Determinants of Procedural Success and Patency Following Subintimal Angioplasty in Patients With TASC C and D Femoropopliteal Arterial Disease

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Background: Subintimal percutaneous transluminal angioplasty (SIA) is a treatment option for long segment occlusions in the lower limb arteries. In the present study the factors influencing success and patency following SIA in patients with TransAtlantic Inter-Society Consensus (TASC) C and D peripheral arterial disease (PAD) were investigated.

Methods and Results: The 63 consecutive SIAs were performed in 54 consecutive patients suffering from limb ischemia with TASC C and D lesions. Follow-up consisted of routine office visits with pulse examination, ankle–brachial index (ABI), and serial surveillance by color duplex ultrasound and scanning at 3- to 6-month intervals for 1 year. The morphology of lesions in all patients were type C (n=13, 20.6%) or type D (n=50, 79.4%). SIA was technically successful in 59 of 63 arterial occlusive lesions (93.6%). Post-procedural ABI was 0.89±0.16. The mean increase in ABI after SIA was 0.45 (range, 0.15–0.87). The primary patency rate at 12 months was 51.7%. Occlusion length, lesions involving the distal superficial femoral artery (SFA), and post-procedural distal run-off vessels (P=0.04, 0.006, 0.018, respectively) were independent patency determinants by multivariate analysis.

Conclusions: The length of the occlusion, lesions involving the distal SFA, and post-procedural distal run-off vessels were strong independent predictors for 1-year patency in TASC C/D severe occlusive femoropopliteal artery disease treated by SIA. (Circ J 2010; 74: 1959–1964)

Key Words: Critical limb ischemia; Patency; Peripheral vascular disease; Subintimal angioplasty

Subintimal angioplasty (SIA) is a minimally invasive percutaneous technique for the re-canalization of occluded iliac and infra-inguinal arteries,1,2 which was first described in 1990 to overcome long and chronic arterial occlusions.3 Usually performed under local anesthesia, SIA involves the creation of a subintimal channel by endoluminal dissection and angioplasty.4 Technical failure of percutaneous transluminal angioplasty (PTA) is often attributed to long-segment occlusions, and SIA may be the most suitable treatment for such patients, as envisied by the ever increasing popularity of SIA as an alternative to surgery for the treatment of long occlusions or diffuse atherosclerotic changes (TransAtlantic Inter-Society Consensus (TASC) B and especially TASC C and D).4 Although it is often stated that the primary patency rate at 1 year post-intervention is quite low compared with the almost 80–90% associated with bypass procedures,5,6 SIA, despite its associated relatively high re-occlusion rate, allows an exceptionally good limb salvage rate in patients with limb-threatening ischemia and relatively good results for long occlusive peripheral artery disease (PAD).2,9 Because patency determinants after SIA for severe occlusive PAD have not been well defined, we evaluated the role of SIA and defined post-SIA patency determinants in a group of patients with severe occlusive femoropopliteal artery disease (TASC C and D).

Methods
From April 2006 to July 2008, 63 SIAs were performed in 54 consecutive patients suffering from chronic limb ischemia (Fontaine classification IIa–IV) with severe occlusive lesions. The morphology of occlusive lesions corresponded to TASC C (13 cases, 20.6%) and D (50 cases, 79.4%). The patients were not candidates for surgery, because of their poor state of health or for anatomical reasons. Exclusion criteria in our study were as follows: fresh occlusion <3 months duration; short occlusion (<5 cm length); previous recanalized or restenotic, reocclusive lesions; and having only 1 stenotic lesion. All patients underwent clinical exami-
nation, ankle–brachial index (ABI) measurement and peripheral computerized tomography (CT) angiography examination before the index procedure.

SIA was always performed under local anesthesia from the ipsilateral or contralateral side using the technique described by Reekers and Bolia. An angled 0.035-inch hydrophilic guide wire (Terumo, Tokyo, Japan) and supporting 4- or 5-Fr catheters (Angled Tapered catheter, Terumo, Tokyo, Japan) were used to create a subintimal dissection plane above the level of the occlusion. As the wire advanced, a loop was naturally formed at the tip of the guidewire. A loss of resistance was often encountered as the wire reentered the true lumen distal to the occlusion. Recanalization was confirmed by advancing the catheter over the guidewire beyond the point of re-entry and performing angiography. The recanalized segment was then dilated at 8–10 atmospheres for 5–10 s using an appropriately sized peripheral angioplasty balloon, followed by primary stent placement (SMART control, Cordis, Miami, FL, USA) with subsequent post-dilatation using a balloon catheter that was 1 mm less in diameter. Procedures in which it was impossible to gain entry, re-entry or obtain an acceptable flow through the canal were regarded as a technical failure.

During the procedure, 5,000 IU of intra-arterial heparin and of intra-arterial glyceryl trinitrate were routinely administered. Patients were prescribed clopidogrel bisulfate for 6 months after the procedure, followed by aspirin indefinitely.

Follow-up consisted of routine office visits that included pulse examination, ABI measurement, and serial surveillance by color duplex ultrasound and scanning at 3- to 6-month intervals for 1 year. Long-term patency was defined as maintenance of both improvement in clinical category and increased ABI (<0.15 below the maximum post-angioplasty value). If the patient showed some recurrent symptoms or revealed a reduction in ABI, then duplex ultrasound and lower extremity CT angiography were used to confirm patency. However, any deterioration in clinical status was considered as a treatment failure. Rates of technical success, outcome, complications, and long-term patency were evaluated using the reporting standards developed by a standard guideline committee.7 Calcification was defined when it was greater than 50% of the total length of the occlusion on intra-operative angiography. Stent fracture was evaluated in at least 2 angiographic views, and was angiographically defined as more than 1 discontinued stent strut and mild (single strut fracture), moderate (more than a single strut fracture), and severe (complete separation of stent segment).12 Technical success was defined as successful recanalization of the artery with resolution of the flow-limiting lesion and resulting fast flow through the peripheral artery on the final angiogram. All patency rates were primary patency rates. All results are reported on an intention-to-treat basis.

### Statistical Analysis

Primary patency rates of the procedure were analyzed by the Kaplan-Meier method and Life table analysis. All examined factors that were related to patency rate in the univariate analyses were included in a multivariable logistic regression model analysis to identify those that were significantly independent factors of patency. Differences were considered significant at P<0.05.

### Table 1. Baseline Clinical and Demographic Characteristics of the Patients With Peripheral Artery Disease

<table>
<thead>
<tr>
<th>Limbs</th>
<th>n=63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71.7</td>
</tr>
<tr>
<td>Male (%)</td>
<td>63 (100)</td>
</tr>
<tr>
<td>Indication (%)</td>
<td></td>
</tr>
<tr>
<td>Fontaine class IIa</td>
<td>3 (4.8)</td>
</tr>
<tr>
<td>Fontaine class IIb</td>
<td>36 (57.1)</td>
</tr>
<tr>
<td>Fontaine class III</td>
<td>9 (14.3)</td>
</tr>
<tr>
<td>Fontaine class IV</td>
<td>15 (23.8)</td>
</tr>
</tbody>
</table>

### Table 2. Baseline Angiographic Characteristics of the Limbs Affected With Peripheral Artery Disease

<table>
<thead>
<tr>
<th>Location of occlusion (%)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CIA and EIA</td>
<td>3 (4.8)</td>
<td></td>
</tr>
<tr>
<td>EIA and SFA</td>
<td>15 (23.8)</td>
<td></td>
</tr>
<tr>
<td>SFA only</td>
<td>36 (57.1)</td>
<td></td>
</tr>
<tr>
<td>SFA and popliteal arteries</td>
<td>4 (6.3)</td>
<td></td>
</tr>
<tr>
<td>SFA and crural arteries</td>
<td>3 (4.8)</td>
<td></td>
</tr>
<tr>
<td>SFA, popliteal and crural arteries</td>
<td>2 (3.2)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as mean or as number (percentage). CIA, common iliac artery; EIA, external iliac artery; SFA, superficial femoral artery; TASC, TransAtlantic Inter-Society Consensus; ABI, ankle-brachial index; SD, standard deviation.
A total of 63 consecutive SIA (54 patients) cases for treatment of TASC C and D femoropopliteal artery disease were identified in this study. Mean age was 72 years (range, 54–85 years) and all patients were men because of specific considerations at the hospital. The baseline demographic, clinical, angiographic characteristics are summarized in Table 1 and 2. Prevalence of factors predisposing to atherosclerosis in this trial is also shown in Table 1. All peripheral vessels were totally occluded; mean lesion length was 226.7 ± 105.4 mm. The quality of the distal run-off was defined by the number of patients with passable calf arteries. Good distal run-off (2–3 arteries) was present in 39 limbs (61.9%) and bad distal run-off (0–1 arteries) was present in 24 limbs (38.1%). Additionally, lesions involving the distal superficial femoral artery (SFA) were present in 35 limbs (55.6%). Mean pre-procedural ABI was 0.43 ± 0.25.

SIA was successful in 59 of the 63 arterial occlusions (93.6%). The SFA was nearly always recanalized, and in 5 cases (8%) the procedure was performed at the popliteal or crural level. Only 3% of successful lesions were solely treated with balloon angioplasty, because those patients showed excellent angiographic results and there was no pressure gradient across the lesion, and stent implantation was performed in most patients (97%). All stent implantations were performed in dissection-creating lesions. In 4 patients, SIA was not successful because of inability to re-enter the distal lumen or to advance the wire, because of a flow-limiting dissection. Complications of this procedure were flow-limiting dissection and hematoma at the puncture site, which occurred in 5% of cases. There were no periprocedural myocardial infarctions, strokes, instances of renal failure, or pulmonary complications, and there were no deaths during the index procedure.

The cumulative primary patency rate was 51.7% at 12 months. Post-procedural ABI was 0.89 ± 0.16. The mean increase in ABI after SIA was 0.45 (range, 0.15–0.87). Recurrence of symptoms or re-occlusion, including stent fracture (4 limbs), was seen in 49.3% of cases. Angiographically
visible stent fractures were detected in 4 cases. All fracture cases were observed as severe and showed occlusion in 3 cases and restenosis in 1 case. Ultimately, some patients (12 limbs) had to be treated by re-intervention and others required bypass surgery (10 limbs) or below-the-knee amputation (9 limbs). There was no mortality during the first 30 days. During the 1-year follow-up, 3 patients died (1 sudden death, 1 respiratory infection, 1 intracranial hemorrhage).

We analyzed the angioplasty patency determinants. The variables examined were history of hypertension, diabetic mellitus, dyslipidemia, renal insufficiency and smoking, the number of patent distal run-off vessels, occlusion length, lesion involving the distal SFA, calcified lesion, TASC classification, and stent length, among others. After univariate analysis, the major factors affecting 1-year patency following SIA were the number of patent run-off vessels, occlusion length, lesion involving the distal SFA, calcified lesion and TASC classification (Table 3). Cumulative probability of patency following SIA in relation to occlusion length, lesion involving the distal SFA, TASC classification and number of patent run-off vessels (P<0.001, P<0.001, P=0.026, P<0.001, respectively) (Figures 1,2). The multivariate regression analysis revealed the factors that independently influence patency rate include occlusion length, the number of patent distal run-off vessels, and lesions involving the distal SFA (P=0.040, 0.018, 0.006, respectively) (Table 4).

**Discussion**

SIA is currently used in many centers for the treatment of PAD, not only TASC B lesions, but also TASC C and D lesions. Although the TASC reports recommend that TASC D lesions be treated with open surgical reconstruction, many patients with TASC C and D lesions have contraindications for surgical treatment because of their poor general status or other reasons. In contrast, SIA is very well tolerated by the majority of patients, even those with relatively bad clinical status.

A technique similar to that described by Reekers and Bolia was used in this study. In our experience the technical success of the device has been satisfactory. Technical failure only occurred in 4 patients, 2 from flow-limiting dissection, 1 from inability to re-enter the distal lumen, and 1 from inability to advance the wire. Therefore, the primary causes of SIA technical failure was inability to re-enter the true lumen in a patent distal vessel, and for this new device systems (Outback catheter, etc) are reported to facilitate re-entry into the true lumen. It is hoped that variations of these methods may help overcome the technical failure of SIA.

According to several reports, SIA is associated with lower patency rates than bypass surgery. In fact, our 1-year primary patency rate result (51.7%) was lower than those reported in other studies, which report overall patency rates for SIA at
12 months ranging from 22% to 74%. We consider that the reason for this is because most of the lesions in the present study corresponded to TASC D (79.4%), which are more complex, long lesions. In a recent meta-analysis, primary patency and limb salvage rates at 12 months were 55.8% (95% confidence interval (CI): 47.9–63.4%, 1,342 limbs), and 89.3% (95% CI: 85.5–92.2%, 2,810 limbs), respectively. In terms of the possible factors that might affect the patency rate of SIA, we found that occlusion length, lesions involving the distal SFA, and the number of post-procedural distal run-off vessels were significantly associated with primary patency (P=0.040, 0.006, 0.018, respectively), using multivariate regression analysis. Although arterial calcification and TASC classification (C or D) were also related to patency (P=0.001, 0.014, respectively) on univariate regression analysis, they were not independent risk factors for re-occlusion (Table 4).

Previous studies have emphasized the importance of the quality of the distal run-off tract from the point of view of both technical success and long-term patency. According to some studies, occlusion length, distal run-off vessels and smoking are independent risk factors for re-occlusion. In a recent study, Setacci et al found that the factors capable of independently affecting patency following SIA for TASC C and D lesions of SFA were renal insufficiency, hypertension, diabetes mellitus, and smoking in patients undergoing SIA for TASC C and D lesions of the SFA. Further research is warranted, including a larger-scale study. Although we did not discuss all data collected in this study, laboratory findings such as serum creatinine, high-sensitivity C-reactive protein and fibrinogen levels also were not related to re-occlusion.

**Study Limitations**

The single-center non-randomized design warrants careful interpretation of the results, and the small sample size might have introduced bias. Also, cilostazol, a unique antiplatelet drug that has vasodilatory effects and inhibits smooth muscle cell proliferation, reduces the rate of target lesion revascularization after PTA in the femoropopliteal artery. We did not evaluate the effect of cilostazol. SIA is becoming a more frequent treatment option for patients with long peripheral arterial occlusions and our study suggests that the occlusion length, the number of run-off vessels and lesions involving the distal SFA are the major predictors of post-procedural patency. Accordingly, when feasible in patients with these risk factors, it would seem prudent during SIA to attempt to recanalize more than 1 of the run-off vessel and to follow-up the patients more frequently after the index procedure.

**Disclosures**

None.

**References**


