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Prevalence of Peripheral Arterial Disease in Patients With Diabetic Charcot Neuroarthropathy

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ABSTRACT

Charcot neuroarthropathy (CN) is a serious complication of diabetes mellitus (DM) that can lead to pedal ulceration, infection, hospitalization, and amputation. Peripheral arterial disease (PAD) is also found in patients with diabetic foot disease; however, its prevalence in patients with CN has not been extensively evaluated. The aim of the present study was to evaluate the prevalence of PAD in a group of patients with CN (with and without ulceration) and compare this to a group of patients with diabetic foot ulceration (DFU) and no CN. We compared the lower extremity noninvasive arterial testing results of 85 patients with DM and CN with those from a group of 126 patients with DFU and no CN. No statistically significant differences were found in age, gender, type of DM (1 versus 2), insulin use, duration of DM, or history of dialysis between our study and control groups. The prevalence of PAD in the patients with CN was 40%. Compared with patients with DFUs, the patients with CN were less likely to have PAD (odds ratio 0.48, 95% confidence interval 0.28 to 0.85; $p = .0111$), ischemia (odds ratio 0.33, 95% confidence interval 0.16 to 0.69; $p = .0033$), or the need for revascularization (odds ratio 0.27, 95% confidence interval 0.10 to 0.73; $p = .0097$). Critical limb ischemia (great toe pressure <30 mm Hg) was 82% less likely in patients with CN than in patients with DFU. PAD in patients with CN is not uncommon; however, ischemia and the need for revascularization were significantly less likely than in patients with DFU without CN.

Charcot neuroarthropathy (CN) is a serious complication of diabetes mellitus (DM) associated with premature mortality and negative effects on quality of life and lower extremity function (1–3). This osseous destructive process can result in foot deformity, ulceration, infection, hospitalization, and, in some cases, major amputation (4,5). Patients with DM are also at increased risk of developing peripheral arterial disease (PAD). It has been estimated that the prevalence of PAD in patients with DM aged >40 years is approximately 10% compared with 5% in the general population (6). Patients with diabetic foot disease have a greater prevalence of PAD, with rates as great as 50% (7,8). To the best of our knowledge, few studies have examined the prevalence of PAD in diabetic patients with CN. PAD can vary in severity, ranging from no ischemia to critical limb ischemia (9). The aim of the present study was to evaluate the prevalence of PAD and associated ischemia in a group of patients with CN. A secondary goal was to compare the prevalence of PAD in patients with CN with that of a group of patients with diabetic foot ulceration (DFU) and no CN.

Patients and Methods

The institutional review board approved the present study. A retrospective review of the data from patients with DM and CN or DFU who had undergone lower extremity noninvasive arterial testing was performed. The studies were performed from November 1, 2010 through June 30, 2015. During the study period, the patients were referred for noninvasive arterial testing if they had had abnormal vascular examination findings, had presented with a new DFU, or had been scheduled to undergo reconstructive surgery for CN. Thus, this cohort of patients did not represent a consecutive series. The diagnosis of CN was determined from clinical and radiographic findings (4). Patients were excluded if they had incomplete noninvasive studies and/or had undergone previous great toe amputation, precluding measurement of the great toe pressure. A complete set of studies included the bilateral ankle-brachial index (ABI), toe brachial index (TBI), absolute great toe pressure measurement, and Doppler wave form analysis. All the studies were performed by certified vascular technologists in certified vascular laboratories. Official interpretation of the studies was performed by vascular surgeons, radiologists, and cardiologists, depending on the site of the vascular laboratory. All patients underwent a detailed lower extremity physical examination and weightbearing radiographs of the foot and ankle. Palpation of the dorsalis pedis and

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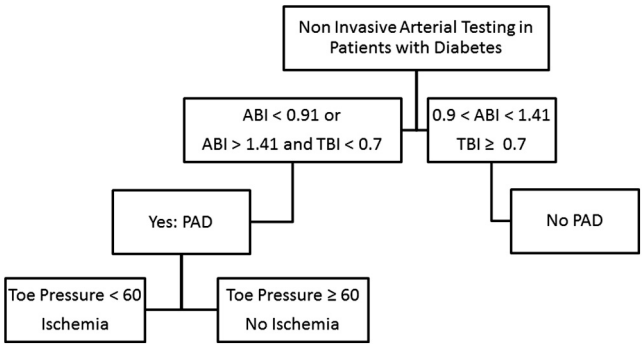

Fig. 1. Flow chart illustrating the diagnosis of peripheral artery disease (PAD) using noninvasive arterial testing. ABI, ankle-brachial index; TBI, toe brachial index.

posterior tibial pulses was performed and were documented as palpable or non-palpable. If all 4 pulses were palpable, the clinical vascular examination findings were considered normal. The inability to palpate ≥1 of the 4 pulses was considered an abnormal finding. Peripheral neuropathy was assessed using the Michigan neuropathy screening index, which includes Semmes-Weinstein monofilament examination, vibratory sensation testing with a 128-Hz tuning fork, Achilles reflex evaluation, the presence or absence of pedal deformity, and the presence or absence of ulceration (10). The demographic data, tobacco use, need for vascular intervention, and a history of infection were recorded for all patients. An ABI of 0.91 to 1.40 was considered normal, and values >1.4 were defined as noncompressible (8,11–14) (Fig. 1). The highest systolic pressure of the dorsalis pedis or the posterior tibial pulse was used to calculate the ABI. A normal TBI was defined as ≥0.70 (8,11,14–18) (Fig. 1). PAD was diagnosed in the presence of an ABI of <0.9 or a TBI of <0.7 on either extremity (8,14,16,17,19,20). Ischemia was defined according the criteria by Mills et al (9) and included 4 grades: no ischemia (great toe pressures ≥60 mm Hg), mild ischemia (great toe pressures of 40 to 59 mm Hg), moderate ischemia (great toe pressures of 30 to 40 mm Hg), and severe ischemia (great toe pressures of <30 mm Hg). Critical limb ischemia was defined as a great toe pressure of <30 mm Hg. For the purposes of the present study, the patients were divided into 2 groups. The study group consisted of patients with CN, with and without plantar ulceration secondary to the bony deformity. The control group included patients with DFU and no radiographic evidence of CN deformity.

The Shapiro-Wilk test was used to determine the normality of the continuous variables. For continuous values with a normal distribution, the mean values ± standard deviation were calculated, and the difference between groups was assessed using the 2-sample *t* test. Non-normally distributed data are reported as the median and interquartile range, and the difference between groups was assessed using the Wilcoxon-Mann-Whitney tests. Frequency distributions of the categorical variables between those with CN and DFU were compared using Pearson's chi-square tests or Fisher's exact tests, as appropriate. All tests were conducted with a significance level of 0.05. Odds ratios (ORs), with the corresponding 95% confidence intervals (CIs), were used to illustrate the magnitude of these associations. All analyses were conducted using SAS, version 9.4, statistical analysis software (SAS Institute Inc., Cary, NC).

Results

A total of 211 patients with DM and complete noninvasive arterial assessments were included in the present study. Our study group consisted of 85 patients with CN, and the control group included 126 patients with DFU and no CN (Table). Of the 85 patients in the CN study group, 59 (70.2%) had a history of ulceration and 26 (29.8%) had no history of ulceration. All the CN-related ulcers were contiguous with the osseous deformity. No statistically significant differences were found in age, gender, type of DM (1 versus 2), insulin use, duration of DM, or history of dialysis between our study and control groups (Table). No significant differences were found between the 2 groups when comparing the laboratory values such as hemoglobin A1c, random serum glucose, serum hemoglobin, and serum albumin levels (Table). Patients with DFU had a significantly greater mean serum creatinine than did patients with CN (1.1 versus 1.0 mg/dL; $p = .03$), although the rates of dialysis treatment and/or renal transplantation were not significantly different between the 2 groups (Table). Patients in the CN group had a significantly higher Michigan neuropathy screening index score ($p = .0003$) and higher body mass index ($p = .005$) than did the patients in the DFU group. Of the patients in the CN group, 62 (73.8%) were obese compared with 74 (62.2%) in the DFU group ($p = .0828$). Also, 28 patients (34.6%) in the CN group had a history of foot infection compared with 56 (52.8%) in the DFU group ($p = .0129$). A history of active or former tobacco use was reported by 21 of 85 patients (25.6%) with CN compared with 48 of 126 patients (39.7%) with DFU ($p = .0380$). No significant difference was found in the number of tobacco pack-years between the 2 groups ($p = .8442$).

Of the 85 patients in the CN group, 34 (40.0%) were diagnosed with PAD compared with 73 of 126 patients (57.9%) in the DFU group (OR 0.48, 95% CI 0.28 to 0.85; $p = .0111$). Of the 85 patients with CN, 11 (12.9%) had ischemia (defined as great toe pressure <60 mm Hg) compared with 39 of 126 patients with DFU (32.0%; OR 0.33, 95% CI 0.16 to 0.69; $p = .0033$; Fig. 2). Five of the 85 patients with CN (5.9%) had mild ischemia compared with 11 of the 126 patients with DFU (8.7%; OR 0.79, 95% CI 0.28 to 2.23; $p = .66$), and 3 of the 85 patients with CN (3.5%) had moderate ischemia compared with 11 of 126 patients with DFU (8.7%; OR 0.38, 95% CI 0.10 to 1.41; $p = .14$). Severe ischemia (i.e., critical limb ischemia) was present in 2 of 85 patients with CN (2.4%) compared with 17 of 126 patients with DFU (13.5%; OR 0.18, 95% CI 0.04 to 0.79; $p = .02$; Fig. 3). Five of the 85 patients (6.0%) in the CN group underwent either an open or endovascular revascularization procedure compared with 24 of 126 patients (19.5%) in the DFU group (OR 0.27, 95% CI 0.10 to 0.73; $p = .0063$). Of the 85 patients in the CN group, 74 (87.1%) had normal Doppler waveforms compared with 72 patients (57.6%) in the DFU group (OR 0.20, 95% CI 0.10 to 0.41; $p \leq .0001$). No significant difference was found between the patients with CN without a history of ulcer (11 of 26; 43.2%) and those with a history of foot ulcer (23 of 59; 39.0%; OR 1.14, 95% CI 0.45 to 2.93; $p = .77$). Also, 61 patients (71.7%) in the CN group had palpable dorsalis pedis and posterior pulses bilaterally compared with 67 (53.2%) in the DFU group (OR 0.45, 95% CI 0.25 to 0.80; $p = .0070$). Overall, 128 of the 211 combined patients (60.7%) had normal clinical vascular examination findings (i.e., all 4 pedal pulses were palpable), and 83 of the 211 patients (30.3%) had abnormal clinical vascular examination findings (absence of ≥1 of the 4 pulses). Sixty-four of 83 patients (77.1%) with abnormal clinical vascular examination findings had PAD compared with 43 of 128 patients (33.1%) with normal clinical vascular examination findings (OR 6.66, 95% CI 3.55 to 12.5; $p < .0001$).

Discussion

To the best of our knowledge, few published studies have evaluated the prevalence of PAD in patients with CN. The reported rates of PAD in patients with CN have ranged from 4.4% to 35.4% (21–24). Most of these studies did not specifically evaluate the prevalence of PAD but, rather, reported on a series of patients with CN (21–23). The precise definition of PAD was not well defined in these studies. Caravaggi et al (21) reported a rate of 4.4% and only included patients with critical limb ischemia using a threshold of transcutaneous oxygen pressure of ≤30 mm Hg. Another center published a case report and a series of 10 patients with critical limb ischemia and CN (25,26). All patients underwent endovascular revascularization, in addition to surgical reconstruction, achieving a limb salvage rate of 90%. Chantelau (22) reported a PAD rate of 12.5% in a study assessing the early diagnosis of CN; however, he did not define the method by which PAD was diagnosed. Sohn et al (23) reported that PAD was present in 26.9% of US military veterans with CN. That study also did not specify how PAD had been diagnosed. The only study we are aware of that specifically evaluated PAD in patients with CN was presented by Bem et al (24). The investigators evaluated 82 diabetic patients with "ulcerated