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Arterial Plaques in Peripheral Arteries Diagnosed by Ultrasound in a Cohort of Patients With Type 2 Diabetes Mellitus: A Single-Center Surveillance

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Abstract

Macroangiopathy (eg, peripheral arterial disease) diagnosis in type 2 diabetes mellitus (T2DM) can be carried out by ultrasound. A surveillance study was performed in 366 consecutive patients (166 patients with T2DM and 200 non-T2DM) aiming to evaluate the frequency of single or multiple arterial plaques (Aplqs) in lower limbs and the relationship with different factors (age, duration of T2DM, glycemic balance, DM treatment, smoking habit, and microalbuminuria). Single and multiple Aplqs, respectively, were found in 10.2% and 38.6% among the patients with T2DM. Age, male gender ($P < .0002$), duration of T2DM ($P < .009$), insulin therapy ($P < .03$), and mediocalcinosis ($P < .001$) were risk factors in patients with T2DM. In conclusion, Aplqs of lower limbs are frequent in T2DM and several factors can play a determining role. Ultrasound is a helpful diagnostic tool.

Keywords

arterial plaque, type 2 diabetes, ultrasound, risk factors, surveillance, peripheral arterial disease

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) is rising worldwide. Macrovascular disease is a consequence of T2DM. Peripheral arterial disease (PAD) in patients with T2DM results in poor prognosis and is associated with high cardiovascular morbidity and mortality.[1,2] Data collected by the Trans-Atlantic Society Consensus II[3] suggest that the strongest relationship is between glycemic status and the frequency of PAD. A 1% rise in glycated hemoglobin A_{1c} (HbA_{1c}) level determines up to 26% of the risk of developing PAD.[4,5]

Ultrasound (US) is effective for diagnosing PAD and it is also helpful to identify the arterial consequences in peripheral arteries.[3,6-7] The ankle–brachial index (ABI) is a suitable marker in clinical practice and it has been approved as a routine assessment in patients with T2DM.[8,9]

The present study first focuses on the frequency of arterial plaques (Aplqs), single or multiple, in the peripheral arteries of patients with the T2DM evaluated by US. The secondary objective is to elucidate the effect of categorical factors (eg, age, duration of T2DM, glycemic balance, anti-DM therapies, smoking, microalbuminuria, and mediocalcinosis) on the frequency of the Aplqs.

Study Population

Consecutive patients (n = 366; from January to December 2013) were referred by their general physician or diabetologist to the noninvasive vascular laboratory in order to perform a US examination; 166 had T2DM and 200 were nondiabetic. The diagnosis of T2DM was based on personal clinical history and on regular prescription of oral anti-DM drugs or insulin. Duration of the T2DM (years) was calculated from the year when patients were diagnosed. The year the patients first began undergoing antidiabetic therapy was also factored in. Patients were asked to show their recent laboratory tests. Glycemic control was defined as an HbA_{1c} level $\leq 6.0\%$ and microalbuminuria recent measurement was requested (normal value ≤ 20 mg/L). Patients were also asked about smoking. Mediocalcinosis in peripheral arteries diagnosed by US was also considered. Clinical and demographic characteristics of the patients are shown in Table 1.

Ultrasound Measurement

The US examination of lower arteries was performed using an Xvision 70 ultrasound system (EsaOte Genoa, Italy) equipped

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Table 1. Demographic and Clinical Characteristics of the Study Population (166 Patients With T2DM).

Demographic and Clinical Features	
Age, years	74.6 ± 2.5
Male, number (%)	86 (51.8)
Female, number (%)	80 (48.2)
Duration of diabetes mellitus, years	9.4 ± 2.3
HbA_{1c}, %	7.2 ± 1.3
Microalbuminuria, number (%)	73 (44.0)
Oral antidiabetic drugs, number (%)	120 (72.3)
Insulin therapy, number (%)	100 (60.2)
Smoking habit, number (%)	38 (22.9)
Statins, number (%)	99 (59.6)

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; T2DM, type 2 diabetes mellitus.

with an 8- to 10-MHz linear probe. The US examination was carried out with patients at rest and after 10 minutes in a room at normal temperature (26°C). The objective was to evaluate the presence of Aplqs in peripheral arteries (common femoral, superficial femoral, popliteal, posterior tibial, and dorsalis pedis) both in patients with T2DM and in healthy individuals. To diagnose the Aplqs, we considered the US echogenic finding patterns inside the lumen of the arteries. We note that in this study, we did not consider the difference in the gray scale grading of the US pathway nor the hemodynamic effect (arterial stenosis degree) determined by the Aplqs on the peripheral arteries. The US finding of calcification of the media of vessel wall in the absence of such lipid or cholesterol deposits was defined as medicocalcinosis.

Categorical Factors

Age, gender, duration of the T2DM (year), glycemic control (HbA_{1c} level), antidiabetic therapy (oral, insulin), microalbuminuria, and smoking habits were considered as categorical elements to explain the frequency of the Aplqs.

Statistical Analysis

Data are shown as mean ± standard deviation. Descriptive statistics were used to evaluate the frequency of multiple Aplqs. To evaluate the difference in frequency of the Aplqs between T2DM and nondiabetic healthy individuals, we used the 2-way contingency test. Concerning the diabetic data set, we analyzed the relationship between single or multiple Aplqs and other categorical variables. First, we considered analysis based on 2-way contingency tables involving pairs of variables through chi-square test. We then carried out a more detailed analysis concerning the relationship between the single or multiple Aplqs and the significant variables by using a 2-sided multinomial regression model; $P \leq .05$ was considered significant.

Results

No Aplqs in arteries of lower limbs was found in 51.2% of patients with diabetes; 10.2% of those had 1 Aplq, and 38.6% of patients with diabetes had multiple Aplqs in peripheral arteries. Furthermore, 36% of nondiabetic patients did not show Aplqs but of the 9.5% of the group that did present with Aplqs, only 24.5% of these showed multiple Aplqs in peripheral arteries (Table 2). The difference in proportions of patients having 2 or multiple Aplqs was significant ($P < .002$; Table 2). High frequency of single or multiple Aplqs was found in older patients with T2DM and progressively rose in groups aged older than 51 years. Single Aplqs were found, respectively, in 3.5% of patients with T2DM aged between 51 and 60 years and in 2.0% of patients aged between 61 and 70 years. The frequency of multiple Aplqs was detected in 7.5% of patients with diabetes aged between 51 and 60 years and in 8.5% aged between 61 and 70 years (Table 3; Figure 1). Conversely, in younger age groups, the frequency of multiple Aplqs was low or absent. The difference in the frequency of patients having multiple Aplqs was significant ($P < .0002$). Concerning the diabetic data set, we analyzed the relationship between the frequency of Aplqs and other variables. First, we considered analysis based on 2-way contingency tables involving pairs of variables through chi-square tests (Table 3). Male gender ($P < .0002$), duration of T2DM ($P < .009$), insulin therapy ($P < .03$), and mediocalcinosis ($P < .001$) using a multinomial regression model were considered statistically significant in patients with T2DM (Table 4).

Table 2. Frequency of Aplqs in T2DM and Nondiabetic Groups and Statistical Comparison.

	Aplqs			
Patients	0	1	2+	Total
T2DM	85 (51.2%)	17 (10.2%)	64 (38.6%)[a]	100.0%
Nondiabetic	132 (66.0%)	15 (9.5%)	49 (24.5%)	100.0%

Abbreviations: Aplqs, arterial plaques; T2DM, type 2 diabetes mellitus.
[a]$P < .0002$ T2DM versus nondiabetic.

Discussion

Many studies[10-15] showed that T2DM is a major risk factor for arterial damage. Type 2 diabetes mellitus accelerates atherosclerosis and plays a role in morbidity for cardiovascular disease (ie, coronary artery disease, myocardial infarction, ischemic stroke, and PAD). Peripheral arterial disease is characterized by the presence of single or multiple Aplqs in 1 or several arteries of the lower limbs. The Aplqs determine the hemodynamic effects related to the different grading of arterial stenosis. Hemodynamic disturbances are efficient in determining lowered blood perfusion to tissues (muscle and skin). Chronic moderate ischemia is elicited by both walking effort (ie, intermittent claudication) and critical hemodymanic disturbances (III and IV stage of Leriche classification or critical limb ischemia) that are elicited by pain at rest and/or by progressive tissue damage (cyanosis, skin trophic alteration, ulcers, etc).

Table 3. Two-Way Contingency Analysis Involving Pairs of Variables Through Chi-Square Tests.

	Classes of Age, Years					
Aplqs	41-50	51-60	61-70	71-80	81-90	Total
0	4.22%	12.65%	16.26%	12.05%	6.02%	51.20%
1	0.00%	2.41%	3.01%	3.62%	1.20%	10.24%
2+	1.81%	5.42%	8.43%	19.28%	3.62%	38.56%

Abbreviation: Aplqs, arterial plaques.

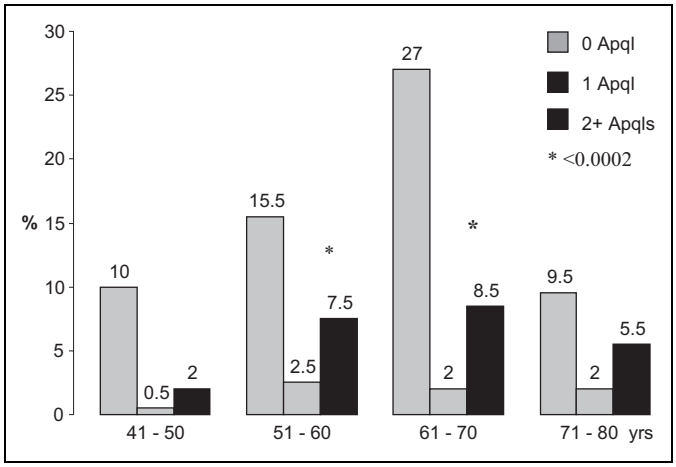

Figure 1. Frequency (%) of Aplqs in different age classes of patients with T2DM. Aplqs indicates arterial plaques; T2DM, type 2 diabetes mellitus.

Table 4. Multinomial Regression Model Analysis in Patients With T2DM and Statistical Significance.

Variable	*P* Value	Significance
Sex	.001	a
Age	.12	
Oral therapy	.63	
Smoking	.48	
Duration of T2DM	.027	b
Metabolic control T2DM	.09	
Insulin therapy	.033	c
Microalbuminuria	.32	
Mediocalcinosis	.001	d

Abbreviation: T2DM, type 2 diabetes mellitus.
[a].002.
[b].009.
[c].03.
[d].001.

Patients with the T2DM have 2- to 3-fold higher risk of developing PAD[16,17] than nondiabetic patients and they also have a higher frequency of critical limb. In patients with PAD, there is a high prevalence of the arterial comorbidities and this rises in those with T2DM; consequently, there is a high risk of a poor clinical outcome.[18,19] Peripheral arterial disease is also considered as a useful marker to estimate cardiovascular risk, and epidemiological studies on the prevalence of the PAD have shown its high frequency in populations older than 65 years.[18,20-22] Nevertheless, PAD is often underdiagnosed and underestimated, and patients with PAD are often undertreated,[3,8,10,23-27] although PAD can be diagnosed early and screened by using US examination and the ABI index.

Failure to notice the signals of suspected damage of the peripheral arteries in patients with T2DM can cause harmful clinical situations. Conversely, the findings of the UK Prospective Diabetes Study (UKPDS) lead us toward aggressive therapy for patients with the T2DM[26] to counteract macroangiopathy. Moreover, other studies have demonstrated the efficacy of aggressive antiplatelet drugs and statins on prognosis of the patients with PAD, particularly in those with the T2DM.[28,29] To our knowledge, this is the first single-center study of Southern Italy that focuses on the role of US method for the diagnosis and monitoring of PAD in patients with T2DM. Our results show a high incidence of atheromatous plaques in patients with T2DM, and longer duration of T2DM was associated with greater number of plaques in lower limb arteries. Our results show a high frequency of atheromatous plaques in the peripheral arteries in patients with T2DM and it correlates with male gender and age and the duration of T2DM. The high frequency of multiple Aplqs in the arteries of lower limbs confirms that patients with T2DM seem to be more prone to develop PAD. It is known that patients with T2DM frequently have narrowing of the distal arteries of the lower limbs (posterior and anterior tibial arteries) and mediocalcinosis of arteries.[18,20-21] In addition, T2DM can also be a major cause of arterial narrowing. We demonstrated multisite damage in the arteries of the lower limbs in patients with T2DM.

We want to emphasize the useful role played by US. Early diagnosis of arterial damage in diabetic patients is efficient to reach 2 important objectives; first, to understand the macrovascular consequences due to T2DM and second, to lower/avoid the incidence of dramatic and nonreversible clinical situations for such high-risk patients (ie, amputation). The diabetic patients enrolled in this study were older and they had T2DM for a mean 9.4 $\pm$ 2.3 years, and we demonstrated that age and duration of the T2DM are important factors in determining the high frequency of Aplqs.

Our patients with T2DM show a low frequency in statin therapy (T2DM 99 of the 166, 59.6%), although these drugs are recommended in diabetic patients to decrease their cardiovascular risk.[30-32] We feel that this can explain the high frequency of the Aplqs in our study. Correspondingly, we emphasize that PAD and T2DM are more frequently diagnosed in older

populations. Adults ranging from middle aged to retirement age are increasing largely due to a prolonged life expectancy. However, as the average age of the population rises, so does the frequency of chronic metabolic diseases (eg, T2DM) and arterial diseases (eg, PAD). Other studies investigated the arterial consequences in patients with T2DM, but unlike others, we have strictly focused on demonstrating the frequency of single or multiple Aplqs in the lower limbs.

In conclusion, our results are consistent with the findings of large epidemiological studies on arteriopathy in the patients with T2DM and the presence of the higher frequency of the Aplqs further underpins previous findings. We underline that older patients with a longer duration of T2DM seem to be more prone to demonstrate arterial damage and developing PAD. We point out that US is an easy and helpful technique to reveal the presence of the Aplqs and it can be effective in asymptomatic patients with the T2DM. Thus, we consider US as a method to monitor the progression of Aplqs and its potential effects on the outcome of patients with T2DM. Furthermore, we believe that in patients with T2DM, we must encourage the use of lipid-lowering drugs (eg, statins) in order to lower the risk of cardiovascular diseases.

Authors' Contribution

S. Signorelli contributed to the conception and design of the study. V. Fiore, M. Mangiafico, and D. Castrogiovanni contributed to the acquisition of data. All authors contributed to the analysis and interpretation of data. All authors were involved in drafting and revising the article and they approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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