Endovascular Techniques for Infrainguinal Peripheral Arterial Disease

Endovascular treatment is increasingly considered as the first-line treatment for atherosclerotic lesions of the femoropopliteal segment. Yet, the success rate of endovascular treatment of femoropopliteal lesions depends on variables such as the presence of diabetes mellitus or chronic kidney disease, stenosis vs. occlusion, lesion length and crural run-off status, factors which are often unfavourable in patients with CLI. (Rueda et al, 2008)

Several studies have demonstrated that surgical revascularization is the standard treatment for limb salvage in patients with CLI due to atherosclerotic disease of infrapopliteal arteries, but endovascular interventions of infrapopliteal lesions represent a far less invasive option and are now considered a valid alternative to surgical bypass in many cases. (Setaccia et al, 2011)

In selected cases of CLI patients, the revascularisation of profunda femoris artery (PFA) by surgical techniques has excellent long-term patency rates. In rare cases of CLI patients with a history of multiple vascular reconstructions in the ipsilateral groin, the surgical exposure of PFA might be technically demanding and endovascular techniques could offer a better therapeutic approach, especially in high-risk patients. However, there is insufficient

evidence for the role of endovascular techniques in patients suffering from profunda femoris artery occlusive disease. (Donas et al, 2010)

The first objective of infrainguinal endovascular treatment is to establish adequate inflow to the infrapopliteal vessels through revascularization of the femoropopliteal segment. This is then followed by an attempt to establish straight line flow to the foot. Attempts to revascularize more than 1 tibial vessel is popular among some endovascular specialists and is one of the advantages of endovascular therapy over surgical bypass. In contrast to the treatment of patients with claudication, where the goal of revascularization is to treat disease causing exercise-induced ischemia, the target lesions for revascularization in patients with CLI are those that are associated with a pressure gradient at rest. Therefore, the lesions treated in patients with CLI are typically either occlusions or critical stenoses. During endovascular therapy for CLI, careful attention to the small vessel runoff in the foot is required. Successful revascularization of the main tibial vessel that results in embolization to the small vessels in the foot is likely to result in clinical failure. Preventing distal embolization during treatment of the target proximal lesion and aggressive treatment of distal embolization when it occurs are important components of endovascular treatment of CLI. (Dattiloa & Casserly, 2011)

Technical Considerations:

Arterial Access:

A sterile field is required in either an Operating Room or an angiography suite with image capability. The most common and safest access site is the Common Femoral Artery (CFA) via either a retrograde or ante grade

approach. To avoid puncturing the iliac artery or SFA, the femoral head is located under the fluoroscopy and used as the guide for the level of needle entry. In addition, there are several useful techniques in helping access a pulseless CFA, including puncturing guided by ultrasound and targeting calcification in a calcified vessel. (Hunink et al, 1993)

Tibial artery interventions are typically performed using either contralateral retrograde common femoral artery (CFA) access or ipsilateral antegrade CFA access. The latter access site has several advantages, including providing superior support in treating complex occlusive disease, facility in treating distal tibial disease due to constraints in the length of interventional equipment, and ability to deal with distal embolization to small vessels in the foot. These advantages are balanced against the increased risk of bleeding at the access site, particularly in obese patients. In most circumstances, the technical advantages offered by antegrade access outweigh the risk of bleeding. (Dattiloa & Casserly, 2011)

Recanalization:

Traversing the lesion with a wire is the most critical part of the procedure. Typically, 0.035-inch guide wires are used for femoropopliteal lesions. Crossing infrapopliteal stenoses is almost universally achieved in an antegrade fashion using 0.014″ interventional wires. Crossing infrapopliteal occlusions is significantly more challenging and requires a more elaborate range of 0.014″ interventional wires with stiffer tips, 0.018″ wires, and, rarely, 0.035″ wires. Hydrophilic-coated wires, such as Glide wires, are useful in navigating through tight stenosis or occlusion. An angled-tip wire with a torque device may be helpful in crossing an eccentric lesion, and a

shaped selective catheter is frequently used in helping manipulate the wire across the lesion. The soft and floppy end of the wire is carefully advanced, crossing the lesion under fluoroscopy, and gentle force is applied while manipulating the wire. Retrograde recanalization of tibial occlusions may be tried by puncturing the target tibial vessel distal to the occlusion. (Figure:4) Once the lesion has been traversed, one needs to pay particular attention to the tip of the wire to ensure a secure wire access and avoid vessel wall perforation or dissection. (Johnston, 1992), (Dattiloa & Casserly, 2011)

Systemic anticoagulation should be maintained routinely during lower limb arterial interventions to minimize the risk of pericatheter thrombosis. Unfractionated heparin is the most commonly used agent, given on a weight-based formula. It is a common clinical practice to use an 80 to 100 mg/kg initial bolus for a therapeutic procedure to achieve the activated clotting time above 250 seconds on the catheter insertion and subsequently 1000 units for each additional hour of the procedure. Newer agents such as low molecular weight heparin, platelet IIb/IIIa inhibitor, direct thrombin inhibitor, or recombinant hirudin have been available and can be used either alone or in conjunction with heparin, particularly in patients sensitive to unfractionated heparin. (Johnston, 1992), (Lyden, 2009)

Figure 4: Retrograde access in posterior tibial artery with placement of 4F sheath.

(Dattiloa & Casserly, 2011)

Subintimal Angioplasty:

Since long complex lesions are usually present in CLI patients, successful endovascular recanalisation of the SFA can sometimes only be performed with subintimal angioplasty (SIA). SIA has been associated with high limb salvage rates between 85% and 90% at 1 year, even despite a low 50% 1-year primary patency rate. These results were recently confirmed by Bolia and Setacci et al. with primary success rates of 80% and 83.5% and limb salvage rates of 85% and 88% at 1 year, respectively.(Bolia , 2005), (Setacci et al, 2009)

A major concern of the popularity of endovascular interventions, especially in complex lesions, is the potential alteration of the level for subsequent open procedures after failed endovascular intervention. Joels et

al. have reported that the problem of alteration of the level of a subsequent open procedure after failed endovascular intervention is acceptable and even when the level alters, it does not necessarily change clinical outcome. They showed that only 23 out of the 276 patients subjected to endovascular recanalisation of the SFA presented with early failure of the procedure and that this altered the level of the subsequent open intervention in one third of the patients. Amputation due to early failure was necessary in only one patient (0.4%). However, they did not include TASC D lesions. (Joels et al, 2008)

In some centers subintimal angioplasty is gaining popularity for long-segment occlusions below the knee. Nydahl et al investigated the use of subintimal PTA for restoring blood flow in the infrapopliteal vessels. This paper reported a one-year limb salvage rate of 85%, even though the subintimal canal was hemodynamically patent in only 53% of the cases. Vraux et al in 2000 found comparably low 12-month primary patency rates (56%) with an 81% limb salvage rate.(Nydahl et al, 1997)(Vraux et al, 2000)

In contrast to the femoral and popliteal arteries, tibial arteries have a thinner wall and an abundance of side branches. As a consequence, attempts to intraluminally pass the occlusion with the end of the hydrophilic guide wire often result in perforation. Therefore it is recommended to start with subintimal dissection with a loop of the hydrophilic guide wire. A serious limitation of the SA is diffuse stenosis or occlusion of the popliteal artery trifurcation, including proximal parts of tibial arteries. Under these circumstances, it is only possible to form a hydrophilic wire loop in the femoro-popliteal segment. Most often, the loop moves into the peroneal artery, which is a direct continuation of the popliteal artery and tibioperoneal

trunk and is less susceptible to obliterating atherosclerosis. This represents a major problem if it is necessary to restore the blood flow in the posterior tibial artery and especially in the anterior tibial artery. As a rule, predilatation of the critically stenosed or occluded proximal part of tibial artery allows forming a hydrophilic guide-wire loop inside the artery stump without much difficulty. (Kaputin , 2010)

The results of conventional angioplasty are poor for multilevel stenosis or long occlusions and good results of SA of tibial vessels occlusions have been confirmed when surgery was not possible or considered high risk. (Vraux & Bertoncello, 2006)

Reentry catheters:

Two devices are available, the Pioneer catheter (Medtronic Vascular) and the Outback (Cordis Corporation, Miami, Florida). Both devices are best suited for vessels that are not heavily calcified and have a well-visualized distal vessel. Briefly, the Pioneer has two .014" wire ports, one with a hollow core nitinol needle. The needle is rotated towards the vessel lumen using intravascular ultrasound guidance (Volcano Corporation, Rancho Cordova, California). The needle is advanced into the lumen and a .014" wire is advanced and secures intraluminal position as the device is withdrawn. With the Outback catheter, fluoroscopic imaging is used to direct a 22-gauge cannula for distal vessel entry. Orthogonal angiography and a fluoroscopic marker provide orientation of the tip toward the reentry site and an angled nitinol needle is advanced into the vessel into the true lumen. (Abbott & Williams, 2007)

Target Lesion treatment:

Balloon Angioplasty:

After the lesion is crossed with a wire, an appropriate balloon angioplasty catheter is selected and tracked along the wire to traverse the lesion. The length of the selected catheter should be slightly longer than the lesion and the diameter should be equal to the adjacent normal vessel. The balloon tends to be approximately 10 to 20% oversized. The radiopaque markers of the balloon catheter are placed so that they will straddle the lesion. Then, the balloon is inflated with saline and contrast mixture to allow visualization of the insufflation process under the fluoroscopy. The patient may experience mild pain, which is not uncommon. However, severe pain can be indicative of vessel rupture, dissection, or other complications. An angiography is crucial in confirming the intraluminal location of the catheter and absence of contrast extravasation. The inflation is continued until the waist of the atherosclerotic lesion disappears and the balloon is at full profile. Frequently, several inflations are required to achieve full profile of the balloon. (Dormandy, 2000)

Occasionally, a lower profile balloon is needed to predilate the tight stenosis so that the selected balloon catheter can cross the lesion. Upon inflation, most balloons do not rewrap to their pre inflation diameter and assume a larger profile. Furthermore, trackability, pushability, and crossability of the balloon should be considered when choosing a particular type. Lastly, shoulder length is an important characteristic when performing PTA to avoid injury to the adjacent arterial segments. After PTA, a completion angiogram is performed while the wire is still in place. Leaving

the wire in place provides access for repeating the procedure if the result is unsatisfactory (Hunink, 1993).

Choice between PTA alone or with stent insertion

Despite excellent initial technical and clinical success rates of PTA of femoropopliteal artery stenoses in series studying the full range of peripheral arterial disease, most including less than 15% CLI patients, the data for CLI are far worse. This was illustrated by a meta-analysis of Muradin et al., which showed clearly inferior 3-year primary patency rates after recanalisation of SFA occlusions in CLI patients compared to claudicants. Technical failure of angioplasty due to dissection or recoil has been largely reduced with the introduction of the bare metal stents, but restenosis has remained a major problem precluding long-term benefit of stenting. Yet, a meta-analysis reported a 3-year patency rate of 58–68% in CLI patients. The self-expanding nitinol stents have further improved endovascular treatment of the SFA and provide more durable results than stainless steel (balloon-expandable) stents. Despite the fact that these studies mainly included claudicants (proportion of CLI patients 14–89%), results of self-expanding nitinol stenting seem beneficial in CLI patients as well. Primary nitinol stenting proved beneficial compared to PTA with provisional stenting especially for longer SFA lesions. Limb salvage rates 36 months after stenting of the SFA in CLI patients have been reported to be 67–75%.(Muradin et al, 2001) (Setaccia et al, 2011)

Similar limb salvage rates were obtained by Taneja and co-workers in 2010 in CLI patients with long-segment occlusions (average 23.8 cm, range 10—39 cm) treated with bare nitinol stents, however primary patency rates

were rather low with 61.5% and 27% after 6 and 12 months, respectively. These studies suggest that endovascular treatment of long femoropopliteal lesions can be; at least clinically; successful. (Taneja et al, 2010)

Fering et al. were the first to demonstrate the safety and utility of primary stenting of infrapopliteal lesions using coronary stents, in a large retrospective series. (Feiring et al, 2004)

In another study by Rand et al that investigated carbon-coated stents (a 0.014-inch coronary balloon-expandable stent with a thin coating of 0.5nm of polycrystalline carbon film to prevent thrombus formation) vs. balloon angioplasty in the infrapopliteal arteries. Although the results at 6 months were superior in the stent group, 9-month clinical follow-up showed similar levels of clinical improvement and limb salvage and similar 1-year patency rates of about 60%. (Rand et al,2006)

Balloon-expandable stents are not flexible and can collapse or fracture in the infrapopliteal segment. Moreover, below-knee stent placement is only possible in cases of unlimited supragenicular inflow. This condition is often absent due to the multisegmental nature of the disease and requires simultaneous endovascular treatment that can often be hazardous, especially in TransAtlantic Inter-Society Consensus D lesions. (Donas et al, 2010)

Other important restrictions of currently available bare or drug eluting balloon-expandable stent platforms for BTK vessels are the small lengths available and the vulnerability to external compression (especially in the distal third of the anterior and posterior tibial artery). This is the reason why the majority of available studies are limited to short focal infrapopliteal lesions up to 3 cm, which are not representative of typical long BTK lesions.

Long, thin-strut, low-profile, self-expanding nitinol stents designed and engineered specifically for the infrapopliteal arteries are available. One RCT designed to compare PTA vs. self-expanding stent. Data showed that bailout stenting of BTK vessels, performed with either balloon-expandable or self-expanding stents for suboptimal balloon dilation, was associated with satisfactory results up to a median of 12 months after treatment: primary patency in 78.9% and limb salvage in 96.4%. Subanalyses focusing on device type showed that balloon-expandable and self-expanding stents avoiding joint segments or pedal vessels perform similarly at early and midterm follow-up. (Kickuth et al, 2007) (Peregrin , et al., 2008)

Drug Eluting Stents

A novel idea that has been tested during recent years has been the use of drug-eluting stents (DES). The proven efficacy of drug-coated stents in the treatment of coronary artery disease gave rise to the idea that they might have a better patency compared to bare metal stents (BMS) in small infrapopliteal vessels. Rastan and his group in Hamburg, Germany performed a double-blind, multicenter, randomized clinical trial comparing Sirolimus-eluting stents (SES) versus BMS for treatment of focal infrapopliteal lesions. There was no statistically significant difference in limb-salvage rate or mortality. However, they concluded that SES achieved significantly higher primary and secondary patency as BMS for focal infrapopliteal arterial lesions. (Rastan et al, 2011)

Another randomized prospective study came from Austria, where they randomized 131 infrapopliteal lesions in 88 patients with CLI to either primary stenting with passive carbon-coated stents or PTA (PTA, 69 lesions;

stent, 62 lesions). At 3 months, 62% of the PTA patients and 82% of patients with stents showed clinical improvement, and the trend reversed at 9 months, when 58% of PTA patients and 47% of stent patients were clinically better than preprocedure. The clinical improvements, primary and secondary patency at 3 and 9 months, were not statistically different between the groups. However, the authors concluded that passive-coated stents have a role in infrapopliteal arterial disease management based on early clinical improvement. (Rand et al, 2011)

Other authors reported positive results of primary stenting using coronary balloon-expandable drug-eluting stents for infrapopliteal disease in small, non-randomized, single center studies. These studies show favorable clinical results for drug-eluting stents in the early follow-up period, with significantly higher angiographic patency and less clinically driven re-interventions compared to simple angioplasty or bare-metal stent. However, these results have to be interpreted with caution because these studies were small in size and had limited follow-up. Notably most of these studies were industry-sponsored. (Scheinert et al, 2006) (Commeau et al, 2006) (Siablis et al, 2007)

Despite the encouraging results with the use of drug-eluting stents below the knee, a major concern remains the length of the stents and their cost. Most of the infrapopliteal lesions are long, and therefore, the application of several short to 20-mm drug-eluting stents is cost-ineffective. Moreover, (Assie et al,2007) (Karnabatidis et al,2009)

Bioabsorbable stent:

The possibility of not having a permanent metallic implant (bioabsorbable stent scaffold technology) has emerged as an exciting technology to combine mechanical prevention of vessel recoil with the advantages of long-term perspective. The bioabsorbable stent could permit the occurrence of positive remodeling with lumen enlargement to compensate for the development of intimal hyperplasia or new lesions. The first published data with coronary application of an absorbable polymeric everolimus-eluting stent were very promising, revealing a nearly complete elimination of both intimal hyperplasia and the need for re-interventions at 1 year. Unfortunately, the same promising results have not been validated for BTK vessels. The prospective multi-centrerandomised trial investigating infrapopliteal absorbable magnesium stents (AMS) vs. angioplasty (AMS-INSIGHT 1 trial)145 indicated that the AMS technology can be safely applied, but it did not demonstrate efficacy regarding longterm patency over standard PTA in the infrapopliteal vessels. Data from 117 patients (147 CLI limbs) showed significantly higher binary restenosis rate at 6 months (68% vs. 42%, $p = 0.01$) with a rate of lumen loss that was nearly doubled (1.4 vs. 0.7mm, $p = 0.001$). It should be noted that the AMS stent was not drug-eluting. (Bosiers , et al., 2009)

Drug-eluting balloon

The concept of using a balloon catheter to directly deliver an antirestenotic drug at the site of arterial disease is of paramount interest. The plan to reduce the risk of restenosis without irreversibly modifying the

structure of the vessel is a new interesting perspective, but limited clinical data are available. (Setaccia, et al., 2011)

Schmidt et al, in 2011, reported their experience with drug-eluting balloons in infrapopliteal arteries. They treated 109 limbs in 104 patients (all for CLI) with a mean lesion length 88 mm. Restenosis rate was 27.4% at 3 months. During a mean follow-up of 65 days, clinical improvement was noted in 91.2% patients, with limb salvage in 95.6% in patients with CLI. This, when compared to results in their own series of long segment stenosis treated with uncoated low-profile balloons with a restenosis rate of 69%, showed a significant improvement of reported short and medium-term patency.(Schmidt et al, 2011) (Rana & Gloviczki. , 2012)

Cutting Balloon

The cutting balloon (Boston Scientific, Boston, MA) was originally developed and used to treat coronary stent restenosis. Three or four microblades or atherotomes, attached in longitudinal fashion on the balloon, cut directly into the stenotic lesion during inflation. It is believed that the microblades penetrate directly into the fibroelastic layer of neointimal hyperplasia and enable effective dilatation and intimal disruption requiring less relative wall tension. As a result, this technique effectively treats a particular stenosis with less neural barotrauma than conventional angioplasty. In one study cutting balloon angioplasty was used to successfully treat popliteal and infrapopliteal vessels for symptomatic limb ischemia. In this report a technical success rate of 100% and a 1-year limb salvage rate of 89.5% were reported. A second study that examined the use of the cutting balloon to treat anastomotic stenotic lesions in lower extremity

bypass grafts revealed a superior long-term patency rate in comparison to conventional angioplasty. (Tsetis & Belli , 2004) (Rastogi & Stavroploulos, 2004) (Swischuk et al, 2008)

Disadvantages of the cutting balloon include the limited offering of balloon lengths, with the longest cutting balloon being 2 cm. This limits the utility of the balloon in the peripheral system, where lesions can be several centimeters in length. Additionally, the atherotomes add to the rigidity of the balloon, making this devise difficult to pass through tortuous vessels, hence the relatively shorter balloon lengths. (Swischuk et al, 2008)

Atherectomy:

Atherectomy is performed by a device that removes a portion of the atheroma from the lumenal surface using a cutting technique. There are different types of atherectomy devices, such as directional shaving devices and rotational devices. The advantage of these devices is the potential to remove some of the plaque and create more space in the lumen, rather than just pushing the plaque aside as all the other methods do. The problem with these devices is the risk of distal embolization during the procedure and the incidence of recurrent stenosis on later follow-up. The most common commercially available device at this time is the Silverhawk $_{TM}$. (Schnieder, 2005)

Blunt microdissection:

The Frontrunner catheter (Cordis Corporation) is a blunt microdissection device that can penetrate the hard caps of fibrocalcific plaques and is approved for both coronary and peripheral CTOs. The device is advanced into the occlusion and the actuating jaws are opened to create plaque fracture

planes. The ability of this device to increase overall success rates for CTO cases is unclear, but some cases of success following guidewire failure have been reported. (Abbott & Williams, 2007).

Laser atherectomy and angioplasty

An Excimer laser atherectomy catheter, with diameters varying from 0.9 to 2.5mm, is tracked over the guidewire to the desired target. Once activated, the Excimer laser utilizes ultraviolet energy to ablate the lesion and create a non-thrombogenic arterial lumen. This lumen is further dilated by an angioplasty balloon. Because the Excimer laser can potentially reduce the rate of distal embolization by evaporating the lesion, it may be used as an adjunct tool for ostial lesions and lesions that can be traversed by a wire but not an angioplasty balloon catheter. (Zhou et al, 2006)

Distal Embolic Protection for Infrainguinal Interventions:

Owing to great success in cardiac, carotid, and renal applications, embolic protection devices (EPD) have been applied to the lower extremity arteries for use during peripheral intervention to prevent distal thromboembolism. The greatest amount of distal embolization has been documented using directional atherectomy devices and mechanical and pharmacologic thrombectomy. (Lookstein & Lewis, 2010)

A recent report by Lam et al detected distal embolization at each step of superficial femoral artery (SFA) intervention, including guidewire crossing, balloon angioplasty, stent deployment, and directional atherectomy by measuring embolic signals using continuous Doppler ultrasound. (Lam et al, 2007)

Factors associated with increased embolization include acute thrombosis, and total vessel occlusion, concentric stenosis, and restenotic lesions. (Lookstein & Lewis, 2010)

It is common sense that patients with clinical presentations ranging from the acutely ischemic limb to chronic claudication, in whom there is poor distal runoff or poor collateral flow, would potentially benefit from EPD use as distal thromboembolism may prove disastrous. (Lookstein & Lewis, 2010)

Several inherent limitations of EPD use in the lower extremities have been identified. Gaining access to selected vessels and through selected lesions may require additional use of smaller guidewires and catheters or predilation. A0.014-inwire has been used to assist the EPD passage through the target lesion. (Lookstein & Lewis, 2010)

The size of the filter basket may be inadequate for collection of thromboembolic debris and cleaning of the basket and device reinsertion may be required. Larger clots remain outside the struts of the filter and cannot be removed by closing the filter. Retrieval of the devices may prove challenging. Several failures of EPDs have been described. Embolization associated with filter deployment or retrieval may occur. Embolism during predilation before EPD placement and embolization due to the filter crossing the lesion have been described in addition to liberation of emboli during filter deployment. In addition, the engendered debris may become dislodged during filter retrieval, resulting in distal embolization. This may occur due to squeezing of filter mesh during basket collapse and retrieval or over the side escape in the event of incomplete apposition of the basket to filter wall. Furthermore, EPD does not provide protection to collateral vessels, which may become occluded during an intervention. Arterial spasm, arterial injury,

and de novo thrombus may occur because of the EPD device itself. (Lookstein & Lewis, 2010)