Atherectomy and DCB in the SFA: A Summary of the Data

Do the outcomes justify the two-part approach to lesions in this challenging anatomy?

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The treatment of superficial femoral artery (SFA) disease is characterized by a number of problems and hurdles to overcome. The first problem is related to the nature of the lesions in the SFA, which are typically long (thus implying a high plaque burden) and highly calcified. Because of the extensive calcification expansion of (laser-cut) nitinol, stents can be problematic, leading to poor vessel wall apposition of the stent, which is known to be a negative predictor of patency. In order to avoid stent placement and/or obtain better stent appositioning, atherectomy (directional, orbital, or laser) has been proposed, yielding satisfactory technical and short-term results, but this technique is still characterized by a relatively high incidence of restenosis in the mid to long term.

Acute elastic recoil of primary lesions can be treated with self-expanding stents, and stenting for stenocclusive disease of the SFA (with or without previous debulking) has improved the midterm outcomes as compared to balloon angioplasty. However, it poses an additional long-term problem, with a relatively high percentage of patients presenting with in-stent restenosis (ISR). Acute elastic recoil of primary lesions can be treated with self-expanding stents, and stenting for stenocclusive disease of the SFA (with or without previous debulking) has improved the midterm outcomes as compared to balloon angioplasty. However, it poses an additional long-term problem, with a relatively high percentage of patients presenting with in-stent restenosis (ISR) which is known to be a negative predictor of patency. In order to avoid stent placement and/or obtain better stent appositioning, atherectomy (directional, orbital, or laser) has been proposed, yielding satisfactory technical and short-term results, but this technique is still characterized by a relatively high incidence of restenosis in the mid to long term.

The concept of drug-coated balloons (DCBs) is based on the local delivery of drugs to the lesion site with an exact control of the drug dosage. Although during passage of the balloon through the valve of the sheath and through the arterial system some drug is lost, an effective and sufficient local concentration is achieved, with very low systemic exposure to the drug. Advantages of the technology are the possibility of a homogeneous drug transfer as compared to stent-mediated drug release, where the drug is only delivered at the level of contact of the stent struts with the vessel wall. DCBs also allow for a drug concentration that is highest at the time of the vessel wall injury, which occurs during balloon angioplasty, and therefore can prevent the initiation of neointimal proliferation. The absence of metal struts makes the technique suitable for treatment of long lesions (especially in small-diameter vessels) and areas where flexion and compression of stents may occur. Results of DCB angioplasty published from various randomized trials are comparable to the results of stenting in short segment (< 10 cm) lesions.

This article provides an update of the data available on the combination of atherectomy and DCB angioplasty in the SFA, both in patients with primary lesions and ISR.

ATHERECTOMY AND DCB FOR PRIMARY LESIONS

In primary lesions of the SFA, the presence of calcification and the high plaque/thrombus burden may inhibit drug uptake and limit the biological effect of paclitaxel from DCBs. Bailout use of self-expanding stents after unsuccessful balloon angioplasty may have a negative influence on the long-term patency rates because the stents will exert a chronic outward pressure on the vessel wall. Therefore, there is a tendency among interventionists to reduce the number of stent implantations (this is also driven by the outcomes of DCB trials).

With the use of debulking, heavily calcified lesions can be treated by removing the perfusion barrier that prevents a proper, homogeneous drug uptake; effective DCB therapy requires homogeneous distribution of drug in the vessel wall. The mechanical recanalization of the vessel allows balloon angioplasty to be performed at a low pressure, reducing the barotrauma to the arterial wall by not overstretching the vessel.
will reduce the likelihood of bailout stenting and will preserve the native vessel (keeping future treatment options, both endovascular and surgical, open).

**Directional Atherectomy Plus DCB**

There is only one study that evaluated the combination of (directional) atherectomy and a paclitaxel-coated balloon in heavily calcified femoropopliteal lesions.\(^{13}\) In this single-center registry, 30 patients were included (18 patients with intermittent claudication, 12 patients with critical limb ischemia [CLI]). In each patient, a directional atherectomy system (TurboHawk, Covidien) and distal filter protection (SpiderFX, Covidien) were used before performing balloon angioplasty with a DCB (In.Pact Admiral, Medtronic, Inc.) for at least 180 seconds. In 90% of the cases, the SFA was treated, and the remaining 10% treated the popliteal artery. Mean lesion length was 115 ± 35 mm. Bailout stenting was necessary in two patients for flow-limiting dissection (2/30; 6.7%). Only two cases had a significant amount of debris collected in the filter. All patients were available for follow-up at 1 year. The limb salvage rate in the CLI group was 100%. Overall, a primary patency rate of 90% was seen (documented by duplex ultrasound). Clinically driven target lesion revascularization (TLR) and target vessel revascularization rates were 10%.

Compared to other studies, the restenosis rates at 1 year and the need for bailout stenting were reduced significantly.\(^ {14}\) In most of the studies that have been performed in the past, patients with severe calcification were excluded. The results of combination therapy in this group of difficult-to-treat patients are, therefore, very promising.

**ATHERECTOMY AND DCB FOR ISR**

ISR is characterized by a heterogenous nature of the lesions, with a cell-dense intimal layer that has a rubbery consistency and a significant volume of cell-poor, hydrated matrix in the outer intima to the stent struts. Due to this unique morphology, ISR lesions tend to feel spongy and recoil quickly. The extracellular matrix accounts for 50% of the total volume of neointimal restenotic lesions, explaining why balloon angioplasty alone does not work in restenotic lesions.\(^ {14}\)

**Conventional Balloon Angioplasty Versus Cutting Balloon Angioplasty**

A randomized study compared conventional balloon angioplasty with peripheral cutting balloon angioplasty in patients who had ISR with lesion lengths up to 20 cm (mean lesion length, 80 mm).\(^ {15}\) Restenosis rates at 6 months were 65% after cutting balloon angioplasty and, even worse, 73% restenosis with conventional percutaneous transluminal angioplasty (PTA). In addition to the morphology of the lesions, the stents used in the SFA are already fully expanded, and thus additional luminal gain by overstretching the stent using balloon dilation will not be feasible or effective. Although the stents can be expanded to a larger diameter with an oversized balloon, after balloon deflation, the stent will recoil to its nominal diameter due to its nitinol encoding.

**Laser Atherectomy Plus DCB**

The first indication that combining laser debulking and DCB angioplasty had better outcomes than plain balloon angioplasty came from an article that described the short-term follow-up of a cohort of 10 patients treated with this combination therapy.\(^ {16}\) The mean follow-up was 7.6 months. Eight women and two men with a mean age of 78.6 years (range, 69–88 years) were treated. All patients experienced relatively early restenosis with a mean time to recurrence of 7.2 months (range, 2–16 months), and the mean lesion length was 115 mm (range, 10–300 mm). Half of the patients presented with CLI (S/10); the other half presented with Rutherford class 3 (intermittent claudication). Two patients had a Tosaka class I lesion;\(^ {17}\) the remaining eight patients all had Tosaka class III lesions (total occlusion). All procedures were technically successful. No residual stenosis was seen angiographically. There were two cases of distal embolization (both in patients with a history of acute or chronic occlusion). Both could be treated successfully with aspiration embolectomy (n = 2) and local (on-the-table) intra-arterial thrombolysis using a bolus of urokinase of 250,000 units (n = 1).

Six patients underwent duplex ultrasound follow-up, one patient had an angiographic control (during angioplasty of an ipsilateral SFA stenosis proximal to the treated segment a year after the index procedure), and the remaining three patients had clinical follow-up with ABI measurements. No TLR was performed. The clinical stage improved in all patients, with nine patients becoming asymptomatic, and one patient having Fontaine class IIa symptoms (Rutherford class 2). The patients who were evaluated with duplex ultrasound and/or angiography (n = 7; mean follow-up, 7 months) did not show any signs of neointimal hyperplasia. One patient underwent a preplanned amputation of a toe shortly after the revascularization procedure. No major amputations or deaths occurred.

The longer-term follow-up of this cohort of 10 patients recently became available, and it appears that the effect of laser debulking followed by DCB is sustained at 2 years.\(^ {18}\) The duration of clinical follow-up...
was 22.2 ± 8.4 months (range, 15–38 months) and for duplex ultrasound follow-up, 23.8 ± 8.5 months (range, 13–38 months). Two patients were lost to follow-up after 13 and 14 months, respectively, and were asymptomatic at that time. One patient had a binary restenosis (> 50% stenosis as shown on duplex ultrasound using a peak systolic velocity ratio threshold of > 2.4) at 36 months. This led to a TLR (n = 1) at 36 months (angiographically, a focal 60% stenosis in the distal popliteal artery was seen). In the remaining patients, no clinically significant restenosis was seen with duplex. Five patients (5/10; 50%) showed absence of restenosis at a mean follow-up of 16.2 months (range, 15–20 months), and 4/10 (40%) had a 25% to 50% stenosis (mean follow-up of this subgroup, 25 months; range, 19–38 months).

### Laser Atherectomy Plus DCB Versus DCB Alone

Similar good results were seen in a study that involved 48 patients who were randomly assigned to treatment using combination therapy of laser debulking and DCB angioplasty (n = 24), or DCB angioplasty alone (n = 24). All patients were suffering from chronic CLI and presented with a total occlusion of the SFA (Tosaka class III). Mean length of the treated stent was 20 ± 10.1 cm in the combination therapy group and 23.3 ± 9.1 cm in the DCB-only group (P = NS). The treated lesion length was 22.4 ± 9.4 cm versus 25.9 ± 8.7 cm, respectively (P = NS).

The occluded tract was limited to the stent only in three patients; in the remaining cases, stent obstruction was associated with proximal and/or distal thrombosis. Two cases of distal embolization were seen in the DCB group and in one patient treated with combined therapy. The patency rates at 6 and 12 months in the combined therapy group (91.7% and 66.7%, respectively) were significantly higher than in the DCB group (58.3% and 37.5%, respectively; P = .01). TLR at 12 months was 16.7% in the combination therapy group, and 50% in the DCB angioplasty-only group (P = .01). The number of major amputations was also significantly reduced (8% vs 46%; P = .003). Ulcer healing was better in the patients who underwent combination therapy.

### Directional Atherectomy Plus Plain Balloon Angioplasty Versus Directional Atherectomy Plus DCB

Further support for the combined approach of debulking and DCB angioplasty for ISR comes from a study in which positive results were obtained using directional atherectomy. In a retrospective analysis, two groups of patients were evaluated. The first group of patients consisted of a historical control group of patients with femoropopliteal restenotic lesions (both native artery and ISR) that were treated with directional atherectomy (Silverhawk, Covidien) and plain balloon angioplasty. The second group consisted of patients with similar lesions treated with directional atherectomy and DCB angioplasty. A total of 89 patients were treated: 60 with PTA as adjunctive therapy (24/60, native artery lesions; 36/60, ISR lesions) and 29 with DCBs (2/29 native arteries, 27/29 ISR). Almost 70% of lesions were ISR, the remainder being restenosis in arteries that were treated without stenting. Lesion length of the entire study population was 171 ± 124 mm (180 ± 136 mm for the PTA cohort; 153 ± 93 mm for the DCB group; P = .276).

The 1-year Kaplan-Meier estimates of freedom from restenosis were 84.7% in the DCB group and 43.8% in the PTA group. The combination of directional atherectomy with adjunctive DCB angioplasty was associated with a better event-free survival at 12 months of follow-up compared to PTA after directional atherectomy. It must be kept in mind that all current atherectomy modalities rely on mechanical scraping or grinding, which are generally inappropriate for softer tissues such as thrombus or neointimal hyperplasia, and the moving components pose an elevated risk for stent disruption and fragmentation. Directional atherectomy is actually contraindicated in the treatment of ISR, and this technique is therefore not recommended.

### DCB as Standalone Therapy

To put these positive results into perspective, a comparison should be made to the outcomes seen with DCB angioplasty or atherectomy (debulking) as standalone therapies. One study evaluated the use of DCBs for the treatment of SFA ISR and demonstrated a 92.1% primary patency rate at 1-year follow-up in a patient cohort with a mean lesion length of 82.9 ± 78.9 mm. In this study, the number of class III lesions was relatively low (20.5%).

The results of 2-year follow-up in this cohort were recently published and showed a decrease in primary patency to 70.3% and a freedom from TLR of 78.4%. The treatment of complex ISR lesions (classes II and III) was associated with an increased rate of recurrent restenosis compared with class I (33.3% for class II and 36.3% for class III vs 12.5% for class I; P = .05). The data from this study evaluating DCB angioplasty in SFA ISR (at 1 and 2 years) show higher restenosis rates as compared to the treatment using combined therapy of debulking and DCB angioplasty in the SFA as found in the above-mentioned studies, even when the mean lesion length in the study from Stabile is shorter. The improvement of outcome with combination therapy can likely be explained by the additional use of debulking.
Debulking seems to be of more importance in treating patients with lesions that are Tosaka class II and higher.

**Laser Atherectomy as Standalone Therapy**

Laser debulking as a standalone therapy has been evaluated in the EXCITE ISR trial and the PATENT registry (Spectranetics Corporation). In the EXCITE ISR trial, the safety of laser atherectomy with adjunct PTA was demonstrated. A 94% procedural success rate was seen, as compared to 83% with PTA alone. Currently, laser atherectomy is the only treatment modality cleared by the US Food and Drug Administration (based on the EXCITE ISR data) for the treatment of peripheral ISR.

In the PATENT study, relatively long and complex lesions were treated (mean lesion length, 123 ± 95.9 mm, with 34.1% of lesions being total occlusions). The primary patency at 6 months (64.1%) compared favorably to that seen in the study by Dick et al (despite shorter lesion length, the patency rate was only 27% in the balloon angioplasty group; see above).

At 12 months, however, the overall primary patency rate showed a drop to 37.8%. The primary patency at 12 months as stratified by Tosaka class was 54.5% for class I, 27.6% for class II, and 24% for class III.

Although it was calculated that, when comparing the three classes, primary patency at 12 months was not significantly different, there was a tendency for longer, more complex lesions to do worse. From this study (and from studies using directional atherectomy), it can be concluded that after debulking, additional therapy is needed in order to prevent recurrence of ISR. Because the burden of intima hyperplasia-associated restenosis and ISR in the peripheral arteries is quite considerable, especially in long lesions, the data obtained in the studies mentioned above support the approach of combining debulking with DCBs, thus avoiding additional stenting procedures.

**CONCLUSION**

There is a growing body of evidence from single-center registries and a small, randomized trial demonstrating that the combination of debulking (atherectomy) and DCB angioplasty improves outcomes both in primary lesions and ISR. Particularly in patients with complex ISR (Tosaka class II and III), the advantages of combination therapy are more pronounced, probably because of the large amount of restenotic material that needs to be addressed. Given the fact that the innermost layer of the substance that forms the ISR consists of noncellular material, the cytotoxic effect of paclitaxel may not be able to reach the cellular (outermost) layer. Atherectomy offers the possibility to remove the smooth muscle cell inner intimal layer and the aqueous outer intimal layer that mainly consists of extracellular matrix. Further studies and larger randomized trials are needed to confirm these positive findings.

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