Eur J Vasc Endovasc Surg (2015) 49, 297–305

Complex Relationship of Body Mass Index with Mortality in Patients with Critical Limb Ischemia Undergoing Endovascular Treatment

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WHAT THIS PAPER ADDS

A complex relationship was found between body mass index (BMI) and long-term outcomes in patients with critical limb ischemia (CLI) after endovascular treatment of isolated infrapopliteal artery lesions. The 3 year overall survival rates were 33.3%, 61.2%, and 69.8% in underweight, normal, and overweight/obese patients, respectively. The survival rate was significantly lower in underweight patients and significantly higher in overweight/obese patients compared with patients of normal weight. Although underweight patients with CLI have a poor prognosis because of comorbidities, low BMI itself is an independent predictor of a poor prognosis in patients with CLI.

Objective: To investigate the relationship between body mass index (BMI) and long-term outcomes of patients with CLI after endovascular treatment (EVT).
Design: Retrospective multicenter study.
Subjects: 1088 consecutive patients (1306 limbs, mean age 72 ± 10 years) with CLI who underwent EVT for isolated infrapopliteal artery lesions were evaluated. These subjects were identified in the J-BEAT III registry.
Methods: The patients were divided into groups based on BMI <18.5 kg/m^2 (underweight, $n = 188$; 219 limbs), 18.5 to 24.9 kg/m^2 (normal weight, $n = 718$; 868 limbs), and >25.0 kg/m^2 (overweight/obese, $n = 182$; 219 limbs). The endpoints were overall survival and freedom from major adverse limb events (MALE).
Results: The median follow up period was 1.5 years (range: 1 month–8.7 years). The 3 year overall survival rates were 33.3%, 61.2%, and 69.8% in underweight, normal, and overweight/obese patients, respectively. The survival rate was significantly lower in underweight patients and significantly higher in overweight/obese patients compared with patients of normal weight (both $p < .0001$). The 3 year rates of freedom from MALE did not differ significantly among the three groups (36.4%, 45.4%, and 52.3%, respectively, $p = .32$). Age, BMI <18.5 kg/m^2, heart failure, aortic valve stenosis, renal failure, triglyceride levels, serum albumin <3.0 g/dL, anticoagulant treatment, non-ambulatory status, and Rutherford 6 classification all were significantly associated with overall survival.
Conclusions: BMI has a complex correlation with mortality in patients with CLI after EVT for isolated infrapopliteal artery lesions. Underweight patients with CLI have an extremely poor prognosis. Such patients have many other factors associated with mortality, but low BMI was identified as an independent predictor of a poor prognosis in patients with CLI. Similarly, normal weight patients had a small but significant increase in mortality compared with overweight/obese patients.

Article history: Received 20 March 2014, Accepted 17 October 2014, Available online 15 December 2014
Keywords: Body mass index, Ischemia/MO, Peripheral arterial disease, Endovascular procedures

INTRODUCTION

The "obesity paradox" emerges from the observation that mortality in patients with hypertension, heart failure,[1,2] and coronary artery disease[3] decreases as their body mass index (BMI) increases, despite the association of obesity with cardiovascular risk factors. BMI has also been found to be inversely related to mortality in patients with

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1078-5884/$ – see front matter
http://dx.doi.org/10.1016/j.ejvs.2014.10.014

peripheral artery disease (PAD).[4,5] However, most patients in these reports presented with claudication alone, whereas patients with critical limb ischemia (CLI) are known to suffer a higher mortality (50—60% at 5 years) compared with those with uncomplicated claudication (20—30% at 5 years).[6]

In vascular surgery, an inverse relationship between obesity and mortality has been proposed in patients with CLI requiring lower extremity revascularization or amputation,[7,8] but this relationship is unclear in patients with CLI after endovascular treatment (EVT) as the primary therapy. EVT is now an alternative first line treatment for patients with CLI because its long-term outcome has been proven non-inferior to that of surgery.[9,10] EVT is also employed in inoperable cases because of age, comorbidities, and general condition. The purpose of this study was to investigate the relationship between BMI and long-term outcomes in patients with CLI following EVT.

SUBJECTS AND METHODS

Study design and population

The J-BEAT (Japanese Below the knee Artery Treatment Trial) III registry is a physician initiated, non-commercial, multicenter registry of consecutive patients with CLI undergoing EVT for isolated infrapopliteal artery lesions between April 2004 and March 2012 in Japan. A total of 1091 consecutive patients (1310 limbs) were identified retrospectively, with subsequent exclusion of three patients (four limbs) with no data for BMI. The patients were divided into three groups based on BMI as recommended by the World Health Organization (Fig. 1): $<$18.5 kg/m^2 (underweight, 188 patients, 219 limbs), 18.5 to 24.9 kg/m^2 (normal weight, 718 patients, 868 limbs), and $>$25.0 kg/m^2 (overweight/obese, 182 patients, 219 limbs). Weights and heights were measured at the time of admission.

Independent researchers collected demographic, angiographic, and procedural data from hospital charts or hospital databases according to pre-specified definitions. Follow up data were obtained from hospital charts or by contacting patients or referring physicians. The relevant review boards or ethics committees in all participating centers approved the study protocol. Written informed consent was obtained from each patient. This study is registered with the University Hospital Medical Information Network-Clinical Trial Registry (UMIN-CTR), as accepted by the International Committee of Medical Journal Editors (No. UMIN 000004917).

Endovascular intervention and follow up protocol

The EVT strategy was limited to the use of balloon angioplasty (without stenting), which was the only strategy permitted in Japan at the time of the study. Balloon angioplasty was performed with repeated dilation of each vessel by inflating optimally sized balloons for 1—3 min at nominal pressure. Satisfactory results were defined as persistent stenosis of $<$50% on angiography and achievement of one straight vascular route to the wound. Antiplatelet agents were administered prior to EVT and continued lifelong. Each patient was evaluated at 1, 3, and 6 months after EVT and then every 6 months after that. Repeat revascularization was performed when indicated by reappearance of symptoms with Rutherford[11] category 4, 5, or 6 and findings of ischemia with significant reduction of ankle-brachial index (ABI) or skin perfusion pressure.

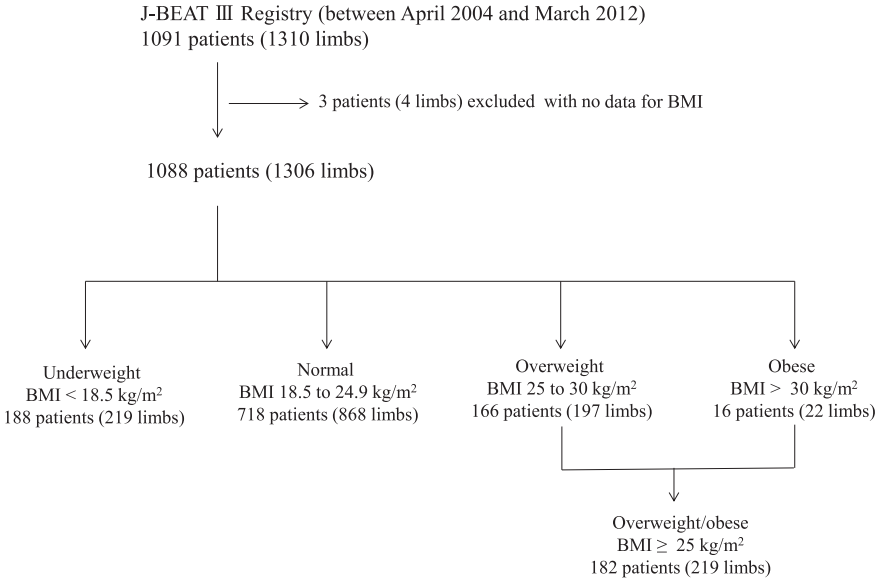

Figure 1. Patient flow charts. A total of 1091 consecutive patients (1310 limbs) who underwent endovascular treatment for isolated infrapopliteal artery lesions were identified retrospectively. Three patients (4 limbs) were excluded because they had no data for body mass index (BMI). The patients were divided into three groups based on BMI $<$18.5 kg/m^2 (underweight, 188 patients, 219 limbs), 18.5 to 24.9 kg/m^2 (normal weight, 718 patients, 868 limbs), and $>$25.0 kg/m^2 (overweight/obese, 182 patients, 219 limbs).