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PRS GLOBAL OPEN

ORIGINAL ARTICLE
Reconstructive

Coronary Artery Disease in Patients with Critical Limb Ischemia Undergoing Major Amputation or Not

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Background: Due to the increase of elderly and diabetes patients, surgeons encounter patients requiring treatment of critical limb ischemia (CLI) in the presence of systemic arteriosclerotic diseases. In this study, we retrospectively investigated the prevalence of coronary artery disease (CAD) in patients with CLI who underwent major (above-the-ankle) amputation or nonmajor amputation (below-the-ankle amputation or debridement of wound).

Methods: We retrospectively investigated 129 consecutive patients surgically managed for CLI in our institution between January 2013 and December 2015. The prevalence of CAD was defined as a cardiac treatment history or significant vascular stenosis (stenosis of > 75%). The outcomes were compared between patients who underwent major amputation (n = 36) and nonmajor amputation (n = 93). Additionally, archived record of 566 patients treated nonsurgically by percutaneous transluminal angioplasty in our institution was investigated to evaluate patients with milder peripheral artery disease.

Results: CAD was present in 83 patients (69%), including 82% of patients who underwent major amputation and 63% of nonmajor amputation group. The prevalence of CAD was significantly higher in the major amputation group ($P = 0.042$). Ejection fraction was not significantly different ($P > 0.05$). Among the 566 CLI patients treated by only percutaneous transluminal angioplasty, 227 (40%) had CAD, which was a significantly lower prevalence than those surgically treated ($P < 0.001$).

Conclusions: The presence of CAD is more frequent in CLI patients who require extended surgical management of the limb than in those who do not. Evaluation of CAD and careful perioperative management are important for patients with CLI patients. *(Plast Reconstr Surg Glob Open 2017;5:e1377; doi: 10.1097/GOX.0000000000001377; Published online 28 June 2017.)*

INTRODUCTION

The prevalence of peripheral arterial disease (PAD) ranges from 3% to 10% worldwide and has been increasing due to progressive growth in the older population, changes in dietary habits, and the increasing incidence of diabetes.[1,2] PAD is often associated with other critical arteriosclerotic diseases, such as coronary artery disease (CAD) or cerebrovascular disease (CVD). High prevalence of CAD in PAD patients has been reported previously.[3,4] This pathologic state is the main cause of death in patients with critical limb ischemia (CLI).[5] Most patients with advanced CLI already exhibit dermatologic ulcerative lesions that require surgical management; these lesions are classified as "Rutherford grade 5.6"[6] and have a high risk of complications accompanying critical arteriosclerotic diseases. Severity of PAD is supposed to be associated with severity of systemic arteriosclerotic state and prevalence of CAD. We must conduct careful perioperative management in patients with severe PAD. However, only a few reports have addressed the prevalence of CAD and CVD of patients with CLI who underwent surgical management, with little evidence of correlation between PAD severity and prevalence of CAD.

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Received for publication March 14, 2017; accepted April 24, 2017.

DOI: 10.1097/GOX.0000000000001377

Disclosure: *The authors have no financial interest to declare in relation to the content of this article. There were no funding sources for this study. The Article Processing Charge was paid for by the authors.*

In our institution, the vascular circulation of almost all patients with CLI is examined preoperatively using cardiac ultrasonography and/or cardiac angiography. We hypothesized that patients who have undergone major amputation have a higher prevalence rate of CAD than do patients who have undergone minor amputation or surgical debridement. The purpose of this retrospective study was to compare the prevalence of CAD in patients with CLI who underwent lower limb amputation, debridement of the limb wound, or percutaneous transluminal angioplasty (PTA).

METHODS

Study Population

This study followed the principles outlined in the Declaration of Helsinki and was approved by the Institutional Ethics Committee of our hospital. Retrospective analyses were performed on a consecutive series of 129 patients with CLI who were surgically managed from January 2013 to December 2015 in our institution. Cardiac ultrasonography or angiography was performed before the surgical treatment. The patients were classified into 2 groups: major amputation group (above-the-ankle amputation, n = 36) and nonmajor amputation (below-the-ankle amputation or debridement of the wound, n = 93). We investigated age, sex, clinical history, smoking habit, follow-up period, and the prevalence of CAD and/or CVD. Additionally, we evaluated the prevalence of CAD and/or CVD in 566 patients with PAD who underwent PTA without surgical treatment in our institution to evaluate patients with milder PAD.

Study Endpoints and Definitions

The primary endpoint of our study was to analyze the prevalence of CAD in our CLI patients. The presence of CAD was defined as a cardiac treatment history or significant vascular stenosis (stenosis of > 75%). A cardiac treatment history was defined as receiving medication for symptoms of myocardial ischemia, such as oral or sublingual nitrates, or having a history of percutaneous coronary intervention or coronary artery bypass grafting. Presence of CVD wad defined as experiencing episodes of cerebral hemorrhage or cerebral infarction. Major amputation was defined as amputation of the lower limb proximal to the ankle (above-the-ankle amputation), and nonmajor amputation was defined as either amputation of the lower limb distal to the ankle (below-the-ankle amputation) or surgical debridement of the wound.

Statistical Analysis

Continuous data are expressed as mean with SD, and categorical data are summarized as frequency (%). Group comparisons were performed using Student's *t* test, the chi-square test, or Fisher's exact test as appropriate. All statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, N.C.). A value of $P < 0.05$ was considered significant.

RESULTS

There were no significant differences between the major (n = 36) and nonmajor (n = 93) amputation groups in age, sex, smoking habit, or other investigation items as baseline characteristics (Table 1). The mean follow-up period from surgical intervention was 12.5 months (range, 1–29 months) in the nonmajor amputation group and 14.8 months (range, 1–34 months) in the major amputation group, with no significant difference ($P = 0.18$).

Among the 129 CLI patients with surgical treatment, 121 patients had undergone cardiac angiography or percutaneous coronary intervention. CAD was present in 83 of the 121 patients (69%), including 82% in the major amputation group (28 of 34 patients) and 63% in the nonmajor amputation group (55 of 87 patients), showing a significantly higher prevalence rate of CAD in the major amputation group ($P = 0.042$; Table 1; Fig. 1). No significant difference was found in the cardiac ejection fraction between the 2 groups. Among the 566 patients with PAD who did not undergo surgical treatment for CLI but underwent PTA, 227 (40%) had CAD, which was a significantly lower prevalence than those surgically treated ($P < 0.001$; Fig. 1).

DISCUSSION

The important outcome of this study was that the prevalence of CAD was significantly higher in the major than nonmajor amputation group. It appears that the risk of CAD was correlated with the severity of limb ischemia. Careful perioperative management is required for major amputation in CLI.

Cardiac function has been considered to have a marked impact on the prognosis of patients with CLI.[7] In an epidemiological investigation that was based on the international Reduction of Atherothrombosis for Continued Health (REACH) Registry involving 68,000 patients in 44 countries, including patients with atherothrombosis or with 3 or more risk factors for atherothrombosis, there were 7,013 patients with PAD with either CAD (53.6%), CVD (23.7%), or both CAD and CVD (14.2%).[8] Furthermore, the Bypass and Endovascular therapy Against Critical limb ischemia from Hyogo (BEACH) Registry of the Japanese population of 459 patients with CLI after undergoing revascularization (Rutherford grade 4–6) showed that the prevalence of CAD was 41.1%.[9] As shown in Fig. 1, comparison of the CAD prevalence among the above-mentioned published reports and our study indicates a significantly higher prevalence of CAD in our patients who underwent surgical intervention, especially in the major amputation group. Lee et al.[10] reported that cardiac angiography examination of 252 patients with CLI showed severe CAD in 57.5% of patients (stenosis of ≥ 70%), and their patients with CAD showed a mean ejection fraction of 53% ± 10%. Our patients had higher prevalence of CAD and lower mean ejection fraction (Table 1), suggesting that CAD is more severe in patients with CLI who require surgical management than in those for whom surgical management can be avoided.

Table 1. Baseline Characteristics and the Prevalence of Coronary Artery Disease and/or CVD in Patients with CLI

Variables	All Patients (n = 129)	With Major Amputation (n = 36)	Without Major Amputation (n = 93)	*P**
Age (y), mean ± SD	74±11	73±12	74±10	0.764
> 75	57 (44)	16 (44)	41 (44)	0.971
Sex				
Male	89 (69)	27 (75)	62 (67)	0.359
Smoking				
No	42 (33)	11 (31)	31 (33)	0.828
Previously yes	28 (22)	7 (19)	21 (23)	
Currently yes	59 (46)	18 (50)	41 (44)	
BMI (kg/m^2), mean ± SD	20.6±4.3	20.1±5.3	20.8±3.8	0.396
Comorbidities, n (%)				
Chronic kidney disease—yes	91 (71)	25 (69)	66 (71)	0.865
Dialysis—yes	76 (59)	24 (67)	52 (56)	0.266
Hypertension—yes	97 (75)	25 (69)	72 (77)	0.347
Dyslipidemia—yes	58 (45)	16 (44)	42 (45)	0.941
Diabetes—yes	92 (71)	27 (75)	65 (70)	0.565
Albumin (g/dL), mean ± SD	3.3±0.7	3.2±0.8	3.4±0.6	0.056
HbA1c (%), mean ± SD	6.9±1.8	6.6±1.3	7.0±1.9	0.187
Multiple drug-resistant bacteria present—yes	45 (35)	9 (25)	36 (39)	0.143
Variables	**All Patients (n = 121)**	**With Major Amputation (n = 34)**	**Without Major Amputation (n = 87)**	***P****
CAD—yes	83 (69)	28 (82)	55 (63)	0.042
CVD—yes	43 (33)	10 (28)	33 (35)	0.405
EF (%), mean ± SD	49.4±14.6	48.1±15.8	49.9±14.1	0.536
< 50%	59 (46)	20 (56)	39 (42)	0.164

Eight of 129 patients with CLI with surgical treatment lack cardiac angiography data or percutaneous coronary intervention data. The prevalence of CAD and/or CVD was calculated in 121 patients. Data are presented as the mean ± SD or the number (%) unless otherwise indicated.
*Analyzed by Student's *t* test for continuous data and by the χ^2 test for categorical data.
BMI, body mass index; HbA1c, hemoglobin A1c; EF, ejection fraction.

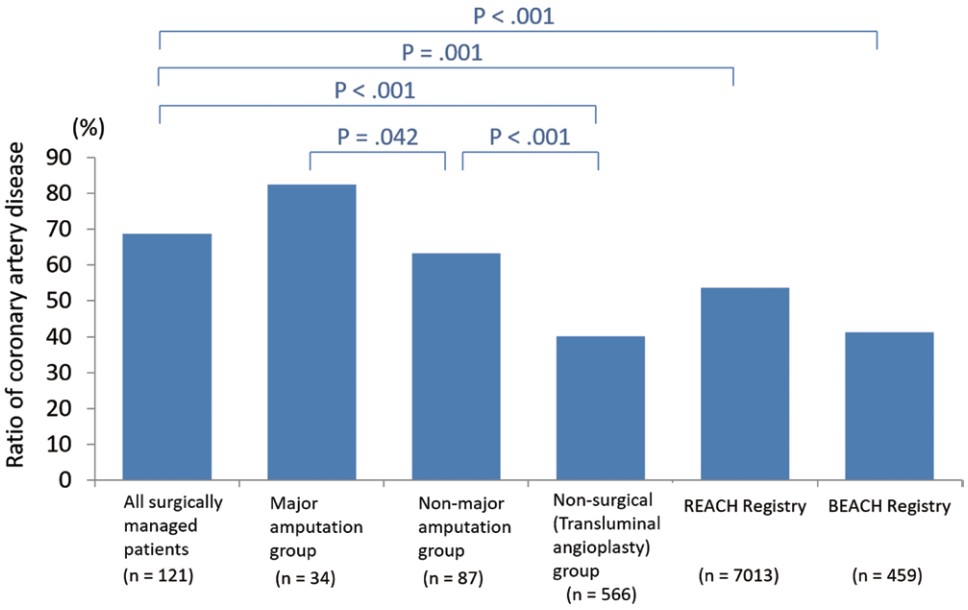

Fig. 1. Comparison of the prevalence of coronary artery disease. Comparisons were done among surgically managed patients (all patients, major amputation group, and nonmajor amputation group), nonsurgically managed PAD patients (PTA group), patients in the REACH Registry, and patients in the BEACH Registry.

The prevalence of CAD in the nonmajor amputation group was significantly higher than that in patients who did not undergo surgical treatment but PTA ($P < 0.001$; Fig. 1). Therefore, even in patients treated by minor amputation or debridement for a localized lesion, careful perioperative management is considered necessary with attention to signs of complications. Based on the findings of published articles and the present study, we consider that detailed cardiac evaluations including cardiac ultrasonography or angiography are necessary for patients with CLI in whom surgical management is to be performed. Cardiac examination data will markedly help in selecting the order of treatment (conduct percutaneous coronary intervention or bypass surgery beforehand or not), appropriate anesthesia method (general anesthesia, lumbar anesthesia, nerve block, or

local anesthesia), optimum surgical method, and perioperative management method. Lee et al.[10] recommended a screening examination using cardiac angiography for patients with CLI. Of their 167 patients with CAD, 78.6% underwent percutaneous coronary intervention in their report. Collaboration between surgeons and cardiologists, including sharing detailed data on cardiac function and CAD, is considered necessary for management of patients with CLI because follow-up treatment may extend over a long period after invasive surgery to save lives and limbs.

This study has several limitations. First, this was a nonrandomized, single-center study with a relatively small number of patients. Second, excluding the BEACH Registry data, differences exist among countries with respect to the definition of CAD, data collection timing, and patients' Rutherford grades, as well as ethnic and life environments. Additionally, adjustment for background factors for a more accurate comparison was not possible because individual data of other researchers' reports were not accessible. A multi-institutional study involving a larger number of patients is therefore desired to confirm whether the findings of the present study can be generalized.

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