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Predictors of Delayed Wound Healing after Endovascular Therapy of Isolated Infrapopliteal Lesions Underlying Critical Limb Ischemia in Patients with High Prevalence of Diabetes Mellitus and Hemodialysis

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WHAT THIS PAPER ADDS

Acceptable limb salvage rates underlie wide use of endovascular therapy (EVT) for patients with critical limb ischemia secondary to isolated infrapopliteal lesions; however, delayed wound healing after revascularization remains a challenge. This study, involving 871 consecutive critically ischemic limbs, examines factors associated with delayed wound healing after EVT. Risk stratification based on these predictors allows wound healing rate estimation.

Objectives: Acceptable limb salvage rates underlie the widespread use of endovascular therapy (EVT) for patients with critical limb ischemia (CLI) secondary to isolated infrapopliteal lesions; however, post-EVT delayed wound healing remains a challenge. Predictors of delayed wound healing and their use in risk stratification of EVT in patients with CLI due to isolated infrapopliteal lesions are explored.

Methods: This was a retrospective multicenter study. 871 consecutive critically ischemic limbs were studied. There was tissue loss in 734 patients (age: 71 ± 10 years old; 71% male) who had undergone EVT between April 2004 and December 2012. The wound healing rate after EVT was estimated by the Kaplan–Meier method. The association between baseline characteristics and delayed wound healing was assessed by the Cox proportional hazard model.

Results: Diabetes mellitus and regular dialysis were present in 75% (553/734) and 64% (476/734) of patients, respectively; 67% of limbs (585/871) had Rutherford class 5 CLI; 8% (67/871) of wounds were located in the heel only; 25% (219/871) of limbs had Rutherford 6 (involving not only the heel); and 42% (354/871) of wounds were complicated by infection. The rate of freedom from major amputation at 1 year reached 88%, whereas the wound healing rate was 67%. Median time to wound healing was 146 days. By multivariate analysis, non-ambulatory status (hazard ratio [HR], 1.58; 95% confidence interval [CI] 1.31–1.91) serum albumin <3 g/dL (HR 1.42; 95% CI 1.08–1.86), Rutherford 6 (not only heel) (HR 1.68; 95% CI 1.33–2.14), wound infection (HR 1.24; 95% CI 1.03–1.50), EVT not based on angiosome concept (HR 1.28; 95% CI 1.06–1.55), and below the ankle (BTA) 0 vessel runoff after EVT (HR 1.45; 95% CI 1.14–1.86) were independent predictors of delayed wound healing.

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Conclusions: Non-ambulatory status, low albumin level, Rutherford 6 (not only heel), wound infection, indirect intervention, and poor BTA runoff were independent predictors for delayed wound healing after EVT in patients with CLI secondary to infrapopliteal lesions, and their use in risk stratification allows estimation of the wound healing rate.

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INTRODUCTION

Critical limb ischemia (CLI), the most severe clinical manifestation of peripheral artery disease (PAD), is characterized by ischemic rest pain or the presence of ischemic tissue loss with or without gangrene.[1] According to the Trans-Atlantic Inter-Society Consensus (TASC) II, the primary objectives of CLI treatment are to relieve ischemic pain, heal ischemic ulcers, prevent limb loss, improve patient function and quality of life (QOL), and prolong survival.[1] When technically possible, revascularization, including bypass surgery (BSX) and endovascular therapy (EVT), are considered optimal treatments for patients with CLI in the latest PAD guidelines.[1–3] Furthermore, EVT has become commonplace as the revascularization strategy for infrapopliteal lesions in patients with CLI because of comparable limb salvage rates to BSX and its less invasive nature.[4] In the management of CLI with tissue loss, delayed wound healing not only lowers QOL but also increases medical costs, even if limb loss is successfully prevented.[5,6]

For BSX, reports have documented 1 year wound healing rates in the 74–85% range, and median wound healing time of 173–186 days post procedure[7,8] with regular dialysis, diabetes mellitus, low albumin level, non-ambulatory status, and Rutherford category 6 as predictors of delayed wound healing.[9]

For EVT, the 1 year wound healing rate and median healing time were 54–86% and 97–145 days, respectively.[10–12] Factors associated with delayed wound healing after EVT were diabetes mellitus, wound infection, below the ankle (BTA) runoff, and body mass index (BMI) < 18.5 kg/m^2.[11,12]

Previous studies have been more limited in the outcomes examined and have not reported the risk stratification for wound healing,[7–12] therefore in this study 871 limbs with ischemic tissue loss due to infrapopliteal lesions were analyzed to assess and risk stratify the wound healing rate and predictors after EVT.

MATERIALS AND METHODS

Study design

This study is a sub-analysis of J-BEAT (**J**apanese **BE**low the knee **A**rtery **T**reatment registry: No. UMIN 000004917), a non-randomized multicenter study approved by the institutional review boards at all 14 participating cardiovascular and vascular institutions in Japan. The study protocol was developed in accordance with the Declaration of Helsinki and approved by the ethics committee of each participating hospital.

Participants

During the study period, 1316 limbs from 1078 CLI patients presenting with isolated infrapopliteal lesions were treated with plain balloon angioplasty. Patients with CLI without tissue loss ($n = 321$ limbs) were excluded from this analysis. Other exclusion criteria were (a) above ankle ischemic ulcer ($n = 17$ limbs); (b) failed EVT, defined as no below knee runoff vessel after EVT ($n = 81$ limbs); and (c) data missing on wound condition ($n = 26$ limbs). Finally, 871 limbs in 734 consecutive CLI patients who had undergone EVT for *de novo* infrapopliteal lesions were enrolled between April 2004 and December 2012.

The database excluded patients who were considered poor candidates for revascularization due to severe comorbidities and impairment at the functional (bedridden without intractable rest pain) and/or cognitive (dementia not requiring institutionalization) levels, or who refused revascularization. Although intervention was not attempted in patients with functionally unsalvageable limbs, non-ambulatory patients without cognitive problems were treated by angioplasty for limb salvage taking into consideration the patient's preference, family cooperation, and lack of control of rest pain with analgesics.

Intervention

Indication and strategy for EVT were decided by consensus among vascular surgeons, interventional cardiologists, and interventional radiologists, depending on general condition, comorbidity and lower limb severity. Patients with >2 year life expectancy, and CLI patients with Rutherford 6 with good autogenous vein (diameter > 3 cm) were commonly selected for primary surgical bypass therapy.

All EVT procedures were performed under local anesthesia. Generally, a 3 or 4Fr sheath was used via an antegrade approach from the ipsilateral common femoral artery. After inserting the sheath, unfractionated heparin (5000 units) was routinely administered into the artery. A 0.014 inch guidewire was advanced into the culprit lesion and it was dilated using an optimally sized balloon catheter at the operator's discretion. Basically, the diameter of the distal part of the healthy vessel was used as reference to decide balloon size. Stent, drug coated balloon, and atherectomy devices were not approved for use in infrapopliteal intervention in Japan.