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Peripheral Artery Disease Severity in Diabetic patients with and without Chronic Renal Failure: An Angiographic Study

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Abstract

Objective: The aim of this study is to investigate the effect of diabetes-associated chronic renal failure (CRF) on the severity of peripheral arterial disease (PAD) using angiography.

Material-Method: The angiographic images of 154 diabetic patients who have undergone balloon angioplasty were examined. Patients were divided into two groups of CRF and non-CRF. PAD severity was determined based on the angiographic images using the Bollinger score system. PAD severity was compared in the lower limb arteries of both groups.

Results: In the study group, 90(58%) patients had only diabetes mellitus (DM), and 64 (42%) had DM and associated CRF. The mean of total, infrapopliteal and suprapopliteal level angiogram scoring of patients with DM and CRF and were 39.42 (std±8.96), 32.69 (std±7.73), 6.67(std±3.09), and with only DM were 31.9 (std±6.45), 28.4(std±6.4), 3.5(std± 2.45), respectively. There was a statistically significant difference between the mean total and suprapopliteal level angiogram scoring of the two groups (p:0.003, p: 0.008).

Conclusion: This angiographic study confirms that the PAD severity at lower extremity arteries in patients with DM and CRF is significantly more than in patients with DM without CRF.

Keywords: Peripheral Artery Disease, Chronic renal failure, Diabetes Mellitus, Angiography

Introduction

Peripheral artery disease (PAD) can be defined as a group of disorders characterized by narrowing and obstruction of the arteries that cause reduced blood flow. PAD due to atherosclerosis is a common chronic disease in diabetic patients. PAD reduces the quality of life by affecting the functional capacity. Diabetes and renal disease are among the independent risk factors of PAD [1]. The prevalence of PAD in patients with end-stage renal disease (ESRD) was reported as 77% [2]. In addition, ESRD is a high risk factor for foot ulcers and amputation in diabetic patients [3]. The rate of amputation is 10 times higher in patients with diabetes associated ESRD than in patients with diabetes alone [4]. Although it is known that ESRD is a risk factor for PAD, there was not adequate study about severity of PAD in patients with CRF. Although angiography is the gold standard method for PAD diagnosis, it is an invasive method; therefore most of the studies on atherosclerosis have been performed with non-invasive methods such as ankle brachial index (ABI) [5-8].

Bollinger et al. described an angiogram scoring method for assessment of lower limb atherosclerosis, including scoring for plaques, stenoses and occlusions [9]. The

Bollinger angiogram scoring method is suitable for differentiating the severity of atherosclerotic PAD. The Bollinger score system was used by Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL) trial for to analyze arterial condition and postoperative outcome in severe limb ischemia patients. Mean below-knee Bollinger angiography score was found as an independent risk factor for both time to death after operation and amputation-free survival [10,11].

In this study, using the Bollinger score system, we aimed to compare PAD severity in cases with and without CRF who have undergone percutaneous balloon angioplasty (PBA) due to diabetic foot wound and CLI.

Material-Method

Study Population and Design

This is a retrospective, single-center study based on the collected data of diabetic patients who had undergone lower extremity balloon angiograplasty of at least 1 vessel. Imaging data between January 2015 and May 2016 were reviewed. Inclusion criteria were the presence of diabetes mellitus and foot wound, patients who had balloon angioplasty for stenosis or occlusion of at least 1 vessel with distal runoff to the foot with technical success. Exclusion criteria were, planned major amputation before angiography, unsuccessful PTA, patients whose data constituted any intervention before angioplasty, patients whose clinical and laboratory data was unavailable.

Patients' gender, age, associated coronary artery disease, comorbid diseases such as hypertension, smoking history, absence or presence of dyslipidemia, and glycated hemoglobin (HBA1C) levels were recorded using the hospital archive system.

CRF was defined as renal failure requiring dialysis. Smoking was identified as a patient who smoked ≥10 cigarettes per day for at least six months. The criteria for dyslipidemia were: total cholesterol ≥200 mg/dL, low density lipoprotein ≥130 mg/dL, high triglyceride ≥150 mg/dL, or the use of medication to lower cholesterol levels.

Patients were divided into two groups of CRF and non-CRF. Lower limb PAD severity was calculated using the Bollinger scoring method in both groups.

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. If there was a hemodynamically significant stenosis or occlusion at any part of the artery, percutaneous treatment was applied after obtaining patient permission. 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.

Imaging Analysis

All angiographic images transferred from the radiology database were evaluated in the workstation by a radiologist with 15 years of experience. 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). For 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 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 three infrapopliteal level arterial segments as, 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.

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). Descriptive statistics for continuous parameters were expressed as arithmetic means ± standard deviation (SD) or median (interquartile range, IQR). The qualitative traits were presented as absolute numbers or percentages. As most qualitative variables were not normally distributed (based on the Shapiro-Wilk test), non-parametric statistical tests were used in the univariate analysis. The Mann-Whitney U-test was used to compare two groups. For qualitative traits, the Fisher's exact test or the chi-squared test was applied. P values <0.05 were considered statistically significant.

Results

In the study period, 154 angiographies were performed in diabetic patients .Of these patients, 102 (66.2%) were men and 52(33.8%) were women with a mean age of 67.2 years (range 51-84). The mean of diabetus mellitus duration of all patients was 22.2 years (range 15-32). Angiographic images of all patients consisted of 33 (21.4%) with only stenosis and 121 (78.6%) which had stenosis with occlusion. The mean of total angiogram scoring was 35.4 (std±8.42) in all patients.

Based on infrapopliteal 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 30.1 (std±7.2) in all patients. All patients were classified into two groups. These were the diabetic foot with CRF group (64/154) and diabetic foot without CRF group (90/154).

Diabetic foot with CRF Group

64 (41.6%) patients with diabetic foot with CRF underwent conventional angiography. The mean of CRF duration 16 years (std±7.4). The mean of total angiogram scoring of this group was 39.42 (std±8.96) and the mean of infrapopliteal level and suprapopliteal angiogram scoring was 32.69 (std±7.73), 6,67 (std±3.09), respectively.

Diabetic foot without CRF Group

90 (58.4%) patients with diabetic foot without CRF underwent conventional angiography. The mean of total angiogram scoring of this group was 31.9 (std±6.45). The mean of infrapopliteal and suprapoliteal level angiogram scoring of this group was 28.4 (std±6.4), 3.5 (std± 2.45), respectively.

There was no statistically significant difference between patient age, gender, diabetic disease duration and comorbid disease such as, 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 suprapoliteal level angiogram scoring of the two groups (p:0.003, p: 0.008). But there was no statistically significant difference in infrapopliteal angiogram scoring between the two groups (p:0.70).

Discussion

In this study, PAD severity in lower limbs of cases with and without CRF who have undergone angioplasty due to diabetic foot injury was calculated using the Bollinger scoring method. There were differences in the PAD severity in cases with and without CRF having diabetic foot injury. In diabetic patients with CRF, the Bollinger score was significantly higher than that of the non-CRF group at total and at the suprapopliteal level only, whereas there was no statistically significant difference between the two groups in the evaluation of the below-the-knee arteries only. There was no difference in smoking history, dyslipidemia, comorbid diseases, or glycated hemoglobin (HBA1C) levels in diabetic patients with and without CRF.

PAD due to atherosclerosis is a common chronic disease. Risk factors for PAD include smoking, diabetes mellitus, high blood pressure, high cholesterol level, and advanced age [12]. PAD is also more common in patients with chronic renal disease requiring dialysis [13,14]. Peripheral arterial disease in diabetic patients progresses rapidly, is more diffuse and affects distal limb arteries, such as the tibial and peroneal arteries, compared with PAD in non-diabetic people [15]. Also CRF is commonly associated with PAD lesions that are more severely calcified and diffuse than those observed in patients without CRF [16,17].

In studies investigating the frequency of PAD in ESRD patients, non-invasive methods such as ankle-brachial index were used. The ankle-brachial index (ABI) is a reproducible, non-invasive index used to screen and detect PAD, with 90% sensitivity and 95% specificity [18]. Although ABI measurements are recommended for screening and determining PAD, but ABI falsely elevated because of their noncompressible vessels caused by vascular calcification in diabetes and ESRD [19,20]. Yang et al. [21] found a mean PAD prevalence of 26% in a meta-analysis study involving 10 studies and 32,864 hemodialysis patients. In these studies, PAD severity was not specified and PAD diagnosis was made using non-invasive methods such as ABI in all of the studies that constituted the meta-analysis. Although PAD is frequent in diabetic cases and ESRD patients, it is a shortcoming that PAD severity is not shown by the gold standard method of angiography in studies.

Bollinger et al. described an angiogram scoring method for assessment of lower limb atherosclerosis, including scoring for plaques, stenoses and occlusions. The Bollinger angiogram scoring method is suitable for differentiating the severity of atherosclerotic PAD, especially in infrapopliteal arteries (9,10). Matsukura et al. [22] stated that the paramalleolar arterial Bollinger score could be used to demonstrate the clinical course after bypass surgery at the infrapopliteal level which they have performed on patients, the majority of whom have DM and ESRD. In this study, patients who have undergone angioplasty due to ischemic diabetic foot injury were enrolled and the PAD severity of the patients was obtained from angiographic images using the Bollinger scoring system [9].

Since angiography is the gold standard method for indicating PAD, more objective results have been achieved with this study compared to studies defined only with ABI. In addition, the absence of any significant difference in age, gender, smoking history, dyslipidemia, duration of diabetes and comorbid diseases that may affect PAD among the study groups suggested that angiography better demonstrates the effect of CRF on PAD between the two groups.

The limitations of this study are retrospective design and a relatively small number of patients. We also evaluated only one extremity that had diabetic ulcer and gangrene

and below the inguinal arterial segments because of antegrade approach of angiography technique.

Conclusion

Angiography better demonstrated PAD severity in lower limb arteries in cases with CRF diabetic foot injury in this study. There was no significant difference in the PAD severity in below-the-knee arteries of diabetic patients with and without CRF, whereas the burden of atherosclerosis was higher particularly in the above-the-knee arteries of diabetic patients with CRF.

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Table 1: Bollinger scoring matrix *

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

*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). h: half the segment length.

Table 2: Demographic characteristics of the patients according to groups.

	DM with CRF n: 64	DM without CRF n:90	P value
Age	68.8 (std±8.01)	66.7(std±8.51)	0.65
Male sex	42 (%65.6)	60 (%66.6)	0.82
Mean DM duration (years)	23 (std ± 11)	19 (std± 14.3)	0.61
Comorbidites			
History of Hypertension	34 (%53.1)	42 (%46.6)	0.41
History of CAD	18 (%28.1)	34 (%37.7)	0.33
History of smoking	28 (%43.7)	42 (%46.6)	0.71
Dislipidemi	22 (%34.3)	38 (%42.2)	0.38
HbA1c %	8.42 (std±1.28)	7.76 (std±1.88)	0.54