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Original article

Clinical outcomes of endovascular treatments for critical limb ischemia with chronic total occlusive lesions limited to below-the-knee arteries

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Abstract

Background: Diabetes mellitus tends to have the greatest impact on the smaller vessels and contributes significantly to occlusive disease from the popliteal artery distally.

Purpose: To evaluate the clinical outcomes after a balloon angioplasty with or without stent placement in diabetic patients with critical limb ischemia (CLI) by chronic total occlusion (CTO) limited to below-the-knee (BTK) arteries.

Material and Methods: From August 2005, patients who presented CLI and CTO limited to the BTK arteries, and who underwent endovascular treatment, were included in this study. The primary endpoints evaluated were technical success, limb salvage, and primary patency. The secondary endpoints evaluated were 30-day access site, intervention site, and systemic complications. Patency and limb salvage were evaluated using the Kaplan-Meier method and compared using Fisher's exact test.

Results: The BTK endovascular treatment (EVT) was performed on 64 limbs. Technical success rate was 93.8% and limb salvage rate was 90.6%. Three of four limbs with technical failure and three of 60 limbs with technical success underwent BTK amputation and the comparison of these rates were significantly different (75% *vs.* 5%, $P = 0.002$). Primary patency rates for the limbs were 75% and 59.1% at 6-month and 12-month follow-up, respectively. Minor complications disappeared through the follow-up periods and there was no 30-day complication or systemic adverse events for the treated vessel.

Conclusion: Even though EVT for CLI in patients with diabetes and CTO in isolated BTK arteries does not have comparable primary patency, it can lead to a very high rate of limb salvage. This result can accentuate the importance of more blood flow to the foot by means of successful revascularization using EVT rather than long-term patency in CTO of isolated BTK arteries.

Keywords: Intervention, fluoroscopy, CT, percutaneous transluminal angioplasty, arteries

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Critical limb ischemia (CLI) represents the most severe clinical manifestation of peripheral arterial disease, and is defined as the presence of ischemic rest pain, ischemia lesions, or gangrene, and it often occurs in conjunction with diabetes, chronic renal insufficiency, and other co-morbidities. In particular, diabetes mellitus tends to have the greatest impact on the smaller vessels (<5 mm) of the body, and therefore in the lower extremities, this contributes significantly to occlusive disease distally to the popliteal artery (1–3).

Two strategies of revascularization are currently used for these amputation-threatening critical limbs to obtain limb salvage: bypass surgery and endovascular treatment (EVT). Although for many years bypass surgery was considered to be the gold standard for patients with steno-occlusive lesions in below-the-knee (BTK) arteries because it achieves good long-term patency, it is not feasible in every patient because of associated co-morbidities. This concept has been challenged by a variety of endovascular techniques such as balloon angioplasty with or without

stent placement (4). However, many studies for BTK EVT included percutaneous transluminal angioplasty (PTA) above-the-knee (ATK) as well as BTK. Further, therapeutic efficacy for PTA limited to BTK in diabetic patients with CLI, and who commonly used to have isolated BTK steno-occlusive lesions, has been reported in few studies (5, 6). In addition, it was difficult to find results pertaining to the evaluation of PTA efficacy when chronic total occlusion (CTO) in isolated BTK.

Therefore, the purpose of this study was to evaluate the clinical outcomes of balloon angioplasty, with or without stent placement, in diabetic patients with CLI by CTO limited to BTK arteries.

Material and Methods

Patients

From August 2005, of 616 patients who underwent infrainguinal arterial intervention, 167 patients (27.1%) who presented with ischemic rest pain, ulcer, or gangrene of the foot underwent PTA in BTK arteries for CLI. Among them, patients with a history of diabetes and CTO lesions limited to the BTK arteries were included. The criteria used for CLI definition were based on the Transatlantic Intero-Society Consensus (TASC II) (7), and diabetes mellitus was diagnosed based on the American Diabetes Association criteria (8). All individuals underwent a CT angiography to detect the CTO lesions defined as occlusions with no antegrade filling of the distal vessel other than via collaterals involving three infrapopliteal arteries with or without foot-vessel involvement. We excluded patients with concomitant above-knee arterial steno-occlusive lesions including the aortoiliac and femoropopliteal arterial lesions, clinical or imaging signs of embolic disease, or who had undergone thrombolysis prior to endovascular or surgical procedures.

This study was a retrospective review of a prospectively maintained database of consecutive patients who underwent BTK endovascular treatment. Written consent was obtained from patients who were informed of the likely outcome and potential complications and Institutional Review Board approved the protocol for this study.

Procedures

Endovascular procedures were performed in an interventional radiology suite by an interventional radiologist under local anesthesia. Before the intervention, Aspirin (100 mg) and clopidogrel (300 ~ 600 mg) were administered orally to all patients. The initial vascular access technique was the ipsilateral antegrade puncture of the common femoral artery using a 4 or 5-Fr introducer sheath in all patients, under ultrasound guidance. After the sheath was introduced, the patients were systemically anti-coagulated intraprocedurally using intravenous heparin with a goal of an activated clotting time of >250 s.

Angiography using non-ionic contrast medium and digital subtraction angiography was performed through the sheath to evaluate the entire BTK arterial trees. The occlusions were crossed using a 0.018″, 0.016″, or 0.014″ guide wire and a balloon catheter was used to support the guide wire. The balloons measured 40–220 mm with a diameter of 2.0–3.0 mm. Diameters of 2.0–2.5 mm were used in the lower part of lower leg and below the ankle, while diameters of 2.5–3.0 mm were used in the middle and proximal part of the lower leg. The balloon catheters were initially inflated to 10–15 atm for 2 min. A second prolonged dilation of up to 5–10 min was performed for an unsatisfactory result, either due to residual stenosis >30% or a flow limiting dissection. If the occlusion did not resolve, drug-eluting stent (Cypher Select; Cordis, Miami Lakes, FL, USA) was placed at the unsatisfactory or dissected segments. If a vessel spasm occurred in relation to the procedures, 0.1–0.2 mg of nitroglycerine was infused as an intra-arterial bolus.

After the procedure, hemostasis was performed by manual compression. Aspirin was administered to all patients post-procedurally. For patients undergoing stent placement, clopidogrel was administered post-procedurally for at least 12 weeks.

Assessment

In general, the patients were monitored by performing a regular physical examination and visual inspection during a monthly follow-up for 3 months and then after every 3 months. CT angiography was performed at every 6-month follow-up.

Primary endpoints included technical success, limb salvage, and primary patency. Technical success was defined as the successful passage of a guide wire either intraluminally or subintimally, performing a balloon angioplasty or stent placement successfully, or obtaining at least one BTK artery restoration in continuity without residual stenosis of <30% at the end of the procedure. Limb salvage was defined as the resolution of rest pain or freedom from amputation, including resolution proximal to the transmetatarsal level. Primary patency was the duration of follow-up during which there was an absence of occlusion or stenosis with the treated segment on CT angiography.

Secondary endpoints included the 30-day complication of the access site, treated vessel (i.e. thromboembolism), and systemic adverse events (myocardial infarction, acute renal failure, and death).

The primary patency for successful balloon angioplasty or stent placement was estimated by the Kaplan-Meier method with 95% confidence intervals and the limb salvage according to whether technical success was achieved or not, was compared using Fisher's exact test. A P value of <0.05 was considered to be statistically significant.

Results

The BTK EVT were performed on 64 limbs (Rutherford category 4; $n = 17$, Rutherford category 5; $n = 29$, Rutherford category 6; $n = 18$) from 49 patients (mean age, 67.4 years; M:F, 38:11) (Fig. 1), with hypertension ($n = 37$), coronary arterial disease ($n = 13$), chronic renal failure ($n = 11$),

Fig. 1 A 65-year-old male patient with diabetes and critical limb ischemia on his right foot. (a, b) Angiography shows CTO in right anterior and posterior tibial arteries. (c) Balloon angioplasty using a 3-mm balloon catheter and 0.018-inch guide wire was performed successfully in both arteries. (d, e) Final angiography shows restoration of blood flow without any residual stenosis in both arteries

or smokers ($n = 21$). The mean follow-up time was 19.3 $\pm$ 13.4 months. CTO lesions in these patients were found in 236 vessels: anterior tibial arteries ($n = 86$), posterior tibial arteries ($n = 77$), peroneal arteries ($n = 42$), as well as pedal and plantar arteries ($n = 31$).

The technical success rate for the procedures was 93.8% (60/64 limbs). Subintimal arterial flossing with antegrade-retrograde intervention (SAFARI) techniques was used in patients who did not enter into the true lumen despite going down to the toes after successful subintimal passage of the guide wire (9.4%, 6/64 limbs). This SAFARI technique selects the distal reentry point by starting a retrograde dissection at the point of distal arterial lumen obstruction by a retrograde subintimal chanel creation after direct puncture with micropuncture set (Cook, Bloomington, IN, USA) of the anterior tibial, posterior tibial, or dorsalis pedis artery. Therefore, in these six patients the BTK EVT were successfully performed via SAFARI techniques. In total five patients underwent drug-eluting stent placement. Technical failures were due to the failure of full expansion of the drug-eluting stent and failure of passage of the guide wire and balloon catheter. The limb salvage rate was 90.6% (58/64 limbs). Three of four limbs with technical failure and three of 60 limbs with technical success underwent BTK amputation. The difference between the rates was statistically significant (75% *vs.* 5%; $P = 0.002$). Primary patency rates for the limbs were 75% at 6-month follow-up and 59.1% at 12-month follow-up.

Thirty-day access site complications occurred in three limbs (4.7%), which included hematoma ($n = 2$) and minimal pseudoaneurysm on ultrasound ($n = 1$). These complications completely disappeared through follow-up periods. There were no 30-day complications for the treated vessel and systemic adverse events including myocardial infarction, acute renal failure, and death.

Discussion

CLI is a chronic condition due to peripheral arterial disease, most commonly atherosclerosis, developed when blood flow does not meet the metabolic demands of tissue at rest. This condition represents the main cause of non-traumatic lower limb amputation. In particular, diabetes is the most important risk factor for CLI because in diabetic patients, atherosclerosis not only develops at a younger age, but also affects more distal vessels, mostly BTK (9–12). This study also evaluated the results of EVT; only for patients with diabetes.

Despite the benefits of pharmacologic therapy, arterial revascularization remains a mainstay in the management of CLI because restoring adequate blood flow to the foot is crucial to providing pain relief, promote wound healing, and avoiding major amputation, in order to ensure limb salvage (7, 8). Even though surgical revascularization remains an important therapeutic option for CLI (7, 8), recent data also support the role of balloon angioplasty as a feasible and safe procedure in this setting, especially when performed with dedicated wires and balloon catheters (4, 13, 14). Furthermore, vascular surgery is not always feasible or recommended in these patients because of high surgical risk, lack of venous conduits, or poor vessel run-off. Furthermore, PTA is often the first choice for lower limb revascularization.

BTK arterial revascularization by means of balloon angioplasty is also being increasingly used and recommended for the treatment of patients with CLI (7, 14). This phenomenon largely depends on technical and technological advancements, such as the introduction of low-profile and dedicated devices, as well as the development of subintimal angioplasty (15, 16) and SAFARI techniques. These improvements have made balloon angioplasty for CLI a reasonable

alternative to surgical treatment (4). In this study, recanalization of the CTO in BTK using the SAFARI techniques was performed in 9.3% of cases because the guide wire did not go to the true lumen and remained in the subintimal tract. Therefore, technical development like the SAFARI technique, in addition to the development of low-profile and dedicated devices, can increase the success rate of balloon angioplasty for the CTO in BTK.

However, few published studies have specifically investigated outcomes in diabetic patients with CLI associated with isolated BTK vessel disease. Moreover, many reports used to deal with the BTK lesions as well as ATK lesions concomitantly. As the small diameter and long length of the BTK vessel – both of which tend to lead to a high restenosis rate, it is possible that the result of PTA for BTK lesions could be different with the result of PTA for ATK lesions.

Ferraresi *et al*. (5) evaluated the long-term results of successful PTA for limb salvage in patient with critical limb ischemia associated with isolated BTK steno-occlusive lesions. They reported that the limb salvage rate was 93% and the major amputation rate significantly lower in patients who underwent a successful procedure than in those in whom the procedure was unsuccessful ($P < 0.05$). Their patients were followed for 2.9 ± 1.4 years and the 1-year target vessel restenosis rate was 42% (35% in stenotic lesions and 53% in occlusive lesions). Sadek *et al*. (6) evaluated patency and limb salvage of endovascular intervention for tibial vessel disease. The technical success rate for all procedures was 91% and limb salvage rates and primary patency rate for patients with CLI at 6, 12, and 18 months were $85\% \pm 0\%$, $81\% \pm 0\%$, and $69\% \pm 0\%$, and $68\% \pm 6\%$, $50\% \pm 8\%$, and $37\% \pm 9\%$, respectively.

In this study, technical success rate and limb salvage rate were over 90% and limb salvage rate in patients who undertook EVT successfully was much higher than other reports, however, comparable with prior reports. After all, successful balloon angioplasty with or without stent placement was able to save critical limbs at follow-up, even in CTO limited to BTK arteries.

We expected that the primary patency until the 12-month follow-up time could be relatively lower in this study than previous reports because this study evaluated the results of balloon angioplasty with or without stent placement for the CTO lesion only. Patients with BTK steno occlusive lesions and with diabetes, that in a nutshell, have the two factors (CTO and diabetes) that can make them poor to keep the revascularized vessel patent. However, the primary patency in this study was not so different than previous reports. One possible explanation was that because isolated BTK lesions in patients with CLI used to include CTO more frequently than in ATK lesions. Moreover, diabetes is common in these patients. The proportions of CTO could be high among enrolled patients in previous studies.

In addition, there was some discrepancy between the rate of limb salvage and patency. This reflects the fact that complete patency of a treated vessel is less important in certain patients than in those with other peripheral arterial disease: the re-canalization temporarily increases blood flow to the foot and this is believed to have a positive effect in eradicating infection and healing ulcers and surgical wounds (5). Some reports suggest that as foot tissue healing reduces oxygen demand, less blood flow is generally required to maintain tissue integrity and keep the limb asymptomatic (17, 18). Ferraresi *et al*. (5) strongly suggested that this was clearly demonstrated by the fact that only three of their 94 patients who underwent a total of 100 successful PTA procedures experienced recurrent CLI in the same limb during the follow-up period.

This study has some limitations. First, this was a retrospective case review. Second, we did not evaluate the patients for a period longer than 12-months, and Doppler ultrasound was not performed during the follow-up period. Third, we did not perform a pre- and postoperative transcutaneous oximetry evaluation. Fourth, we did not analyze the follow-up data of the stenotic vessels without CTO lesion, which may be affective to the result of the CTO lesions.

In conclusion, EVT including balloon angioplasty with or without stent placement for CLI in patients with diabetes and CTO limited to BTK arteries does not have comparable primary patency. When compared with the limb salvage rate, it can lead to a very high rate of limb salvage. This result can accentuate the importance of more blood flow to the foot by means of successful revascularization by EVT rather than long-term patency of EVT in CTO limited to BTK arteries.

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Conflict of interest: None.

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