Hybrid rotablation and drug-eluting balloon strategy

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Abstract

Aim: The aim was to assess the safety and efficacy of rotational atherectomy followed by drug-eluting balloon (DEB) in patients with a high risk of bleeding.

Methods: A retrospective review was carried out of hospital records of consecutive patients who underwent the hybrid procedure.

Results: The average age of the 23 patients was 74 years. Risk factors for bleeding included renal failure (35%), oral anticoagulation use (26%) and peptic ulcer disease (35%). All patients had procedural success. No bleeding was reported over the 24-month follow-up period. Dual antiplatelet therapy was stopped successfully in six patients (26%) at three months. Two patients had confirmed target-lesion failure (restenosis). Two patients died over the study period but the cause of death was not known to be cardiovascular disease related.

Conclusion: For patients at high risk of bleeding who require rotablation, the use of a drug-eluting balloon may be a safe, effective alternative.

Keywords: rotablation, drug-eluting balloon, calcification

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The revascularisation strategy for dealing with calcified lesions includes adequate lesion preparation to avoid complications and improve clinical outcomes. The techniques to prepare lesions include balloon angioplasty, using semi-compliant and non-compliant balloons, cutting balloons, rotational atherectomy and, recently, intravascular lithotripsy. Post lesion preparation, the current recommendations and practice are to use drug-eluting stents (DES) requiring dual antiplatelet therapy (DAPT), which includes P2Y12 inhibitors (clopidogrel, ticagrelor or prasugrel) for six to 12 months, and aspirin lifelong.

Hybrid rotablation and drug-eluting balloon strategy is a new concept for calcified lesions and has a number of potential benefits. Most patients referred with calcified lesions are elderly and have numerous co-morbidities and risk factors for bleeding, including atrial fibrillation, oral anticoagulants, renal failure and peptic ulcer disease. The use of drug-eluting balloons (DEBs) offers a strategy for reducing bleeding risk, as the post-procedure addition of P2Y12 inhibitors to aspirin for secondary prevention is required for only one month, following which they can be discontinued.

Patients with calcified lesions often have diffuse disease and long lesions, potentially requiring long, small stents. These are prone to under-expansion, malapposition, delayed endothelialisation and chronic inflammation, stent fracture, neo-atheroma and polymer reactions, all of which place patients at increased risk for early, late and very late stent thrombosis. Therefore, by eliminating the need for any stent implantation, DEBs may significantly reduce the risk of these stent-related adverse events.

DEBs are designed to act as delivery vehicles to the target lesion of chemotherapeutic agents (paclitaxel, sirolimus), which have been coated on the balloon. The currently available DEBs have different excipient/coating techniques (Table 1).

The main DEBs available for use in our practice were the SeQuent® Please (B Braun) and IN.PACT Falcon (Medtronic). The SeQuent® Please DEB uses iopromide (a contrast medium) to act as the excipient to retain the drug on the balloon and to facilitate delivery of the drug to the vessel wall due to its lipophilicity. The dose of paclitaxel used is 3 μg/mm². The half-life of the drug is almost two months. The IN.PACT Falcon DEB uses urea as an excipient with the antiproliferative agent paclitaxel (3.5 μg/mm²). Although sirolimus-coated DEBs have recently been developed and used with promising clinical

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<tr>
<th>Chemotherapeutic agent</th>
<th>DER type</th>
<th>Excipient/coating technique</th>
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<tr>
<td>Paclitaxel</td>
<td>SeQuent® Please</td>
<td>Lipromide matrix coating</td>
</tr>
<tr>
<td></td>
<td>Pantera Lux</td>
<td>BTHC matrix coating</td>
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<td></td>
<td>IN.PACT Falcon</td>
<td>FreePac matrix coating</td>
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<td>Dior</td>
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<td>Elutas</td>
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<td>Lutonix</td>
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<td>Danubio</td>
<td>BTHC excipient</td>
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<td>Sirolimus</td>
<td>Magic touch</td>
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Table 1. Drug-eluting balloons

DEB, drug-eluting balloons; BTHC, butyryl-tri-hexyl citrate.
outcomes in de novo lesions, we did not use any DEBs containing sirolimus in our cohort of patients.

Rotablation or rotational atherectomy has been practiced worldwide and standard protocols have been developed to improve the clinical outcomes of patients with calcified lesions. The new concept of a hybrid approach that combines the use of rotablation with a DEB adds to the pool of novel and beneficial interventional therapies for patients with calcified lesions.

Although a strategy of hybrid rotational atherectomy and DEB is considered a viable alternative in patients with multiple co-morbidities and high risk for bleeding, data on effectiveness and safety are limited. There are no randomised, control trials comparing this strategy to conventional approaches, and the published observational experience consists predominantly of small, retrospective, single-centre cohorts.

Given the paucity of available published data, we aimed to add to the information on effectiveness and safety of a hybrid approach to calcified lesions in a real-world setting by sharing our recent experience from a different geography and population. This was a retrospective review of the patient records, files, angiograms and other available relevant material. Parameters included demographic, clinical (hypertension, diabetes and dyslipidaemia) and laboratory data, medication and angiographic data (Tables 2, 3). Consecutive adult patients who underwent a hybrid percutaneous intervention, defined as the combination of rotablation and DEB therapy for calcified lesions, in a minimum of one lesion were included in the analysis. Patients who did not have a complete set of procedural and follow-up data available for review were excluded.

Patients were given clopidogrel either prior to or post intervention. Ticagrelor and prasugrel were not used. Elective patients were only given intravenous heparin during the procedure to keep an activated clotting time level between 250 and 350 s. Enoxaparin 1 mg/kg bd subcutaneously was given for acute coronary syndrome patients unless the patients were on warfarin.

Rotablation was performed if the lesions were heavily calcified or uncrossable with a balloon. It was performed using the Rotablator (Boston Scientific, MN). The burr sizes ranged from 1.25 to 2.0 mm. The speed of the burr ranged between 170 000 and 180 000 rpm. Post rotablation, pre-dilatation of the lesion was performed with a semi-compliant balloon, non-compliant or cutting balloon for lesion optimisation and then followed with a DEB, which was inflated for 60 to 90 seconds at nominal pressures. The DEB was generally sized 1:1 per the vessel diameter and at least 2 mm longer on both sides of the lesion.

### Methods

The study was conducted using anonymised patient data from a high procedure-volume group cardiology practice in Johannesburg, South Africa between June 2015 and December 2018. The percutaneous procedures of interest were performed by one of two experienced interventional cardiologists.

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The strategy in case of flow-limiting dissections (TIMI < 3) or significant recoil (> 30%) was to then use a DES. No bare-metal stents were used.

**Results**

There were 23 patients who had the rotablation and DEB strategy. The indication for the hybrid procedure was non-ST-segment myocardial infarction in 13 patients and unstable angina in 10 patients. The average age was 74 years and 78.3% were males. The majority of patients were dyslipidaemic (78.3%) and hypertensive (74%); 30.4% were diabetic and 13% were smokers. Seven patients (30.4%) had a prior coronary artery bypass graft. The mean left ventricular ejection fraction was 52% and three (13%) patients had severe aortic stenosis (two patients had prior transcatheter aortic valve implantations and one had a prior balloon aortic valvuloplasty).

Risk factors for bleeding included chronic renal failure (35%), the use of oral anticoagulation (26%), atrial fibrillation (13%) and peptic ulcer disease (35%). The mean haemoglobin level was low, at 12.7 g/dl, and the mean creatinine level was raised, at 158 μmol/l, with an estimated glomerular filtration rate (eGFR) of 58 ml/kg/min. Mean total cholesterol was 4.4 mmol/l and the low-density lipoprotein cholesterol was 2.4 mmol/l.

The majority of the procedures were performed via the femoral route (87%) and 13% were performed radially. Cutting balloon was used in 13% of calcified plaques. The 1.25-mm burr was used in 61% of cases, followed by the 1.75-mm burr (35%) and the 1.5-mm burr (27%). The average length of DEB used was 37 mm. The DEB included SeQuent® Please (65%) and IN.PACT Falcon (35%). After the procedure, six patients received DAPT for a minimum of one month, 10 for six months, and 13 for 12 months and one for longer than 12 months, and for two there were no follow up data. There were 15 patients who had stents inserted in other lesions.

Procedural success was reported in all 23 patients. Twenty of the 23 patients had follow-up information available at 24 months. Six patients (26%) were not on DAPT beyond three months in a significant proportion (> 25%) of patients, that bleeding rates in this high-risk cohort over a 24-month period were extremely low, and that restenosis rates were acceptable.

DEBs have been used in current daily practice for in-stent restenosis (ISR), small-calibre vessels, bifurcation lesions, ostial lesions and undilatable lesions. The BELLO study (Balloon Elution and Late Loss Optimization) was a randomised, multicentre study of small coronary vessels (< 2.8 mm), which showed that apaclitaxel DEB was associated with less angiographic late loss and similar rates of restenosis and revascularisation as a paclitaxel-eluting stent, but more evidence is needed to compare DEB and newer-generation DES.

However, in a meta-analysis of over 5 000 patients looking at the most appropriate coronary PCI strategy, including sirolimus- and paclitaxel-eluting stents, DEBs, bare-metal stents and balloon angioplasty, sirolimus-eluting stents yielded the most favourable angiographic and clinical outcome for the treatment of small coronary arteries. In our study, the 2.5-mm DEB and the 1.25-mm burr were used in 60.9% of patients in small-calibre vessels.

Restenosis rates of 30 to 40% after rotablation alone or following angioplasty alone were unacceptably high, which decreased to 23 to 43% following bare-metal stents. There is a much more acceptable restenosis rate currently of one to 5% in the DES era. However the increased bleeding risk of being on DAPT suggests one should consider DEB.

Paclitaxel DEBs have been shown to be superior to balloon angioplasty for ISR in terms of major adverse cardiovascular events (MACE) and target-lesion revascularisation (TLR) for up to 36 months in a multicentre, randomised study, which showed that the multiple TLR was more frequent in the plain old balloon angioplasty (POBA) group, compared to the DEB group (13.2 vs 1.4%, p = 0.021). The MACE rate was significantly reduced in the DEB group compared to the POBA group (20.8 vs 52.6%, p = 0.001). The disadvantages of stent complications such as malapposition and under-expansion, delayed endothelialisation and chronic inflammation are eliminated with no permanent implant and have led to new developments in the field of interventional cardiology. In our study, two patients (8.7%) had target- vessel restenosis. This restenosis rate was much lower than the POBA rates of 23 to 43% but higher than the DES restenosis rate of one to 5%.

Bioresorbable vascular scaffolds (BVS) have been developed with the attractive concept of resorbable material, avoiding the late complications of permanent metal scaffolds. The BVS have been shown to be efficacious but due to definite stent thrombosis of 2.6% at 12 months, have not been shown to be superior to DES. Recently, novel drug-eluting metal absorbable scaffolds consisting of absorbable magnesium scaffold backbones as an alternative to polymeric scaffolds have showed a favourable safety profile. The polymer-free umirolimus stent has been shown to be superior to bare-metal stents in primary safety and primary endpoints in patients after one month of DAPT. Further trials have also shown evidence to stop DAPT after
one month in patients with high bleeding risk with zotarolimus stents.\textsuperscript{23}

The attractive concept of stentless PCI has gained interest in the interventional cardiology community. Stentless PCI has been reported recently from Japan, which suggests that rotational atherectomy and DEB might be an alternative for patients who may be unsuitable for DES implantation. Case reports of successful outcomes of patients with calcified diffuse lesions, patients with severe thrombocytopenia and those with chronic kidney disease, as well as patients with ostial lesions also recommend that one should consider this hybrid strategy.\textsuperscript{12,14,15}

The study by Rissanen \textit{et al.} enrolled 65 patients, who were followed for a period of 17 months; 82\% of patients had at least one risk factor for bleeding. Risk factors in this study included anticoagulation (40\%), anaemia (45\%), active malignancy (1.5\%), prior stroke (22\%), severe renal dysfunction with an eGFR < 30 ml/kg/min (3\%), age > 80 years (31\%) and prior bleeding requiring intervention (25\%). MACE occurred in 20\% of patients at 24 months. The incidence of significant bleeding was 9\% at 12 months.

This study, which was published in 2017, was the first to show that PCI using DEB after rotablation was safe and effective. Compared to our study, we had a similar elderly population with 34.8\% aged > 80 years, fewer patients on anticoagulation (26.1\%) and more with severe renal dysfunction (13\%). More studies are needed to show the prevalence of rotablation and different novel ways to approach revascularisation in these patients with calcification and high risk of bleeding.

There were limitations to this study. This was a retrospective audit of files, which would limit one’s acquisition of data and follow up. Patients were not routinely followed up with repeat coronary angiography, which could have affected the incidence of restenosis and new TLR.

Conclusion
The hybrid approach of rotablation and DEB is a novel approach in patients with coronary calcification and a bleeding risk. These patients are more commonly elderly male patients with renal failure. Bleeding risk can be reduced in these high-risk patients as DAPT could be stopped by three months in a significant proportion (> 25\%) of patients. This study has also shown that bleeding rates in this high-risk cohort over a 24-month period was extremely low and that restenosis rates were acceptable. In our cohort, we have confirmed prior observations that the procedure of DEB following lesion preparation with rotational atherectomy is safe and effective for patients with a high risk of bleeding.

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References


