in Table 4. Follow up data was available for all patients at 30 days, 25 patients at one year and 19 patients at 2 years. There were no deaths, myocardial infarctions, strokes or major bleeds during the period of follow up. Target lesion revascularisation occurred in six lesions over two years (14%) and target vessel revascularisation occurred in eight vessels treated (22%). All six lesion failures occurred in patients who had previously failed DCB treatment to the same lesions prior to their procedure with rotational atherectomy. The four remaining lesions that had previously failed DCB treatment were free of TLR out to a mean follow up of 18 months.

4. Discussion

There are several factors that provide rationale for lesion debulking prior to DCB angioplasty in in-stent restenosis. Models and trials studying predictors of restenosis in drug eluting stent implantation suggest that stent underexpansion due to noncompliant vessel architecture is a predictor of restenosis by restricting the final diameter of the vessel and altering the uniformity of drug delivery to the vessel wall [14–16]. Rotational atherectomy prior to DCB angioplasty provides ideal lesion preparation and may aid in a more uniform application of drug to the vessel wall. It also allows greater lesion expansion prior to and during DCB angioplasty.

The results from this study suggest that for selected ISR cases, lesion debulking with rotational atherectomy prior to DCB angioplasty is a safe and potentially effective procedure.

From a safety perspective, previous studies of rotational atherectomy in de novo coronary lesions show arterial dissection rates of 11–13% and acute occlusion of 3–4% [17–19]. Rotational atherectomy in ISR may have a lower incidence of complications with rates of slow flow of 3% and very low rates of occlusion and dissection [20]. In the studied cohort, there were no coronary dissections or acute vessel closures suggesting at least comparable safety to routine rotational atherectomy. The lack of rarer complications such as perforation, pericardial effusion, burr entrapment and myocardial infarction was reassuring despite the relatively small cohort size and comparable with other rotational atherectomy trials in ISR.

Table 3
Procedural outcomes. DCB – drug coated balloon. MACE – major adverse cardiac event. SD – standard deviation.

Lesion success	43 (100%)
Mean residual stenosis by QCA	11.2%
DCB/lesion (range)	1.07 (1–2)
Lesions per procedure (range)	1.1 (1–3)
Mean burr size (SD)	1.7 mm (1.25 to 2.0 mm)
Mean burr/artery ratio	0.55
Mean DCB diameter (SD)	2.8 mm (0.4)
Mean DCB length (SD)	21.8 mm (5.7)
Procedural MACE (%)	0 (0)
Coronary perforation (%)	0 (0)
Drug eluting stent deployed in another lesion in target vessel (%)	2 (4)
Drug eluting stent as bail-out in target lesion (%)	0 (0)

Table 4
Clinical outcomes. TLR – target lesion revascularisation. TVR – target vessel revascularisation. CVA – cerebrovascular accident.

	1 m, no. (%)	1 m - 1y, no. (%)	1y - 2y, no. (%)
No follow up available	0 (0)	1 (4)	7 (27)
Death	0 (0)	0 (0)	0 (0)
Myocardial infarction	0 (0)	0 (0)	0 (0)
TLR	0 (0)	4 (9)	2 (5)
TVR	0 (0)	6 (16)	2 (6)
CVA	0 (0)	0 (0)	0 (0)
Major bleed	0 (0)	0 (0)	0 (0)

Rates of TLR and TVR in our cohort were comparable to rates in trials of DCB use alone for ISR. Importantly, all of the TLR occurred in lesions that had already failed DCB angioplasty alone. Four lesions that had already failed DCB angioplasty were free of TLR or TVR for a mean follow up of 18 months after rotational atherectomy followed by DCB angioplasty. We suspect that this may be the patient group that this technique is most relevant for and the results of this study suggest that lesion debulking prior to DCB inflation may be of benefit in patients who have already failed conventional treatment.

5. Study limitations

Without randomisation, it is difficult to assess the additional effect of lesion debulking prior to DCB angioplasty. Patients were selected either because they had failed conventional therapy or the angiographic appearance of their lesions was suitably unfavourable that debulking was thought to be required including characteristics such as calcification, length, tortuosity and vessel diameter. ISR in drug eluting stents was also favoured over ISR in bare metal stents which presumably were treated more often with drug eluting stent deployment. While it would follow that these patients should have a high rate of TLR with conventional therapy, further study is required to confirm this. The lack of surveillance coronary angiography also makes accurate assessment of asymptomatic lesion failure unfeasible.

Further, intravascular imaging is often suggested as a method for determining the aetiology of ISR and distinguishing particularly between stent underexpansion, intimal hyperplasia and neoatherosclerosis. Other information regarding previous stenting procedures such as how many layers of stent were present could also have been obtained in this way. Intravascular imaging in this patient cohort would have been useful in determining which patients would benefit most from this technique but this was not the practice at our institution in the studied period. It would follow that rotational atherectomy for underexpanded stents would be more perilous and less effective than for intimal hyperplasia and as such, we would suggest routine intravascular imaging in further studies in this area.

While safety results were reassuring, rarer complications such as perforation, emergency coronary artery bypass graft surgery and mortality did not occur in the study group but would require a larger cohort to properly assess.

Future larger randomised trials could further stratify which lesions that have failed conventional treatment may benefit from lesion debulking prior to DCB angioplasty, compare this technique to drug eluting stent deployment and further study safety outcomes to ensure that the favourable safety outcomes demonstrated in this smaller group are reproduced in a larger cohort.

6. Conclusions

Lesion debulking with rotational atherectomy followed by DCB inflation is a feasible treatment option for selected cases of ISR. Further study is needed to fully assess its efficacy in comparison to conventional treatment.

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