Percutaneous transluminal angioplasty in severe diabetic foot ischemia: outcomes and prognostic factors

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SUMMARY

Objectives: To evaluate the outcomes of severe ischemic diabetic foot ulcers for which percutaneous transluminal angioplasty (PTA) was considered as the first-line vascular procedure. Factors associated with successful PTA were sought.

Research design and methods: In 32 consecutive diabetic patients with foot ulcers and severe limb ischemia, PTA was performed if feasible; if not, primary bypass grafting was done when feasible. All patients were followed until healing or for at least one year. Patients with worsening ulcers after PTA underwent bypass grafting. Clinical and angiographic factors influencing outcomes after PTA were sought by univariate and multivariate analysis.

Results: PTA was done in 25 of the 32 (78%) patients, and considered clinically successful in 13 (52%). After 1 year, the healing rate was 70% and the limb salvage rate 90%. Successful PTA was significantly associated with a higher post-PTA transcutaneous oxygen pressure (P = 0.03) and presence of at least one patent pedal vessel (P = 0.03) in the univariate analysis; only a patent pedal vessel was significant in the multivariate analysis.

Conclusion: Primary PTA in diabetic patients with severe ischemic foot ulcers provides similar outcomes to usual results obtained in severe ischemia in absence of diabetes. The presence of one patent pedal vessel on arteriography before PTA is the best prognostic factor.

Key-words: Diabetic foot ulcer · Peripheral arterial disease · Percutaneous transluminal angioplasty.

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RÉSUMÉ

Angioplastie transluminale percutanée dans l'ischémie sévère du pied diabétique: résultats et facteurs pronostics

Objectif : Évaluer l'évolution des ulcères ischémiques sévères du pied diabétique ayant bénéficié d'une procédure de revascularisation par angioplastie transluminale percutanée (PTA) en première intention. Analyse des facteurs associés au succès de l'angioplastie.

Matériel et méthodes : Réalisation, quand elle était jugée faisable, d'une angioplastie (PTA) chez 32 patients diabétiques hospitalisés successivement, présentant un ulcère ischémique dans un contexte d'ischémie critique des membres inférieurs (CLI). En cas d'échec, les patients ont bénéficié quand cela était possible d'un pontage artériel distal. Tous les patients ont été suivis jusqu'à cicatrisation ou pendant au moins 1 an. En cas d'aggravation de l'ulcère après PTA, un pontage distal a été réalisé. Les facteurs cliniques et angiographiques influençant le pronostic après PTA ont été étudiés en analyse univariée et multivariée.

Résultats : Une angioplastie a été réalisable chez 25 des 32 patients (78 %), et considérée comme un succès clinique dans 13 cas (52 %). Après 1 an, le taux de cicatrisation était de 70 % et le taux de sauvetage de membres de 90 %. Le taux de succès de l'angioplastie était significativement associé à l'élévation de la pression transcutanée en oxygène post angioplastie (P = 0.03) et à la présence d'au moins un axe artériel perméable au niveau du pied (P = 0.03) en analyse univariée ; en analyse multivariée seule la présence d'au moins un axe artériel au niveau du pied est significativement associée.

Conclusion : L'angioplastie en première intention chez les patients diabétiques présentant un ulcère ischémique sévère du pied permet une évolution similaire à celle constatée habituellement pour la CLI en l'absence de diabète. La présence d'un axe artériel au niveau du pied perméable avant angioplastie est le meilleur facteur pronostic.

Mots-clés : Ulcération du pied diabétique · Artérite des membres inférieurs · Angioplastie transluminale percutanée.

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Introduction

In patients with diabetic foot ulcers, the presence of peripheral occlusive arterial disease (PAOD) increases the risk of major amputation. For the last 10 to 15 years, surgical bypass grafting has been the standard treatment for diabetic patients with ischemic foot ulcers [1]. Surgical bypass grafting is an invasive procedure, whereas an alternative for achieving revascularization is percutaneous transluminal angioplasty (PTA), which is associated with low morbimortality, lower costs, and short hospital stays [2]. In addition, PTA can be used repeatedly to treat recurrent ulcers, and preserves the saphenous veins.

In severe limb ischemia, PTA is now accepted as a satisfactory alternative to surgery [3, 4], but diabetes is often reported as associated with poorer outcomes [5-7]. However, Faglia et al. [8] recently reported excellent results after extensive use of PTA in patients with diabetic foot ulcers and variable degrees of PAOD. More studies are therefore needed to establish the place and limitations of PTA in the management of ischemic foot ulcers in diabetic patients.

We prospectively evaluated outcomes in patients with diabetic foot ulcers and severe limb ischemia treated with primary PTA if feasible. Factors associated with ulcer outcomes after PTA were sought, with special attention to absence of patent pedal artery on arteriography, which in many cases precludes distal pedal bypass grafting.

Research design and methods

Patient selection

From March 2000 to November 2001, all consecutive diabetic patients admitted to a diabetic foot unit were evaluated for the presence and severity of PAOD. Inclusion criteria were severe limb ischemia defined as absence of foot pulses associated with a transcutaneous oxygen pressure ($TcPO_2$) no greater than 30 mm Hg at the dorsum of the foot [9, 10]. In presence of important edema perturbing TcPO2 measurement, patients were not included. All included ulcers were grade 2 or 3 and stage C or D according to the University of Texas Wound Classification System [11].

Treatment protocol

Arteriography was used to evaluate the morphology, location, and hemodynamic impact of arterial lesions. PTA was performed if deemed feasible by two interventional radiologists and a vascular surgeon. Lower leg arteries that had stenoses < 30% and were opacified at least down to the malleolar level were defined as "patent" and were noted in each treated limb before and after PTA. Pedal vessels (dorsal pedal and common plantar arteries) were classified as "patent" when at least one pedal artery was clearly opacified during arteriography. When PTA was not considered feasible (femoro-popliteal and/or leg arteries complete occlusion), femoro-popliteal or distal bypass grafting was performed if feasible. All patients received standard medical treatment including offloading, wound care, and antibiotic therapy if needed. Osteomyelitis was medically treated (two antibiotics until healing).

Ulcer size area was determined in rule millimeters. The larger ulcer was considered the study ulcer.

PTA procedure

PTA was performed with digital fluoroscopy guidance, immediately after diagnostic evaluation of the lower leg. Whenever possible, percutaneous antegrade puncture of the ipsilateral common femoral artery was used to introduce a 0.035" guidewire into the superficial femoral artery, followed by a 4-6 French sheath. Femoro-popliteal and infrapopliteal angioplasty was performed as needed. The goal of the treatment was the maximal runoff. Distal lesions were crossed with a 0.014" standard guidewire and occlusions were preferably crossed with a hydrophilic 0.035" guidewire. If possible, total occlusions were recanalized through the occluded arterial lumen; if not, the subintimal technique was used. The balloon diameter was equal to the measured size of the artery. Femoro-popliteal and infrapopliteal lesions were treated with a low-profile balloon dilatation catheter advanced over the guidewire to the most distal lesion possible. Several inflations of 1-3 minutes' duration at 8 to 20 atmospheres were performed over the entire length of the lesion. Stents were not used on infrapopliteal arteries. In patients requiring PTA of the proximal femoral artery, retrograde puncture of the contralateral common femoral artery was used to insert a long 6 or 7 French sheath across the aortic bifurcation. Procedural success was defined as a residual stenosis of the treated lesion of less than 30% as measured by arteriography.

After successful PTA, heparin was given intravenously for 48 hours and a combination of aspirin (75-300 mg/d) and clopidogrel (75 mg/d) orally for 1 month. Then, either aspirin or clopidogrel was used as maintenance antiplatelet treatment.

TcPO2 measurement

TcPO2 measurement was made with an electrochemical transducer (TCM 400, Radiometer S.A., Copenhagen, DK). The monitor was calibrated against air. The measurement site was cleaned with disinfectant solution, and the probe attached in presence of contact liquid supplied by the manufacturer, at the first intermetatarsal place or as near as possible to the dorsum of the foot. The transducer was heated to 44°C and hyperemic stabilization occurred within 20 minutes, at room temperature.

Clinical variable definition

Neuropathy was defined as insensitivity to the 10-g 5.07 Semmes-Weinstein monofilament using standard methods

[12]. Osteomyelitis was diagnosed on probing to bone with local infection and suggestive features on weekly bone radiographs [13]. Renal impairment was defined as creatinine clearance < 60 ml/mn.

Follow-up

Patients were monitored daily as inpatients in the foot unit until clinical improvement was noted and as outpatients by the same team until ulcer healing or at least 12 months. Short-term and long-term clinical success of PTA was evaluated based on ulcer size and appearance. Clinical failure of PTA was defined as an increase in ulcer size with necrotic and inflammatory symptoms (whereas infection was as controlled as possible with antibiotic treatment adapted to repeated microbiological results) and led to bypass grafting if this procedure was feasible. Clinical success of PTA was defined as disappearance of necrotic and inflammatory symptoms and partial (at least 30% decrease in ulcer size) or total healing of the ulcer without bypass grafting or major amputation, i.e., amputation at or above the ankle. Toe or transmetatarsal amputation was classified as minor amputation. Limb salvage was defined as absence of major amputation. Duplex ultrasonography or angiography was not performed at follow-up and, consequently, patency cannot be described.

Statistical methods

In the life tables for healing rate and limb salvage, patients who died before healing were treated as censored.

Factors associated with clinical PTA success were sought by performing a univariate analysis with Fisher exact tests for categorical variables and Wilcoxon tests for continuous variables; then, factors significant at the 0.05 level were entered into a stepwise logistic regression model. All computations were performed using the SAS System 8.02 for Windows.

Results

Patient population

During the 20-month inclusion period, 110 diabetic patients were admitted to our diabetic foot unit. Among them, 32 had clinical evidence of severe limb ischemia with reliable $TcPO_2$ measure: all had no palpable distal pulses and mean $TcPO_2$ at admission was 15 ±7 mmHg. *Table I* reports their demographic and clinical characteristics. Ulcers were localized under the forefoot or toes for 27, under the hindfoot for 2, and at the lateral part of the foot for 3 of them.

PTA procedure

PTA was carried out in 25 (78%) patients and considered unfeasible in 7 patients. Before PTA, 11 of the 25 (46%) patients who underwent this procedure had no patent lower leg arteries and 7 (29%) had no patent pedal vessels. There were two procedural failures that left the vascular status unchanged. So, in 23 PTA treated patients, the mean number of treated arteries was 1.6 (range, 1-4). Localization and nature of the treated lesions are described in *table II*. Eight PTA procedures involved only the femoral axis, 13 only the popliteal and/or infrapopliteal axis, and four both the femoral and the infrafemoral axes. After PTA, 23 of the 25 (80%) patients had at leasts one patent lower leg artery. A puncture site hematoma developed in 2 patients, one of whom required a blood transfusion; one patient had a nonfatal myocardial infarction 12 hours after PTA.

Table I
Demographic and clinical data.

n	32
Age (years)	67 ± 10
Men	24 (85)
Diabetes duration (years)	22 ± 12
Type 2 diabetes	27 (84)
Active smoking	3 (9)
History of previous ulcer	18 (56)
HbA_{1c} (%)	7.5 ± 1.5
Neuropathy	29 (91)
Renal impairment	4 (12,5)
Absence of foot pulses	32 (100)
Necrotic lesion	29 (91)
Osteomyelitis	14 (44)

Data are N (%) or mean ± SD.

Clinical results

In the PTA group, TcPO2 increased from 15.5 ± 6 to 23.6 ± 10 (NS) as measured 72h post-PTA. Mean follow-up was 8.5 ± 5.5 months (range, 1.5-24). One patient in the

Table II
Localization and nature of treated lesions (n).

	stenosis	occlusion
Iliofemoral arteries (common iliac, external iliac and common femoral arteries)	6	0
Superficial femoral and popliteal arteries	13	3
Tibioperoneal artery	4	1
Anterior tibial artery	3	1
Posterior tibial artery	1	0
Peroneal artery	4	1

PTA group was lost to follow up after 2 months. Five of the 31 patients followed up for at least 1 year died during this period, 3 of malnutrition and 2 of coronary heart disease. They had all received PTA, but no bypass graft was feasible in these patients. Healing rate and limb salvage rate are shown in *figure 1*. In the entire cohort after 1 year, the healing rate was 70% and the limb salvage rate was 90%.

Bypass grafting was performed in 6 of the 7 patients who did not undergo PTA, and was required in 6 of the 25 who underwent attempt of primary PTA. The patient who was lost to follow-up after 2 months was classified as a clinical PTA failure because his wound had worsened at the last visit. This left 13 (52%) patients with clinical PTA success (9 with total and 4 with partial healing) in the PTA group. In the entire cohort, this left 59% (19/32) of "PTA failure" (unfeasible or clinically unsuccessful).

Factors associated with clinical PTA success

Clinical and arteriographic features in the 25 patients who underwent PTA are reported in *table III*. The increase in $TcPO_2$ in each group did not reach significance. In univariate analysis, clinical PTA success was significantly associated with higher 72 h-post-PTA $TcPO_2$, and with the presence of at least one patent pedal vessel (dorsal pedal and/or common plantar arteries) on arteriography before PTA. In stepwise multiple logistic regression analysis, only presence of a patent pedal vessel was independently associated with clinical PTA success (odds ratio for clinical failure, 0.07; 95% confidence interval, 0.006-0.745).

Discussion

Studies in patients with PAOD found that the cumulative limb salvage rate was similar with infrapopliteal PTA as the primary treatment for critical limb ischemia and with surgical revascularization, but diabetes was associated with poor outcomes in several studies of PTA for critical limb ischemia [3, 4, 15, 16]. In our study of a population with severe ischemia, the rate of clinical success after PTA (defined as partial or total ulcer healing with no bypass grafting or major amputation) was 52%. The overall 1-year limb salvage rate was comparable to that in a population of patients with critical limb ischemia including only 30 to 50% of diabetic patients [3, 15], suggesting that diabetes may not necessarily indicate a poor prognosis. Outcomes in our study were less favorable than in the study by Faglia *et al*. [8], who reported a 95% limb salvage rate and a 100% healing rate after 14 ± 7 months follow-up with no secondary bypass procedures, but in a heterogeneous cohort of diabetic patients with mild to severe ischemic foot ulcers. This difference can be ascribed to the much more severe

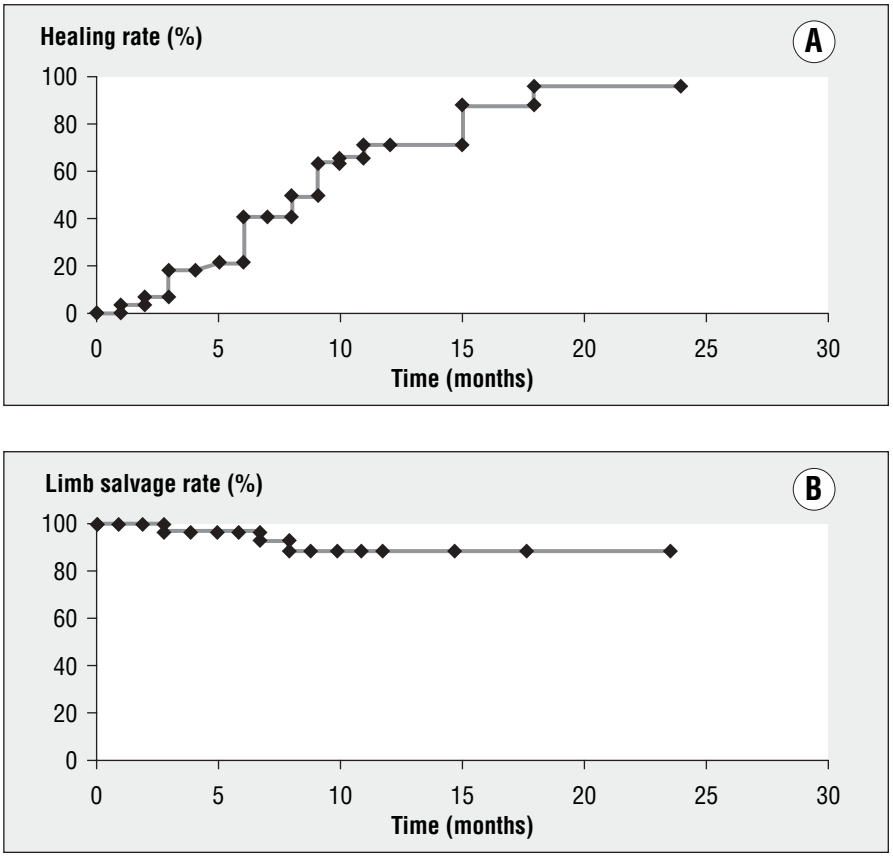

Figure 1
Healing rate (A) and limb salvage rate (B) as a function of time in the 32 patients included in the study.

Table III
Factors associated with clinical success of percutaneous transluminal angioplasty as the first-line revascularization procedure for patients with diabetic foot ulcers and severe ischemia.

	Clinical success	Clinical failure	P value
n	13	12	
Age (years)	62 ± 15	70 ± 10	0.20
Type 2 diabetes	10 (77)	10 (83)	1.00
Diabetes duration	21 ± 10	24 ± 14	0.85
HbA_{1c} (%)	7 ± 1.5	8 ± 1.90	0.27
Men	8 (62)	10 (83)	0.39
History of ulcer	6 (46)	7 (58)	0.70
Active smoking	2 (15)	1 (8)	1.00
Osteomyelitis	8 (62)	3 (25)	0.11
Neuropathy	12 (92)	10 (83)	0.59
$TcPO_2$ before PTA (mmHg)	17 ± 7	14 ± 6	0.39
$TcPO_2$ after PTA (mmHg)	27 ± 9	20 ± 9	0.03*
≥1 patent pedal artery before PTA	12 (92)	6 (50)	0.03*
≥1 patent lower leg artery after PTA	13 (100)	10 (83)	0.22

Data are N (%) or mean ± SD.
PTA: percutaneous transluminal angioplasty.

ischemia in our patients (all of whom had a pre-PTA $TcPO_2$ value of less than 30 mm Hg) and to the severity of their ulcers. But above all, Faglia *et al.* used criteria to select patients for the PTA group which might have exclude the more severely ischemic patients.

Another purpose of the present study was to look for clinical and angiographic parameters associated with clinical outcomes after PTA. We especially wanted to see if PTA was successful in patients without patent pedal arteries on arteriography, a situation where distal bypass graft is rarely feasible. Indeed, good angiographic opacification of at least one pedal artery before PTA was the only factor independently associated with clinical PTA success. PTA was successful in only 1 of 11 patients with no patent pedal vessel. Moreover, obtaining a continuous patent artery at the malleolar level did not independently predict clinical success. Similarly, in a study of 32 diabetic patients with foot ulcers, the number of patent crural arteries after PTA was not associated with ulcer healing [17]. Thus, we may assume that improving arterial flow in the tibial area is necessary but not sufficient to obtain a good clinical result. Further support for this conclusion comes from a prospective trial in critical limb ischemia, in which improving arterial filling in the most severely ischemic area, even via collaterals, was more closely associated with PTA success than obtaining a continuous artery at the tibial level [18].

In conclusion, these results suggest that PTA should be considered routinely for first-line revascularization in patients with ischemic diabetic foot ulcers, even in presence of severe ischemia, as a means of obtaining good clinical outcomes in some. But in patients with no patent pedal artery, in whom distal pedal bypass grafting is rarely feasible, PTA does not seem to be not an effective solution.

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