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Angiographic Restenosis and Its Clinical Impact after Infrapopliteal Angioplasty

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WHAT THIS PAPER ADDS?

- Although restenosis after plain angioplasty for infrapopliteal lesion occurs at a high rate because of the generally long and diffuse nature of arteriosclerotic disease in this region, the impact of restenosis on patient and limb prognosis after angioplasty has not been systematically studied. Therefore, our study assessed the angiographic restenosis rate 3 months after infrapopliteal angioplasty and evaluated the impact of early restenosis on clinical outcomes in patients with critical limb ischemia after infrapopliteal angioplasty. Although the subsequent occurrence of restenosis has been considered not to affect limb salvage, leading to a perceived lack of relevance of durability of infrapopliteal angioplasty in the clinical setting, results from this prospective multicenter registry indicate that occurrence of angiographic restenosis after angioplasty in critical limb ischemia patients is extremely high in the early phase and adversely affects clinical outcomes at 3 and 12 months.

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EVT, endovascular therapy; BSX, bypass therapy; CLI, critical limb ischemia; TASC, Transatlantic Inter-Society Consensus; ABI, ankle-brachial index; ADL, activity of daily life

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ABSTRACT

Objective: To assess 3- and 12-month angiographic restenosis rates and their clinical impact after infrapopliteal angioplasty.
Design: Prospective multicenter study.
Materials and methods: We analyzed 68 critical ischemic limbs (tissue loss: 58 limbs) from 63 consecutive patients due to isolated infrapopliteal lesions who underwent angioplasty alone. Primary endpoint was 3-month angiographic restenosis rate; secondary endpoints were 12-month angiographic restenosis rate, and 3- and 12-month rates of mortality, major amputation and reintervention. Three- and 12-month frequency of ambulatory status and of freedom from ischemic symptoms, and time to wound healing in the ischemic wound group, were compared between restenotic and non-restenotic groups. Angiographic restenosis predictors were assessed by multivariable analysis.
Results: 95% of cases had 3-month angiography; restenosis rate was 73%: 40% restenosis and 33% re-occlusion. Twelve-month follow-up angiography was conducted for the patients without 3-month angiographic restenosis, and restenosis rate at 12 months was 82%. Non-administration of cilostazol and statin, and chronic total occlusion were 3-month angiographic restenosis predictors. Three- and 12-month mortality was 5% and 12%, respectively. Despite no patients having undergone amputation, 15% had persistent ischemic symptoms, and 48% of limbs underwent reintervention within 12 months. During the same study period, ambulatory status and limbs with complete healing were more frequently observed in the non-restenosis group than in the restenosis group. In the tissue loss group, time to wound healing in the restenosis group was longer than in the non-restenosis group (127 days vs. 66 days, $p = 0.02$).
Conclusion: The extremely high angiographic restenosis rate after infrapopliteal angioplasty may adversely impact clinical status improvement.

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Introduction

Long-term durability and a high limb salvage rate have made surgical bypass therapy (BSX) the standard treatment modality for patients with critical limb ischemia (CLI)[1,2] In the BASIL (bypass vs. angioplasty in treatment of severe leg ischemia) trial on CLI patients with infrainguinal arterial occlusive disease, a revascularization technique (BSX or EVT) was recommended based on the presence of useable vein and life expectancy.[3,4] However, in clinical practice, these patients are often not suitable surgical candidates due to concomitant disease and advanced age, which has led many to favor endovascular therapy (EVT) as first-line therapy in this high-risk target population.[5–7] Recently, similar amputation-free survival rates in patients with CLI due to infrapopliteal lesions were observed for the two revascularization strategies after propensity matching analysis.[8] However, restenosis after plain angioplasty for infrapopliteal lesion occurs at a high rate because of the generally long and diffuse nature of arteriosclerotic disease in this region, and a recent trial also documented that restenosis of extensive infrapopliteal disease occurs in the early phase.[9] However, the impact of restenosis on patient and limb prognosis after angioplasty has not been systematically studied. Also, the 12-month angiographic restenosis rate remains unknown. Therefore, our study objective was to assess the 3- and 12-month angiographic restenosis rate after infrapopliteal angioplasty, and to evaluate the clinical impact of restenosis on the prognosis for patients with CLI after infrapopliteal angioplasty.

Methods

Participants

Participants were enrolled from January to March 2011 in this prospective multicenter registry study. During this period, 235 limbs in 216 consecutive CLI patients were treated with EVT in one of six cardiovascular or vascular centers in Japan. The database included 68 limbs from 63 consecutive patients who successfully underwent angioplasty alone for de novo infrapopliteal lesions, and who also consented to undergo follow-up angiography at 3 months. All patients were symptomatic secondary to isolated infrapopliteal lesions (Rutherford 4–6) in critical ischemic limbs. Patients with CLI due to infrapopliteal lesions combined with femoropopliteal lesions (54%, 120 limbs in 115 patients) or with ilio-femoral lesions (14%, 32 limbs in 28 patients) were excluded from this study. Ten patients (15 limbs) who refused 3-month follow-up angiography were excluded. Patients who presented with acute limb ischemia requiring emergent revascularization or functionally unsalvageable limbs were also excluded from this analysis. BSX was selected by consensus among vascular specialists. During the study inclusion period, 26 CLI patients were initially treated with bypass therapy by a vascular surgeon without prior endovascular intervention. The study protocol was developed in accordance with the Declaration of Helsinki, and approved by the ethics committees of all centers. This study was also registered in the University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR), which was approved by the International Committee of Medical Journal Editors (no. **UMIN000006488**, J-BEAT angio registry: **J**apanese **BE**low-the-knee **A**rtery **T**reatment for the **angio**graphical assessment registry). All patients gave written informed consent prior to revascularization.

Protocols

After admission, lower limb arteries were routinely and anatomically evaluated by duplex ultrasound. For assessment of hemodynamic status in lower limb ischemia, ankle-brachial index (ABI) and skin perfusion pressure (SPP) were measured. SPP was generally measured on the dorsal and plantar sides of the foot. In the SPP test, which uses a laser Doppler instrument (PAD 3000; Väsamed, Inc., Eden Prairie, MN, USA) to quantitatively evaluate microcirculatory perfusion in the skin, a laser Doppler sensor is located beneath a pressure cuff for application and release of pressure to the limb. All patients also underwent digital subtraction angiography before the procedure. A consensus of vascular specialists, including vascular surgeons, interventional cardiologists and radiologists, judged whether EVT was indicated for each patient. Because 98% of lesions were Transatlantic Inter-Society Consensus (TASC) 2000 D in an infrapopliteal artery, indication for EVT was decided by consensus depending on lower limb severity and general condition based on our published risk stratification.[10]

All EVT procedures were performed under local anesthesia by a cardiologist or vascular surgeon. Anatomical indication was judged by digital subtraction angiography, and lesions with $\geq$75% diameter stenosis were treated. Selection of EVT approach was left to the operator's discretion. Generally, a 3Fr 55 cm sheath (Medkit, Japan) was used for the antegrade approach from the ipsilateral common femoral artery. After placing the sheath, unfractionated heparin (5000 units) was routinely injected into the artery. A 0.014-inch guide wire was advanced into the culprit lesion and an optimally sized balloon catheter was introduced. For treatment of chronic total occlusion (CTO), the intraluminal approach was generally used, with the subintimal approach with wire loop technique being used in cases of failed wire crossing. Vessel diameter and lesion length were visually assessed using preprocedural duplex and the balloon catheter as reference. A 100 mm or 120 mm balloon was commonly used and balloon inflation was held at nominal pressure for at least 180 s. Stent and atherectomy devices were not approved for use in infrapopliteal intervention in Japan. Angiosome-based intervention was done for the target lesion and, if an angiosome-based straight line was obtained, other lesions with residual stenosis were not treated. However, if treatment of the angiosome-based target lesion was unsuccessful, a non-angiosome-based lesion was treated. Dual antiplatelet therapy (aspirin at 100 mg/day and either ticlopidine at 200 mg/day or cilostazol at 200 mg/day) was started at least 1 week prior to EVT and continued lifelong.

Follow-up and outcomes

All patients were followed up at 1 week, 1, 2, and 3 months after revascularization, and thereafter every 3 months until 12 months. All patients had follow-up angiography scheduled at 3 months after balloon angioplasty. Additionally, to assess the 12-month restenosis rate, 12-month angiography follow-up was scheduled for patients without angiographic restenosis at 3 months. If a patient did not return to the hospital, phone calls were made to check limb status and the patient's general health. All patients with open ulcers were individually followed and complete wound healing was judged by a plastic surgeon. Severity of wounds before revascularization, especially of those involving infection and extension, was carefully assessed by a plastic surgeon who decided indication for antibiotic therapy and amputation timing. Duplex, ABI and SPP were routinely measured before and after the EVT procedure as the standard assessment modality for limb healing or worsening.

Definitions

Ischemic tissue loss was defined in accordance with TASC as tissue loss associated with an ankle pressure $<$70 mmHg or a toe pressure $<$50 mmHg. When these measurements could not be obtained due to intractable rest pain or a non-compressible artery

because of severe calcification, SPP was measured at the dorsal and plantar sides of the foot. An SPP <40 mmHg was defined as indicating ischemic tissue loss.[11] Atherosclerosis risk factors have been reported previously.[12] Coronary artery disease was defined as history of any revascularization of the coronary arteries. Cerebrovascular disease was defined as a history of stroke and/or cerebral hemorrhage. End-stage renal disease (ESRD) was defined as a glomerular filtration rate (GFR) <15 L/min/1.73 m^2 or regular dialysis. EVT procedural success was defined as obtaining one straight-line flow to the ulcer or gangrene region without occurrence of any flow limiting dissection. EVT with angioplasty was considered hemodynamically successful when post-procedural SPP level increased by more than 40 mmHg, which is associated with a high limb salvage rate. Reintervention included repeat angioplasty. Below the knee, above the knee and forefoot amputation was defined as major amputation. Ambulatory status was defined as being capable of walking and this was judged by a physical therapist.

Study endpoints

Primary study endpoint was 3-month angiographic binary restenosis rate per lesion. Follow-up angiography in two different angulations was performed using an antegrade approach via a 3 Fr sheath. Angiograms were analyzed on site by two investigators based on visual estimation. Binary restenosis was calculated using a 50% diameter reduction threshold. Secondary endpoints were 12-month angiographic binary restenosis rate, 3- and 12-month mortality, freedom from ischemic symptoms and reintervention rate. Additionally, we classified the overall patient and limb populations into two groups based on the presence/absence of 3-month angiographic restenosis, and subsequently compared frequency of ambulatory status, frequency of freedom from ischemic symptoms at 3 and 12 months, and time to wound healing in the ischemic wound group during the chronic phase. Also, factors associated with angiographic restenosis were assessed by multivariable analysis. Follow-up angiography was scheduled at 3 months for all participants and at 12 months for patients without 3-month angiographic restenosis after balloon angioplasty.

Statistical analysis

Data are shown as means ± standard deviation. An unpaired *t*-test was used to compare continuous variables with normal distributions. Chi-square test was used to compare proportions between groups. Statistical significance level was set at $p < 0.05$. Independent outcome determinants were determined by multivariable analysis including all univariable parameters with a *p*-value of <0.10. Statistical analysis was performed using SPSS (SPSS Inc., Chicago, IL, USA).

Results

Participant flow through the trial

Fig. 1 shows participant flow through the trial. Sixty-three consecutive patients (109 infrapopliteal arteries in 68 limbs) were enrolled in this study between January and March 2011 with last follow-up completed in March 2012. Timing of the 3-month follow-up ranged from April to July 2011. Complete clinical follow-up at 3 months was available for all study participants except for those who had died. Three patients with 3 limbs and 7 infrapopliteal lesions could not be assessed because they died before the scheduled 3-month follow-up angiography, and follow-up angiography was consequently conducted in 95% (60/63) of study participants.

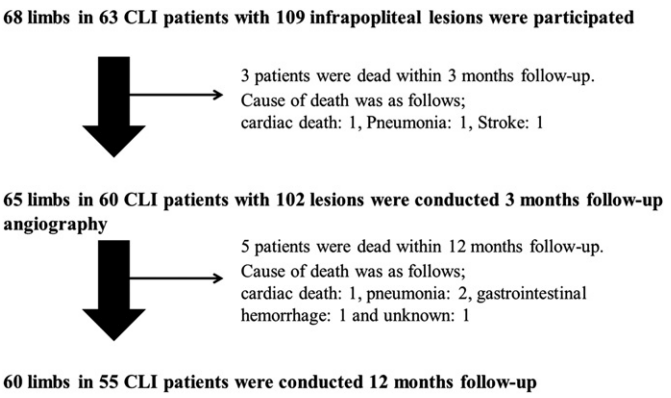

Figure 1. Participant flow through the J-BEAT angio registry.

Five patients died after 3-month angiography and 60 limbs in 55 CLI patients underwent a 12-month clinical follow-up.

Overall characteristics

Overall patient characteristics are shown in Table 1. Sixty-two percent (39/63) of patients suffered from diabetes mellitus and 57% (36) had ESRD on dialysis. Eighty-five percent of limbs (58/68) were complicated with tissue loss defined as Rutherford 5 or 6. ABI was slightly decreased at 0.74 but SPP level was insufficient for ulcer healing. Average treated lesion length was 140 mm, and 98% (64/65) of lesions were defined as TASC 2000 D. Because of inclusion of a high number of patients with diabetes mellitus and ESRD

Table 1
Overall patient characteristics.

Age	75 ± 8
Male gender	57% (36)
BMI (body mass index)	22 ± 3
Patient ADL (ambulatory/wheelchair/bedridden) before angioplasty	30/31/2
Risk factors	
Hypertension	79% (50)
Hyperlipidemia	41% (26)
Diabetes mellitus	62% (39)
Current smoking	25% (16)
ESRD (GFR<15)/regular dialysis	60% (38)/57% (36)
Cardiovascular disease	
Coronary artery disease	43% (27)
Ejection fraction (%)	60 ± 13
Cerebrovascular disease	19% (12)
Medications	
Antibiotics	27% (17)
Cilostazol	51% (32)
Statin	27% (17)
Tissue loss	85% (58)
ABI before angioplasty	0.74 ± 0.17
SPP (dorsal side/plantar side) mmHg	
before angioplasty	28 ± 15/33 ± 18
after angioplasty	47 ± 28/48 ± 21
at 3 months	43 ± 19/43 ± 22
C-reactive protein level (mg/dL)	1.9 ± 2.7
Lesion characteristics	
TASC D lesion	98% (64)
Reference vessel diameter (mm)	2.4 ± 0.4
Lesion length (mm)	140 ± 90
% Diameter stenosis (pre/post/3 months)	97 ± 9/27 ± 17/74 ± 36
Residual stenosis greater than 30% diameter stenosis just after angioplasty	19% (19)
Chronic total occlusion (pre/3 months)	62% (63)/ 30% (31)
Vessel calcification	49% (52)

ADL: activity daily life.

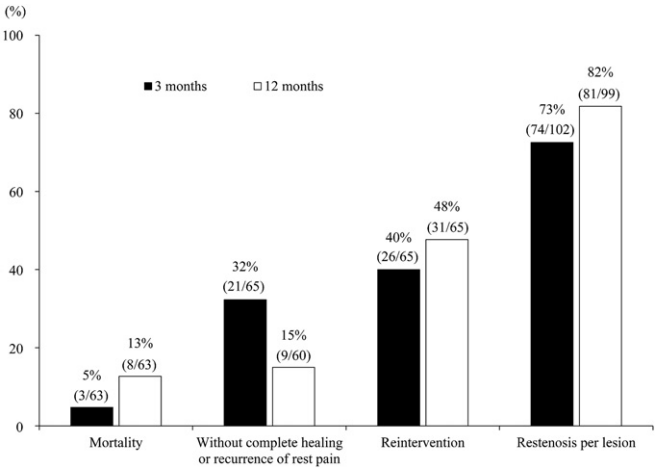

Figure 2. Outcomes at 3 and 12 months.

on dialysis, approximately half of lesions involved calcification as readily visible densities noted within the apparent vascular wall by angiography. Forty-eight percent (30/63) of patients were ambulatory before angioplasty.

Outcomes at 3 months

Outcomes at 3 months are shown in Fig. 2. Three-month angiographic restenosis as primary endpoint was found in 73% (74/102) of lesions. At 3 months after angioplasty, 32% (21/65) of limbs lacked complete ulcer healing or had rest pain recurrence, and 40% (26/65) of limbs had undergone reintervention using angioplasty. Five limbs required reintervention because of subcritical limb ischemia with severe stenosis. Fig. 3 shows the findings in the 102 lesions angiographically assessed at 3 months. At baseline, there were 39 stenotic and 63 occlusive lesions. In the stenosis group, 41% (16/39) of lesions did not develop angiographic restenosis at 3 months while 51% (20/39) of lesions had restenosis and 8% (3/39) of lesions were re-occluded. In the occlusion group, 19% (12/63) of lesions did not develop angiographic restenosis at 3 months while 49% (31/63) of lesions re-occluded and 32% (20/63) of lesions had restenosis. Distributions were significantly different among groups. Table 2 shows predictors for 3-month angiographic restenosis. After

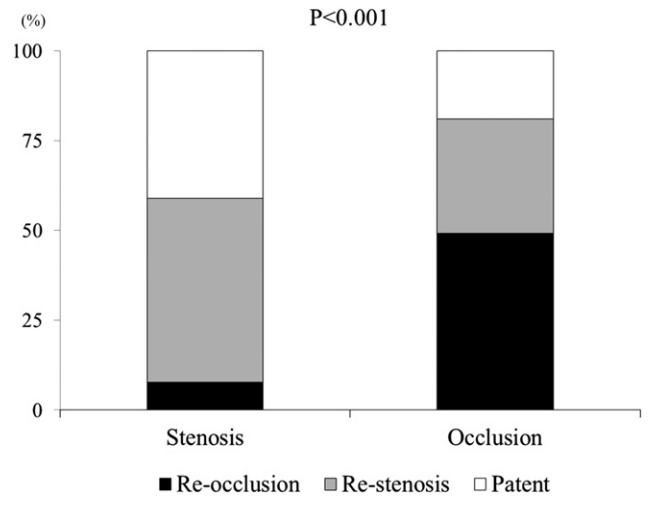

Figure 3. Findings in the 102 lesions angiographically assessed at 3 months.

Table 2
Multivariate analysis for angiographic restenosis at 3 months.

Variables	Adjusted odds ratio [95% CI]	*p* value
Hypertension	0.090 [0.014, 0.587]	0.012
Administration of cilostazol	0.299 [0.107, 0.834]	0.021
Administration of statin	0.168 [0.048, 0.590]	0.005
Lesion length (mm)	1.002 [0.996, 1.009]	0.439
Chronic total occlusion	4.809 [1.651, 14.01]	0.004

Multivariate logistic regression analysis was performed.

multivariate logistic regression analysis, administration of cilostazol (adjusted odds ratio: 0.299, 95% confidential interval [CI]: 0.107–0.834; $p = 0.021$) and statin (adjusted odds ratio: 0.168, 95% CI: 0.048–0.590; $p = 0.0005$) was negatively associated while CTO (adjusted odds ratio, 4.809; 95% CI: 1.651–14.01; $p = 0.004$) was positively associated with 3-month restenosis.

Comparison of characteristics between patients and limbs with and without 3-month angiographic restenosis

Comparison of characteristics between patients with and without restenosis is shown in Table 3. There were no significant differences in distribution of atherosclerosis risk factors and comorbidities, except for administration of cilostazol. Fig. 4 shows the comparison of frequency before angioplasty, and at 3 and 12 months, of ambulatory status between patients with and without restenosis. Frequency of ambulatory status before angioplasty and 3 months later was not significantly different between patients with and without restenosis (before angioplasty: 48% vs. 57%, $p = 0.54$; 3 months: 54% vs. 64%, $p = 0.51$). However, frequency of ambulatory status at 12 months was greater in the non-restenosis group than in the restenosis group (92% vs. 55%, $p = 0.04$). Regarding comparison of characteristics between limbs with and without restenosis in

Table 3
Comparison of characteristics between patients with and without 3 months angiographic restenosis.

	Patients with restenosis ($n = 46$)	Patients without restenosis ($n = 14$)	*p* value
Patient status			
Age	74 ± 8	77 ± 8	0.21
Male	52% (24)	71% (10)	0.24
BMI	22 ± 3	23 ± 3	0.77
Patient ADL (ambulatory/ wheelchair/bedridden) before angioplasty	22/22/2	8/6/0	0.85
Patient ADL (ambulatory/ wheelchair/bedridden) at 3 months	25/19/2	9/4/1	0.81
Patient ADL (ambulatory/ wheelchair/bedridden) at 12 months	24/17/1	12/1/0	0.07
Risk factors			
Hypertension	76% (35)	86% (12)	0.44
Hyperlipidemia	41% (19)	50% (7)	0.57
Low-density lipoprotein	101 ± 38	90 ± 28	0.33
Diabetes mellitus	59% (27)	64% (9)	0.71
HbA1c	6.2 ± 1.4	6.4 ± 1.8	0.67
ESRD on dialysis	52% (24)	64% (9)	0.43
Coronary artery disease	41% (19)	43% (6)	0.99
Ejection fraction (%)	59 ± 14	64 ± 9	0.28
Cerebrovascular disease	17% (8)	11% (1)	0.35
Medication			
Cilostazol	39% (18)	71% (10)	0.03
Statin	26% (12)	43% (6)	0.23

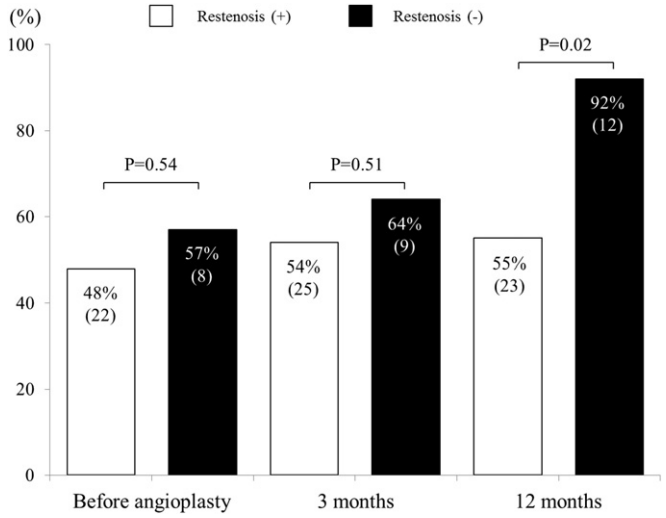

Figure 4. Comparison of frequency of ambulatory status between patients with and without restenosis before angioplasty, and after 3 and 12 months.

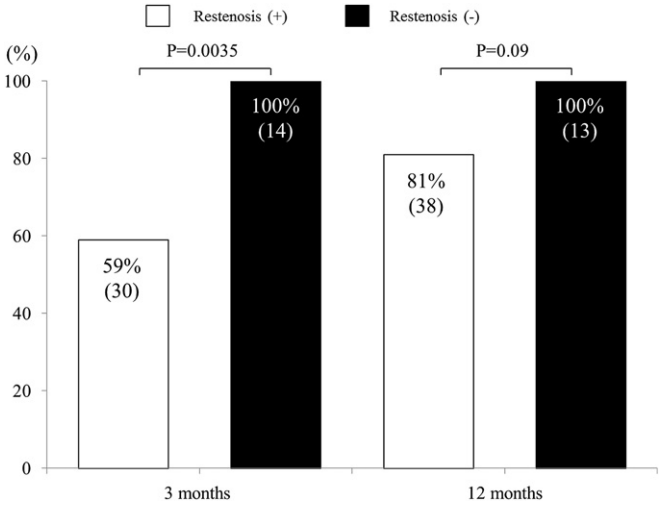

Figure 5. Comparison of frequency of complete ulcer healing or lack of rest pain with and without restenosis after 3 and 12 months.

Table 4, Rutherford classification was similar between groups. Pre and post procedure and 3-month SPP were not significantly different between the restenosis and non-restenosis groups. However, 3-month SPP at both dorsal and plantar sides was numerically lower in the restenosis than in the non-restenosis group. SPP $>$ 40 mmHg, indicative of sufficient blood flow for ulcer healing, at the plantar side was more frequently observed in the non-restenosis group than the restenosis group. Twelve-month reintervention rate was 59% in the limbs with 3-month angiographic restenosis. Fig. 5 shows the comparison of frequency at 3 months and 12 months of complete ulcer healing or lack of rest pain in limbs with and without restenosis. Frequency of complete ulcer healing or lack of rest pain was higher in the non-restenosis group than in the restenosis group at 3 months (100% vs. 59%, $p = 0.0035$). The same tendency was observed at 12 months but the difference did not reach statistical significance (100% vs. 81%, $p = 0.09$). Eighty-three percent (54/65) of limbs had Rutherford 5/6 status before angioplasty and 7% (4/55) of ischemic wounds were not completely healed at 12 months. In limbs with complete wound healing ($n = 51$) in the chronic phase, average time to wound healing in the overall population was 112 $\pm$ 79 days, and it was longer in the restenosis group than in the non-restenosis group (127 $\pm$ 83 vs. 66 $\pm$ 40 days, $p = 0.02$).

Outcomes at 12 months

Fig. 2 shows the 12-month outcomes. Fourteen limbs in 14 patients were free from 3-month angiographic restenosis and one of these patients died within 12 months. Two patients were lost to 12-month angiographic follow-up and therefore 85% of limbs (11/13) with 23 lesions underwent 12-month angiographic follow-up. Twelve-month angiographic restenosis as secondary endpoint was present in 82% (81/99) of lesions. At 12 months after angioplasty, 15% (9/60) of limbs lacked complete ulcer healing or had rest pain recurrence, and 48% (31/65) of limbs had undergone reintervention using angioplasty. At 3 and 12 months, no patients had undergone major amputation.

Discussion

Our prospective and multicenter registry examined the 3-month angiographic restenosis rate after infrapopliteal angioplasty for patients with CLI. Three-month angiographic follow-up was conducted in 95% (60/63) of cases and the restenosis rate was 73% (74/102). By multivariable analysis for predictors of 3-month angiographic restenosis, non-administration of cilostazol and statin, and CTO were positively associated with angiographic

Table 4
Comparison of characteristics between lower limbs with and without restenosis.

	Limbs with restenosis ($n = 51$)	Limbs without restenosis ($n = 14$)	p value
Tissue loss	84% (43)	79% (11)	0.69
C-reactive protein level (mg/dL)	2.0 $\pm$ 2.7 [1.9]	1.9 $\pm$ 3.1 [0.95]	0.84
Wound infection	26% (13)	29% (4)	0.99
TASC 2000 classification C/D	2/49	1/13	0.37
ABI	0.73 $\pm$ 0.16	0.76 $\pm$ 0.17	0.51
SPP (dorsal side/plantar side) mmHg			
before angioplasty	28 $\pm$ 15/34 $\pm$ 18	30 $\pm$ 15/33 $\pm$ 20	0.66/0.86
after angioplasty	47 $\pm$ 22/46 $\pm$ 21	48 $\pm$ 10/55 $\pm$ 23	0.88/0.18
at 3 months	41 $\pm$ 19/40 $\pm$ 23	49 $\pm$ 18/50 $\pm$ 19	0.18/0.23
SPP >40 mmHg before/after/at 3 months (dorsal side)	18% (9)/53% (27)/ 47% (24)	31% (4)/77% (10)/77% (10)	0.29/0.21/0.09
SPP >40 mmHg before/after/at 3 months (plantar side)	29% (15)/57% (29)/ 44% (19)	39% (5)/69% (9)/75% (14)	0.53/0.42/0.05
Time to wound healing (days)	127 $\pm$ 83	66 $\pm$ 40	0.02
12 Months reintervention rate	59% (30)	7% (1)	0.0006

restenosis. At 3 months limbs with incomplete ulcer healing or with rest pain recurrence and at 12 months patients with non-ambulatory status were more frequently observed in the restenosis group.

Based on results from a meta-analysis, although technical success and subsequent durability of infrapopliteal angioplasty are limited in comparison to bypass surgery, clinical benefit is acceptable because limb salvage rates are similar between the two treatment modalities.[13] Therefore, occurrence of restenosis appeared not to affect limb salvage, leading to a perceived lack of relevance of durability of infrapopliteal angioplasty in the clinical setting. However, results from this prospective multicenter registry indicate that occurrence of restenosis during the wound-healing process after angioplasty for patients with CLI will delay or hinder ischemic wound healing and achievement of ambulatory status in the chronic phase. Therefore, it adversely impacts improvement of clinical outcomes in CLI patients. In this study, the 3-month angiographic restenosis rate was slightly higher than found in earlier studies.[9] This might be attributed to the fact that more than half the patients were on dialysis therapy, leading to a more severe form of atherosclerosis complicated by calcification. Regarding factors associated with restenosis, there is general agreement that restenosis is more frequently observed in lesions with CTO than in those without it.[14,15] However, from the angiographic perspective, presence of CTO is a novel predictor for restenosis after infrapopliteal angioplasty. Cilostazol and statins have an inhibitory effect on restenosis after percutaneous coronary intervention, and several studies in patients with peripheral artery disease identified improvement of walking distance in intermittent claudication,[14–16] and reduction of restenosis after femoropopliteal stenting and of need for revascularization in claudicant patients.[17–19] It could be speculated that antiproliferation of vascular smooth muscle cells and improvement of endothelial cell function with cilostazol and statin therapy may lead to inhibition of neointimal hyperplasia following balloon angioplasty for infrapopliteal lesions.[20,21] Recently, cilostazol and statins were shown to improve amputation-free survival and limb salvage rate after EVT for infrainguinal disease in patients with CLI.[20,21] Therefore, these results favor use of cilostazol and statin as first-line oral drugs for patients with CLI treated by infrapopliteal angioplasty.

Limitations

There were several limitations to this study. Although this was a prospective and multicenter study, it included a small number of CLI patients. Also, control groups of patients who were unsuitable for revascularization and patients treated with bypass therapy were not included because we did not manage those cases. Quantitative vascular analysis to evaluate the degree of restenosis in long infrapopliteal lesions was not conducted because it is technically and clinically challenging. Therefore, visual assessment by angiography was used to precisely determine binary restenosis. Finally, selection of medication, especially antiplatelet therapy, was decided by physicians' prescription leading to a risk of selection bias.

Long-term efficacy outcomes of traditional angioplasty have been systematically studied and found to be comparable to those of BSX.[8] Consequently, occurrence of restenosis after infrapopliteal angioplasty has not been generally considered as a critical issue after an endovascular approach for patients with CLI. To the best of our knowledge, this is the first report on the relationship between restenosis after angioplasty and clinical outcomes in patients with CLI due to isolated infrapopliteal lesions. A randomized trial with a large number of patients to investigate the long-term clinical efficacy of next-generation infrapopliteal devices is warranted.

Conclusion

The 3-month restenosis rate of diseased infrapopliteal arteries was extremely high after treatment with plain balloon angioplasty. Occurrence of restenosis in the early phase may adversely impact improvement of clinical outcomes after endovascular intervention.

Financial Disclosure

None.

Conflicts of Interest

None.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ejvs.2012.07.017.

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