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Arteriographic findings in diabetic and nondiabetic patients with critical limb ischemia☆

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A B S T R A C T

Objective: To compare angiographic findings of diabetic and nondiabetic patients with critical limb ischemia.
Methods: We included 161 patients with infrainguinal critical limb ischemia (CLI). We evaluated the clinical and arteriographic (number and presence of opacification of leg arteries) of the two groups of patients. Statistical analysis was performed using EPI-INFO.
Results: Most patients were category 5 of Rutherford's Classification and had femoropopliteal disease. Seventy-two percent of nondiabetic and 67% of diabetic patients had opacification of the fibular artery ($p = 0.25$), which is the most present artery in both groups. Diabetic patients had less opacification of the posterior tibial artery in the univariate analysis (29% vs. 47%, $p = 0.008$). But only female sex showed a significant risk for the absence of the posterior tibial artery in logistic regression (OR = 2.6; $p = 0.01$).
Conclusion: The peroneal artery was the most frequently found artery in angiograms of diabetic and nondiabetic patients with CLI. Diabetic and nondiabetic patients did not differ in angiographic findings of the leg.

Análise das arteriografias de diabéticos e não diabéticos com isquemia crítica da perna

Palavras-chave:
Diabetes *mellitus*
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Complicações do diabetes

R E S U M O

Objetivo: Comparar características angiográficas de pacientes diabéticos e não diabéticos com isquemia crítica.
Métodos: Foram incluídos 161 membros inferiores de pacientes com isquemia crítica infrainguinal. Avaliaram-se as características clínicas e arteriográficas (número e presença de opacificação das artérias da perna) dos dois grupos de pacientes. A análise estatística foi realizada pelo EPI-INFO.

☆ Study conducted at Complexo Hospitalar Universitário Professor Edgard Santos, Universidade Federal da Bahia, Salvador, BA, Brazil.

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Resultados: A maioria dos pacientes era categoria 5 da Classificação de Rutherford e apresentava doença do território fêmoro-poplíteo. Opacificação da artéria fibular foi encontrada em 72% dos não diabéticos e em 67% dos diabéticos (p = 0,25), sendo esta a artéria mais presente em ambos os grupos. Os diabéticos apresentaram menor índice de opacificação da artéria tibial posterior na análise univariada (29% vs. 47%; p = 0,008). Na regressão logística, apenas o sexo feminino se mostrou significante para a ausência da artéria tibial posterior (OR = 2,6; p = 0,01).

Conclusão: A artéria fibular foi a mais encontrada nas angiografias de diabéticos e não diabéticos com isquemia crítica. Diabéticos e não diabéticos não diferiram em relação ao padrão angiográfico da perna.

Introduction

Diabetes mellitus (DM) is considered one of the main risk factors for peripheral vascular disease.[1] The overall prevalence of peripheral arterial disease (PAD) in diabetic patients is approximately 12%.[2] In Brazil, the prevalence of PAD is 10% among diabetics and 2.6% among nondiabetic patients.[3] Melton et al. have shown in the monitoring of diabetic patients, that the cumulative incidence of peripheral vascular disease in this population was estimated at 15% for those with more than 10 years of diagnosis, and 45% after 20 years of disease.[4] Most of these patients had absence of infrapatellar pulse[4] (74% without dorsalis pedis pulse and 80% without posterior tibial pulse).

Patients with critical limb ischemia, characterized by pain at rest, ulcers or gangrene secondary to peripheral vascular disease, are at high risk of cardiovascular events such as myocardial infarction and cerebrovascular accident, as well as limb loss.[1] In Brazil, studies have shown the high cost of hospitalizations for diabetic foot complications,[5] and peripheral vascular disease increases the risk of amputation in these patients.[6]

The literature reports that although diabetic patients have a lower chance of arterial reconstruction, they seem to have similar results to others with peripheral arterial occlusive disease (PAOD) in infrainguinal revascularizations.[7,8] Possible differences in the arteriographic pattern may be one of the causes of the lesser opportunity of revascularization in diabetic patients. The aim of this study is to determine whether there are differences in the angiographic pattern of diabetic and nondiabetic patients with critical limb ischemia due to infrainguinal PAOD.

Methods

The study included patients consecutively admitted for treatment of critical limb ischemia due to infrainguinal PAOD, of atherosclerotic etiology, at Hospital Universitário Professor Edgard Santos (HUPES). This research project, number 292011, was approved by the Ethics Committee in Research of HUPES Complex in August 2011. Data collection was performed retrospectively from patients' records, clinical follow-up reports and arteriographies performed and filed at the Service of Vascular Surgery of HUPES Complex of Universidade Federal da Bahia, for inpatients admitted for treatment in the period between December 2005 and December 2011 .

During this period, the treatment records of 213 patients admitted for treatment of critical ischemia due to infrainguinal atherosclerotic disease were found and reviewed. On physical examination, all patients had normal femoral pulses, characterizing infrainguinal disease, with absence of dorsalis pedis and posterior tibial pulses. We included only those cases in which the ischemic limb arteriography was filed in the Service, with digital subtraction arteriography performed through ipsilateral femoral puncture at HUPES.

Due to the absence of documented angiographic study, 52 patients were excluded. Therefore, this study included 161 patients, which meant the treatment of 175 ischemic lower limbs. Critical bilateral ischemia was found in 14 patients during the period considered for the study, but the lower extremities with less severe disease in these cases were excluded from the analysis, totaling 161 lower limbs for final analysis.

All patients' data are recorded in the clinical follow-up files, which belong to the Service, containing detailed information on the patients. A protocol was designed to collect data from the medical records in the outpatient clinic and angio-radiology unit. The arteriographies were evaluated together by two vascular surgeons, blinded to the diagnosis of diabetes, presence of opacification of any segment of the lower-limb arteries [popliteal, anterior tibial (AT), posterior tibial (PT) and peroneal].

Patients were divided into two groups (diabetic and nondiabetic), with the aim of comparatively analyzing the arteriographic pattern in both groups. Patients were considered diabetic when they had a prior diagnosis of the disease and received treatment for it. This was also the criterion used for systemic arterial hypertension. The history of ischemic heart disease and chronic renal failure was considered according to the medical record notes of such a diagnosis, through the patient's clinical history. The patient was considered a smoker if he or she had the habit of smoking at the time of treatment.

The two groups of patients were comparatively evaluated regarding the following aspects: Rutherford Classification of the lower limb with critical ischemia,[1] number of lower-limb opacified arteries at the arteriography (0 or none, 1, 2 or 3), and the presence of opacification of any segment of the AT, PT and peroneal arteries. The Rutherford classification for chronic ischemia of the lower limbs consists of the categories: (0) asymptomatic, (1) mild claudication, (2) moderate claudication, (3) severe claudication, (4) ischemic rest pain, (5) minor tissue loss and (6) major tissue loss. Patients in categories 4, 5 and 6 are considered as having critical limb ischemia, and are at higher risk of limb loss.[1]

The presence of refilling of the popliteal artery was evaluated in the 117 limbs that showed occlusive disease of the femoropopliteal sector during physical assessment of pulses with absent popliteal pulse. It was considered for the analysis the presence of any opacified segment of lower-limb arteries due to the presence of advanced occlusive disease and critical ischemia in all cases, with no popliteal pulse in 117 cases and absence of both distal pulses (posterior tibial and dorsalis pedis) in all cases.

Data were tabulated in Microsoft Excel® and analyzed using Epi-info software, release 3.3.2, February 2005. The Chi-square (χ^2) test was used to test the association between diabetes mellitus and other qualitative variables, correlating them to the arteriographic assessment. Mean age was compared by analysis of variance (ANOVA). Logistic regression was used to analyze the risk factors that were significantly correlated to the absence of opacification of a certain artery, when they reached statistical significance ($p < 0.05$) in the Chi-square test, which occurred only with posterior tibial artery. The significance level was set at 5% ($p < 0.05$) for rejection of the null hypothesis, i.e., that there is no statistical difference between the groups regarding the studied variables.

Results

Of the 161 patients studied, 54% were diabetic, 73% hypertensive, 67% were smokers and 53% were male. As for the topographic diagnosis of arterial obstruction through pulse examination, 73% had femoropopliteal occlusive disease, with absence of popliteal and distal pulse at physical examination, and the remaining 27% had infrapatellar disease, with normal popliteal pulse. The mean age of patients was 70.08 years, ranging between 44 and 93 years. As for the Rutherford classification[1] for chronic critical ischemia, 80% of limbs were in Category 5, 15% in Category 6 and 5% in Category 4. A comparative analysis of the clinical characteristics of diabetic and nondiabetic patients is shown in Table 1. More than 90% of the cases had necrotic tissue (gangrene) and the presence of some degree of opacification of the leg arteries was studied because impacts in revascularization surgical procedures in these cases.

When performing the evaluation of digital arteriographies of the 161 lower limbs regarding the number of leg arteries identified, most patients in both groups had only one artery at the examination (Table 2).

The 117 limbs with femoropopliteal disease were studied separately in relation to the opacification of the popliteal artery, comparing data from diabetic and nondiabetic patients, with no significant differences (Table 3).

The peroneal artery was the one identified in most cases in both diabetics and nondiabetics (Table 3). When studying the AT artery, diabetics and nondiabetics did not differ significantly regarding its presence (Table 3). The opacification of the peroneal and AT arteries did not differ significantly between genders, and were not associated alone to SAH or smoking.

Table 1 – Comparative analysis of the clinical characteristics of diabetic and nondiabetic patients with critical ischemia due to infrainguinal PAOD.

Characteristic	Diabetics (87 cases) n (%)	Nondiabetics (74 cases) n (%)	*p* value
Gender			
Male	36 (41%)	49 (66%)	0.0008
Female	51 (59%)	25 (34%)	
Hypertension	72 (83%)	45 (61%)	0.001
Current smoking	50 (58%)	58 (78%)	0.002
PAOD topography			
Femoropopliteal	59 (68%)	58 (78%)	0.07
Infrapatellar	28 (32%)	16 (22%)	
Mean age	71 years	69 years	0.3
History of CVD	19 (22%)	11 (15%)	0.13
Chronic renal failure	10 (12%)	5 (7%)	0.16
Rutherford classification			
Category 4	4 (5%)	4 (5%)	0.9
Category 5	70 (80%)	59 (80%)	
Category 6	13 (15%)	11 (15%)	

PAOD, peripheral arterial occlusive disease; SAH, systemic arterial hypertension.

Table 2 – Comparative analysis of the number of opacified leg arteries in the digital angiograms of diabetic and nondiabetic patients with critical ischemia due to infrainguinal PAOD.

Number of opacified arteries	Diabetics n (%)	Nondiabetics n (%)	*p* value
0 (none)	3 (3%)	2 (3%)	
1	59 (68%)	41 (55%)	0.25
2	22 (26%)	24 (32%)	
3	3 (3%)	7 (10%)	

Table 3 – Comparative analysis of the presence of opacification of leg arteries in the digital angiography of diabetic and nondiabetic patients with critical ischemia due to infrainguinal PAOD.

Artery	Diabetics n (%)	Nondiabetics n (%)	*p* value
*Popliteal**			
Present	43 (73%)	36 (62%)	0.1
Absent	16 (27%)	22 (38%)	
Peroneal			
Present	58 (67%)	53 (72%)	0.25
Absent	29 (33%)	21 (28%)	
Anterior tibial			
Present	29 (33%)	23 (31%)	0.38
Absent	58 (67%)	51 (69%)	
Posterior tibial			
Present	25 (29%)	35 (47%)	0.008
Absent	62 (71%)	39 (53%)	

*Analyzed only in 117 patients with femoropopliteal obstruction (absent popliteal pulse).

The posterior tibial (PT) artery was significantly more present in angiographic examinations of nondiabetic patients (Table 3). However, diabetic patients had a significantly higher percentage of women and hypertensive patients. Thus, using the χ^2 test, we evaluated the possibility of correlation of other risk factors for atherosclerosis and non-opacification of the PT artery. The female sex (21% vs. 52%, p = 0.00002), SAH (30% vs. 57%, p = 0.001), DM (Table 3) and smoking (44% vs. 25%, p = 0.009) were significantly correlated in the univariate analysis using the χ^2 test with opacification of the PT artery. The patients with PT opacification were also significantly younger (67 vs. 72 years, p = 0.0048). The multivariate logistic regression analysis was performed, including the variables that had statistical significance (female gender, age, smoking, diabetes and SAH), and only the female gender was significant, showing to be a risk factor for non-opacification of the posterior tibial artery in the lower-limb angiograms (p = 0.01) (Table 4).

Discussion

Cardiovascular disease is the leading cause of death in the Brazilian population,[9] and diabetes mellitus is one of its risk factors. A recent study shows an increase in mortality by diabetes in most Brazilian cities.[10] Diabetes is also an important risk factor for peripheral vascular disease and patients with critical limb ischemia have a mortality rate of around 20% as early as in the first year after disease presentation.[1] The literature shows particularities of atherosclerotic disease in diabetic patients, such as the fact that it occurs earlier, being more frequent and more severe, with diabetes being the leading cause of lower limb amputations in the world.[11,12] To find characteristics and peculiarities of peripheral vascular disease in Brazil may demonstrate which population groups are more exposed to the disease, helping research on the disease treatment and prevention.

In this study, we compared diabetic and nondiabetic patients with critical limb ischemia due to PAOD and found no difference between the mean age of the two groups, which was around 70 years for both. Although the literature reports that peripheral vascular disease in diabetic patients occurs earlier,[13-15] perhaps the advanced form of the disease, leading to critical ischemia, occurs later, at a similar age range of nondiabetic patients.

Overall, there was a slight male predominance. However, when comparing the groups, females were statistically more prevalent among diabetics, as shown in studies by other

Table 4 – Multivariate logistic regression analysis of risk factors related to the absence of opacification in the posterior tibial artery in leg angiographies.

Risk factor/variable	Odds ratio	95% confidence interval	*p* value
Diabetes mellitus	1.44	0.6-2.9	0.32
Systemic arterial hypertension	1.72	0.7-3.8	0.18
Age ≥ 70 years	1.72	0.8-3.5	1.12
Female sex	2.60	1.2-5.5	0.01
Current smoking	0.66	0.2-1.4	0.31

authors who focused on diabetic foot complications.[5,16-18] This finding may be explained by a parallel with coronary heart disease, in which the protective effect of the female sex is eliminated by diabetes, as well as the fact that diabetes doubles the risk of cardiovascular disease in men and triples it in women.[19,20] The higher prevalence of hypertension among diabetic patients with PAOD found in our sample has also been mentioned by other authors.[6,18,21]

As for the arterial territory affected by PAOD, diagnosed by physical examination of pulses, most of our patients in both groups had femoropopliteal disease. The infrapatellar disease, with normal popliteal pulse was little prevalent in our sample and the difference was not significant between diabetics and nondiabetics.

Atherosclerotic disease in diabetics, according to the literature, is prone to involvement of infragenicular arteries, with reports of a greater proportions of tibioperoneal illness among diabetic patients when compared to nondiabetic ones and lower propensity to aortoiliac disease in diabetics.[8,18,22] However, histological studies have shown that atherosclerotic lesions in the lower limbs appear to have indistinguishable morphology and distribution in both groups.[18,23]

Our study found no differences in the angiographic patterns of diabetic and nondiabetic patients in relation to opacification of the leg arteries, except for the PT artery, with both groups having similar behavior in relation to the number of visualized arteries. However, other authors, who also performed arteriographic studies, showed differences between diabetic and nondiabetic patients, reporting that diabetics have greater infrapatellar involvement by atherosclerotic disease.[21,24] A possible explanation for this may be the fact that we only included cases with critical limb ischemia, predominantly patients in category 5 of the Rutherford classification,[1] with advanced atherosclerotic disease, different from the study by Jude et al.,[21] who also included in their series patients with claudication.

We also differed regarding the methodology from the study by Rueda et al.,[24] as we did not measure the arterial stenotic lesions in our patients, choosing to assess only the presence of opacification in some arterial segments, as we believe that the presence of this refilling has a more objective meaning, directly influencing the type of revascularization of the ischemic limb. We searched the arteriographies for the presence of any refilling of leg arteries, unlike Graziani et al.,[25] who created a morphological classification of the lesions based on arteriographies only in diabetic patients with critical limb ischemia. However, the study by Graziani et al.[25] is similar to ours as it found a high prevalence of combined occlusive disease in the femoropopliteal and infrapatellar sectors in diabetic patients, with high rates of occlusion in the AT and PT arteries.

Our patients also showed multisegmental peripheral vascular disease, and it is noteworthy that we termed the disease "femoropopliteal" when there was no femoral pulse on physical examination, but atherosclerosis was not exclusive in this sector. The obstructive disease was diffuse in both groups, with a minority of patients showing refilling of the three leg arteries. In cases with femoropopliteal disease, there was no difference between diabetic and nondiabetic patients in relation to the popliteal artery refilling. The presence of this refilling can mean the chance of a lower-complexity revascularization. However, this study did not consider the length of the opacified segment of the arteries.

The peroneal artery was the only one of the leg arteries that was present in most of the angiograms, in both diabetics and nondiabetics. Graziani et al.[25] reported a greater incidence of occlusions, when compared to the stenosis, in the AT and PT arteries of diabetic patients, but not in the fibular artery, which showed significantly more stenoses than occlusions, which, we believe, corroborates our findings. In the 1960s, the anatomopathological study by Strandness et al.[26] found that diabetics had the PT, AT and fibular arteries more frequently affected than nondiabetic patients, whereas other histological studies showed a similar pattern of atherosclerotic disease between diabetics and nondiabetics.[18,27-29] While the arteriographic studies do not determine the morphological characteristics of the atherosclerotic plaque and may fail to detect it, either due to the examination technique or the presence of lesions that do not lead to significant stenoses,[30] histological studies often do not analyze the entire length of the artery in question, but only sections of selected fragments.

The influence of the female gender on the arteriographic pattern of PAOD deserves to be highlighted. Women had lower percentage of PT artery opacification when compared to men. This difference remained significant after logistic regression. Nguyem et al., in a multicenter study with over 1000 patients, found that among patients with critical limb ischemia submitted to revascularization, women of black ethnicity had a higher risk of graft failure and limb loss.[31] It was not the purpose of our study to establish a correlation between the angiographic pattern in women and the risk of limb loss, but such angiographic characteristics may have significance in the prognosis and treatment of these patients, which needs to be further studied. The women from our sample smoked less, but had more diabetes, more arterial hypertension and were older. These particularities of the female gender are likely to influence the pattern of PAOD and will be further studied in our research.

The literature has shown that the angiographic pattern of occlusive arterial disease has prognostic value for the limb, being a risk factor for amputations in diabetics.[32] In our study, we found no differences in the angiographic pattern between diabetics and nondiabetics; it only shows the limitations inherent to a retrospective study and we did not assess whether the opacified arteries were eligible for revascularization. However, it shows new aspects of a disease with high prevalence and high rates of morbimortality. Future researches are needed aiming at the in-depth study of the peculiarities of peripheral atherosclerotic disease in diabetics and in the female gender.

Conclusion

In our sample of patients with advanced vascular disease of the lower limbs, diabetic and nondiabetic patients did not differ regarding the angiographic pattern of the extremity. The fibular artery was the best preserved artery in the leg arteriographies in both groups. Female patients were more likely to have PT artery involvement.

Conflicts of interest

The authors declare no conflicts of interest.

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