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ScienceDirect

Journal of the Chinese Medical Association 81 (2018) 565−570

www.jcma-online.com

Original Article

Angiographic assessment of atherosclerotic load at the lower extremity in patients with diabetic foot and charcot neuro-arthropathy

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Received May 28, 2017; accepted September 15, 2017

Abstract

Background: The aim of this study was to investigate atherosclerotic load at the lower extremity in patients with diabetic foot and charcot neuro-arthropathy and compare them with patients with diabetic foot without charcot neuro-arthropathy.
Methods: This retrospective study consists of 78 patients with diabetic foot who had lower extremity angiography with antegrade approach. All patients were classified into two groups; neuro ischemic wounds with charcot neuro-arthropathy (30/78) and without charcot neuro-arthropathy (48/78).Atherosclerotic load at the side of diabetic foot was determined by using the Bollinger angiogram scoring method. Comparison of atherosclerotic load between the two groups was performed.
Results: The mean of total and infrapopliteal level angiogram scoring of all patients was 33.3 (standard deviation, sd:±17.2) and 29.3 (sd:±15.6), respectively. The mean of total and infrapopliteal level angiogram scoring of neuroischemic wounds with charcot neuro-arthropathy group was 18.1 (sd:±11.6) and 15.7 (sd:±10.4), respectively. The mean of total and infrapopliteal level angiogram scoring of neuroischemic wounds without charcot neuro-arthropathy group was 42.8 (sd:±12.7) and 37.7 (sd:±12.0), respectively. There was a statistically significant difference between the two groups of mean total and infrapopliteal angiogram scoring ($p < 0.01$).
Conclusion: This angiographic study confirms that the atherosclerotic load in patients with diabetic foot and chronic charcot neuro-arthropathy is significantly less than in patients with neuroischemic diabetic foot wounds without chronic charcot neuro-arthropathy.

Keywords: Angiography; Atherosclerosis; Charcot neuro-arthropathy; Diabetic foot

1. Introduction

Foot complications associated with diabetes have a prevalence of 15%−20% in all patients with diabetes and remain the most common cause of nontraumatic amputations of the lower extremity.[1] Charcot neuro-arthropathy (CN) is a progressive disease affecting the bones, joints and soft tissue of the foot and ankle. Of all patients with diabetes, 0.1−7.5% have CN and 29% of patients with diabetes and peripheral neuropathy have CN.[2,3] CN can lead to severe and debilitating structural deformity of the foot.[4] Atherosclerotic peripheral arterial disease (PAD) is a group of disorders characterized by narrowing or occlusion of the arteries resulting in gradual reduction of blood supply to the limbs. Patients with diabetic foot disease have a greater prevalence of atherosclerotic PAD,

Conflict of interest: The authors declare that they have no conflict of interest related to the subject matter or materials discussed in this article.

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https://doi.org/10.1016/j.jcma.2017.09.006

especially infrapopliteal arterial stenosis and occlusions which are more severe in patients with diabetes. Due to the natural course of diabetes mellitus, PAD can be expected in CN cases. Until today, few studies have examined the prevalence of atherosclerotic PAD in patients with diabetes and CN.[5,6] To our knowledge, there have been no studies that have specifically evaluated the pattern and quality of PAD in this population. Additionally, none have focused on the atherosclerotic load in patients with diabetes and CN by using angiography. Bollinger et al. described an angiogram scoring method for assessment of lower limb atherosclerosis, including scoring for plaques, stenoses and occlusions.[7] The Bollinger angiogram scoring method is suitable for differentiating the severity of atherosclerotic PAD, especially in infrapopliteal arteries (see Fig. 2).[8]

The Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL) trial used the Bollinger score system to analyze arterial atherosclerotic load in limb ischemia patients. In this trial, mean below-knee Bollinger angiography score that was shown atherosclerotic load, was found as an independent risk factor for both time to death after operation and amputation-free survival.[9,10] Also, technical success rates of infrapopliteal angioplasty were depended to atherosclerotic load in patients with PAD.[11] Although emphasis of atherosclerotic load has been demonstrated in treatment of patients with PAD, the effect of atherosclerotic load in patients with CN is unknown yet.

In this study, we aimed to investigate the atherosclerotic load at the lower extremity using the Bollinger angiogram scoring method in patients with diabetic foot wounds and chronic CN and compare them with patients who had diabetic foot wounds without chronic CN.

2. Methods

2.1. Study population and design

We abstracted the medical records of people with diabetic foot wounds receiving lower extremity conventional angiography imaging from the Radiology Service database of a single academic medical center. After institutional review board approval, imaging data between October 2014 and March 2016 were evaluated. There were 125 angiography studies with evaluable foot radiographs performed at our institution for evaluation of diabetic foot during the study period. Modified Eichenholtz classification system[12] was used for CN and chronic CN diagnosis was made with clinical such as decreased or absent warmth, edema and erythema and plain radiography such as: remodeled and new bone formation, decreased osteosclerosis and/or possible gross residual deformity.

2.2. Patient inclusion criteria

Patients with diabetes and foot ulceration or gangrene who had angiography with antegrade approach and who had plain radiography of the foot and clinical data for CN were included in this study. All patients had undergone magnetic resonance angiography (MRA) before conventional angiography for confirming peripheral arterial disease.

2.3. Patient exclusion criteria

Patients with diabetic foot and without any peripheral arterial disease suspicion at MRA, patients whose data

Fig. 1. Sixty year old male who had diabetic foot and charcot neuro arthropathy at talonavicular, calcaneo-cuboid joints. Also lateral radiography shows subluxation of cuboid.

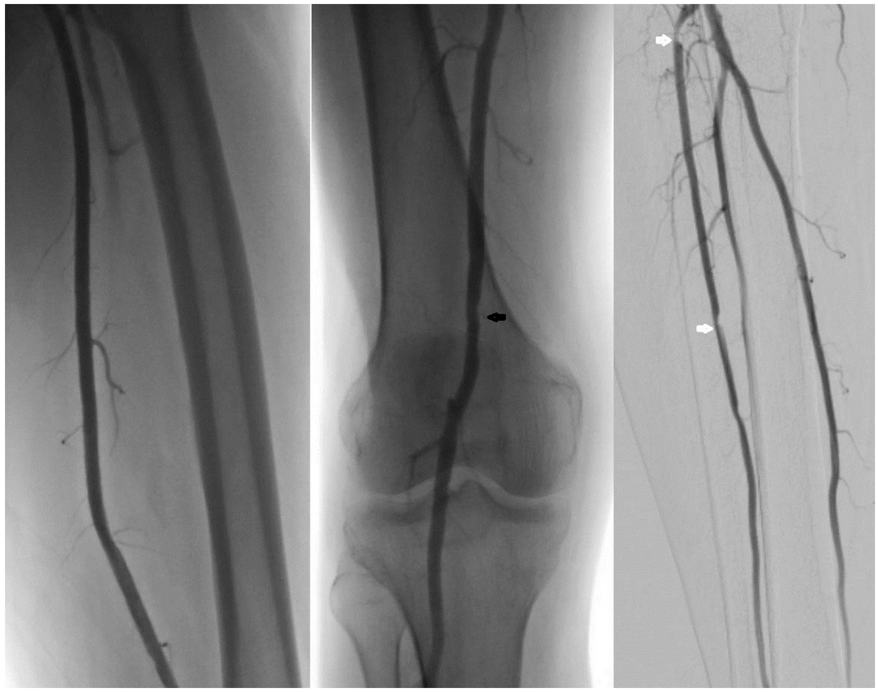

Fig. 2. Conventional angiogram of the patient in Fig. 1. Popliteal artery has plaques (black arrow) and there are stenoses at tibialis anterior artery (white arrows). Patients' angiogram score was 12.

constituted any intervention before angiography, who did not have plain radiography of the foot and who had suspicion of acute CN, acute or chronic osteomyelitis, cellulitis, septic arthritis or other inflammatory arthritis.

2.4. Interventional procedure

Interventions were performed mainly by an antegrade approach from the superficial artery under ultrasound guidance and with the use of 5-French sheaths. The contrast material was 300 mg/ml iodinized contrast agent, average contrast amount was 25 cc, injected by hand via the sheath. Infrapopliteal arteries were scanned by digital subtraction angiography. All procedures were performed by a single interventional radiologist with more than 20 years of experience in peripheral vascular intervention. Following the removal of the vascular sheath, hemostasis was achieved by manual compression. If there was a hemodynamically significant stenosis or occlusion at any part of the artery, percutaneous treatment was applied after obtaining patient permission. All patients were observed on the surgery ward for two or three hours and were discharged if no acute complications (bleeding or thrombosis) were detected.

2.5. Imaging analysis

All angiographic images and plain radiographies transferred from the radiology database were evaluated in the workstation by a radiologist with 14 years of experience. Patients were divided into two groups: with CN group and without CN group according to clinic and plain radiography of the foot. A scoring system, originally developed by Bollinger et al.,[7] was used to assess the angiographies. This system consists of an additive score describing the severity of the lesions visualized within each segment of the artery. Each of these segments was scored according to the severity and extent of disease (Table 1). Four severities of lesion are characterized in the Bollinger angiogram scoring method; occlusion of the lumen, stenosis ≥50% of the luminal diameter, stenosis <50% but >25%, and plaques impinging ≤25% of the diameter. Each type of lesion is further categorized as follows by its extent as single lesion, multiple lesions affecting less than half of the segment, and multiple lesions affecting more than half of the segment. To calculate the additive scores, the individual scores for each of the three lesion severities are summed in accordance with the rules as; in the presence of occlusions, stenoses and plaques are not considered, when both severities of stenoses are present

Table 1
Bollinger scoring matrix[a].

Occlusion	Stenosis >50%	Stenosis<50%	Plaques	Location
	4	2	1	Single
13	5	3	2	Multiple <h
15	6	4	3	Multiple >h

h = half the segment length.

[a] The vertical columns represent the different severities of atherosclerotic lesions observed, the horizontal ones the location of the lesions detected in each of the arterial segments. The numbers appearing in the single field correspond to the score numbers. The additive score for each artery is obtained by adding the scores (see text for details).

plaques are not considered, for each severity of disease, only one extent of disease category is scored. Two suprapopliteal level as; superficial femoral artery, popliteal artery and four infrapopliteal level arterial segments as; tibioperoneal trunk, anterior tibial artery (ATA), posterior tibial artery (PTA), peroneal artery (PRA) were assessed. Total angiogram scores were calculated as the sum of suprapopliteal and infrapopliteal level arteries angiogram scores. The results for all patients were studied in order to assess intra-observer reliability of the scoring method. Angiographic images for each patient was studied more than twice after a one-week interval, and the reliability of each patient's score confirmed.

2.6. Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 17.0 statistical software for Windows (SPSS Inc, Chicago, IL, USA). Comparisons between patients with and without Charcot neuro-arthropathy were performed using Student's *t*-test for continuous variables and the $\chi 2$ test for discrete variables. P values < 0.05 were considered statistically significant.

3. Results

In the study period, 125 angiographies were performed in patients with diabetic foot, but 78 patients met inclusion and exclusion criteria. Thus, the study consists of 78 patients with diabetic foot. Of these patients, 59 (75.6%) were men and 19 (24.3%) were women with a mean age of 66.4 years (range 51−84). The mean of disease (diabetus mellitus) duration of all patients was 22.2 years (range 8−32). The most common comorbid disease was chronic renal insufficiency (30.8%). Angiographic images of all patients consisted of 10 (12.8%) with only stenosis and 59 (75.6%) which had stenosis with occlusion. The mean of total angiogram scoring was 33.3 (standard deviation, sd:±17.2) in all patients.

Based on infrapopliteal artery occlusions; only one artery occlusion was seen in 24 (30.8%) patients, 29 (37.2%) patients had two artery occlusions, and 8 (10.3%) patients had three artery occlusions. ATA was the most affected artery in all patients (23.1%). ATA and PTA were the most affected binary arteries (17.9%). The mean of infrapopliteal angiogram scoring was 29.3 (sd:±15.6) in all patients.

All patients were classified into two groups. These were the diabetic foot with CN group (30/78) and diabetic foot without CN group (48/78).

3.1. Diabetic foot with CN group

30 (38.5%) patients with diabetic foot with CN underwent conventional angiography. CN was in the right foot in 12/30, left foot; 15/30 and bilateral; 3/30. The mean of total angiogram scoring of this group was 18.1 (sd:±11.6) and the mean of infrapopliteal level angiogram scoring was 15.7 (sd:±10.4) in all patients. There was no statistically significant difference of angiogram scoring according to side of foot (p:0.82).

3.2. Diabetic foot without CN group

48 (61.5%) patients with diabetic foot without CN underwent conventional angiography. The mean of total angiogram scoring of this group was 42.8 (sd:±12.7). The mean of infrapopliteal level angiogram scoring of this group was 37.7 (sd:±12.0).

There was no statistically significant difference between patient age, gender, diabetic disease duration and comorbid disease such as chronic renal insufficiency, hypertension and coronary artery disease, of the two groups ($p > 0.05$). Demographic characteristics of the patients were demonstrated in Table 2. There was a statistically significant difference between the mean total and infrapopliteal angiogram scoring ($p < 0.01$) of the two groups (Table 3). In both groups, a total of 52 patients who had stenosis and/or occlusions were treated with percutaneous transluminal angioplasty successfully. Others were referred to surgery.

4. Discussion

This study focused on the angiographic load of lower limb atherosclerosis, comparing patients who had neuroischemic and ischemic diabetic foot ulcers, with and without CN. The severity of atherosclerotic lesions was evaluated using Bollinger angiogram scoring.[7] To the best of our knowledge, no published study has evaluated load of atherosclerosis in patients with diabetes and CN. This study demonstrates that patients with neuroischemic or ischemic diabetic foot ulcers and without CN have a significantly higher atherosclerotic load than patients with diabetes and chronic CN. This fits well with general observations regarding people with and without CN.

Diabetes mellitus (DM) has particular effects on the musculoskeletal system, especially the foot.[13] Vasculopathy, neuropathy, and infection are the three major pathological processes that lead to the development of diabetes-related foot complications.[14] CN is a condition associated with peripheral neuropathy, and is characterised by bone and joint fracture,

Table 2
Demographic characteristics and occlusive artery numbers of diabetic patients with Charcot neuro-arthropathy and without Charcot neuro-arthropathy.

	Diabetic foot with CN	Diabetic foot without CN
n (%)	30 (38.5%)	48 (61.5%)
Gender (% male)	24 (80%)	35 (72.9%)
Age (years)	65.5 ± 7.5*	67 ± 8.61
Disease duration (years)	23.4 ± 11.6	21.2 ± 13.1
Comorbid	11 (36%)	18 (37.5%)
Chronic renal insufficiency	6 (20%)	8 (16.7%)
Coronary artery disease	5 (16.6%)	8 (16.7%)
Hypertension		
Occlusive artery number	17 (100%)	45 (100%)
One artery occlusion	12 (40%)	12 (25%)
Two artery occlusion	5 (16.7%)	24 (50%)
Three artery occlusion	1 (3.3%)	7 (14.6%)
Four ≤ artery occlusion	0	2 (4.2%)

n = number, CN = Charcot neuro-arthropathy, * mean ± standard deviation.

Table 3
Comparison of Bollinger angiogram scores in diabetic foot with Charcot neuro-arthropathy and without charcot neuro-arthropathy group patients by arterial segments.

	Diabetic foot with CN (n:30	Diabetic foot without CN (n:48	*p*
Total AS	18.1 ± 11.6*	42.8 ± 12.7	< 0.001
Suprapopliteal AS	2.60 ± 3.40	5.31 ± 3.19	0.001
Superficial Artery AS	1.7 ± 2.58	2.92 ± 1.86	0.030
Popliteal Artery AS	0.97 ± 1.62	2.44 ± 2.47	0.002
Infrapopliteal AS	15.7 ± 10.4	37.7 ± 12.0	< 0.001
Tibioperoneal trunk AS	0.53 ± 1.19	4.92 ± 5.25	< 0.001
Anterior tibial artery AS	5.60 ± 5.44	10.33 ± 4.91	< 0.001
Posterior tibial artery AS	6.27 ± 5.71	12.38 ± 4.19	< 0.001
Peroneal artery AS	2.90 ± 4.08	9.83 ± 5.63	< 0.001

AS = Angiogram score, n = number, * mean ± standard deviation.

dislocation, instability and gross deformities.[15] In patients who develop ulcers, the risk of amputation is high, and below the knee amputation is often indicated.[16] Acute CN patients are often misdiagnosed as having osteomyelitis, cellulitis, deep venous thrombosis, or gout.[17] Although plain radiography is the primary initial imaging method for evaluation of the foot in diabetic patients, it can often be normal in acute stage of CN. Magnetic resonance imaging and positron emission tomography scanning of foot are being accepted as a solution for differential diagnosis.[18,19] Plain radiographs are valuable in the chronic CN and only chronic CN patients with diabetic wound were included in this study.

Atherosclerosis is also a serious and frequent problem in DM. Atherosclerotic PAD manifests as critical limb ischemia (CLI), characterized by ischemic rest pain and/or tissue loss. CLI is one of the other causes of lower limb amputation in patients with diabetes.[20] CLI can be defined as a serious PAD and if left untreated, the natural history of it is a 25%–45% chance of major amputation.[21] Arterial imaging is challenging in diabetic patients because the disease is often multisegmental with a predilection for the infrapopliteal arteries. Conventional angiography, MRA and computerized tomographic angiography have been used as imaging modalities in lower extremity ischemia. Conventional angiography provides the highest degree of spatial resolution and image quality. Also, conventional angiography is the best method for to determine atherosclerotic load in arteries. In present study, the Bollinger angiogram scoring method was used to determine the load of atherosclerosis in the lower extremity. This method was found suitable for showing the load of atherosclerosis.[8] Patients with diabetes and Charcot deformity associated with atherosclerotic PAD also have a major risk of ulceration and infection. Although complications of the foot in diabetes in which relative ischemia is a common contributing factor,[18] there was no sufficient information between CN and arterial supply to the foot. Few published studies have evaluated the prevalence of PAD in patients with CN.[5,6] PAD was identified in 40% of patients with CN, although ischemia was present in only 13% using the criteria defined by the Society of Vascular Surgery.[22] In only one study, diagnosis of PAD was determined from the angiographic findings. That study demonstrated that patients with foot ulcers without CN had a PAD rate of 48% compared with a rate of 35.4% in patients with ulcerated CN, but load of atherosclerotic PAD was not shown in that study. Recently, Wukich et al.[5] have shown that ischemia and the need for revascularization were less in patients with diabetic foot ulceration without CN by using lower extremity noninvasive arterial tests such as the bilateral ankle-brachial index (ABI) and toe brachial index. Although ABI measurements are recommended for screening and determining PAD, but ABI falsely elevated because of their noncompressible vessels caused by medial artery calcinosis (MAC) in diabetes.[23] Also, in recent years, an association among CN and MAC has also been established.[5]

The pathogenesis of CN remains poorly understood. More recently, Jeffcoate et al. suggested that acute CN is characterized by an overly aggressive inflammatory response that results in edema, osteolysis, joint destruction, and deformity.[24] Adequate perfusion is necessary to permit the development of inflammation. So in acute CN, the load of atherosclerosis may be low, but in this study we evaluated only chronic CN and we found significantly lower atherosclerosis load in diabetic patients with CN.

The limitations of this study are retrospective design and a relatively small number of patients because of constrictive inclusion and exclusion criteria. We also evaluated only one extremity that had diabetic ulcer and gangrene and seven arterial segments because of antegrade approach of angiography technique.

In conclusion, this study showed us that the atherosclerotic load in patients with diabetic foot and chronic CN is significantly less than in patients with diabetic foot without chronic CN. Also, this finding suggests us that inflammatory response may be not only in the acute phase but also in the chronic phase of CN. However further studies are needed to confirm our findings.

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