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Research Article

Evaluation of Cardiovascular Risk in Patients with Type 1 Diabetes: How Ankle Brachial Index Can Be Usefull?

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Abstract:

Background: Patients with type 1 diabetes (T1D) face a significantly higher mortality risk compared to the general population, primarily due to elevated rates of cardiovascular disease (CVD). Detecting cardiovascular disease at its preclinical stage is essential for effective primary prevention in this relatively young population. This study aims to assess the link between steno-risk and subclinical atherosclerotic disease, as detected by the Ankle-Brachial Index (ABI), in T1D patients and determine the prevalence of these abnormalities among them.

Methods: A cohort of 312 adults with T1D (151 males and 161 females, mean age 31 ± 12 years) was examined. Patients were categorized based on their ABI values (ABI < 0.9 indicating peripheral arterial disease (PAD), ABI ≥ 1.3 indicating arterial calcification (AC), and ABI between 0.9 and 1.3 indicating normal ABI). The study analyzed the relationship between ABI anomalies and cardiovascular risk factors and their association with the steno-risk category.

Results: Among the patients, 138 (44.2%) had a normal ABI, 112 (35.9%) had PAD, and 62 (19.9%) had AC. AC was more prevalent in men than in women (p = 0.006). A family history of stroke was common in both the PAD and AC groups (p = 0.042 and p = 0.046, respectively). Patients with AC were often older (36 ± 13 vs. 30 ± 12; P = .012), had a longer duration of diabetes (20 ± 11 vs. 14 ± 9; P < 0.001), a higher prevalence of hypertension (25.8% vs. 14.5%, P = 0.05), and a higher prevalence of smoking (19.3% vs. 9.4%, P = 0.046). A higher number of subjects with AC were found in the Steno-Risk 10–20% and Steno-Risk ≥20% categories compared to the Steno-Risk < 10% (37.5 vs. 15.5; 29 vs. 15.5, p = 0.0106, respectively).

Conclusion: This study demonstrates that an ABI > 1.30 is more common in older patients with type 1 diabetes and is associated with a longer duration of diabetes, male gender, smoking, hypertension, and a family history of stroke. Furthermore, an ABI > 1.30, indicating arterial calcification, is significantly linked to moderate and high cardiovascular risk assessed by steno-risk in patients with type 1 diabetes. The ABI may serve as a straightforward tool for screening atherosclerosis in T1D.

Keywords: Ankle-Brachial Index; Peripheral Arterial Disease; Steno Type 1 Risk Engine; Type 1 Diabetes Mellitus; Medial Calcifications.

Introduction

Type 1 diabetes (T1D) represents 10 to 15% of all the causes of diabetes. It has seen a clear increase in its incidence, both in children and adults, over the last three decades (1, 2). Indeed, Algeria, which was considered an intermediate incidence zone during the years 1990-1999, became a high incidence zone in 2016 (3). Furthermore, it is well known that cardiovascular mortality in type 1 diabetic patients is higher than that of the general population (4). Early detection of ccardiovascular disease (CVD) at the preclinical stage is primordial for effective primary prevention in this relatively young people. International recommendations regarding the prevention and management of CVD in T1D come from the extrapolation of data on type 2 T2D diabetes, although the pathogenesis of CVD and risk predictors in these two forms of diabetes are not completely identical (5). Few means of screening for early CVD are available and can detect subclinical atherosclerosis disease such as measuring the intima media thickness of the carotids or the ankle brachial index (ABI) (6). Other tools in the form of cardiovascular risk scores have been proposed to predict the first fatal or non-fatal CVD event among the T1D population such as the Steno Type 1 Risk Score (Steno-Risk) which is validated in Denmark and in certain countries in Europe. This score has a powerful predictive value for cardiovascular events at 5 years and 10 years in T1D (7) but its validation in other populations requires prospective longitudinal studies. With this background, the aim of the present study is to assess the relationship between steno risk and subclinical atherosclerosis disease detected by the ABI in T1D patients and to determine the frequency of these abnormalities among them.

Material and Methods

Study design and population

This is a cross-sectional, single-center study in a cohort of three hundred twelve individuals with T1D (151 M /161F, age range 16–75 years). All participants attended the Outpatient Diabetes Clinic of Mustapha University Hospital, Algiers (ALGERIA) fromJanuary 2016 to December 2018; they underwent yearly evaluation for the routine screening of chronic complications. The medical records of each patient's most recent visit were used to collect duration of diabetes, insulin therapy,smoking status, physical activity and the status of microangiopathy and cardiovascular complications. The patients had a careful questioning about the personal and family history of cardiovascular disease, as well as a clinical examination to assess the body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP). A measurement of The Ankle-Brachial Index is carried out in these patients. A metabolic assessment by measuring albuminuria,lipid profile (total cholesterol, HDL cholesterol,triglycerides), and HbA1c.

Measurements and definitions

Plasma concentrations of glucose and lipids were measuredby standard methods; glycated hemoglobin (HbA1c)by High-performance liquid chromatography (HPLC);albumin concentration in spot urine by immunoturbidimétric assay and plasma and urine creatinine by colometric methods. BMI was calculated as weight in kg/height in m2.Lowdensity lipoprotein (LDL) cholesterol was calculatedby Friedwald's formula. eGFR was calculated using the MDRD formula. Smoking status was defined as smokingone or more cigarettes per day.Hypertension wasdiagnosed as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg and/or use of antihypertensive drugs. Hypercholesterolemiawas defined as LDL cholesterol > 100 mg/dl or useof cholesterol-lowering drugs.

The ABI was calculated as (systolic pressure of the ankle in each leg)/ (the higher of the two arm systolic pressures). All the subjects entered in one of the following cohorts: ABI < 0.9 peripheral arterial disease (PAD), ABI ≥ 1.3 arterial calcification (AC), ABI between 0.9 and 1.3 normal.The Steno-Risk equation(www.sdcc.dk/T1riskengine) was used in 277 patients to estimate 10-year CVD risk (setting<10% as low; 10%-20% moderate; and ≥ 20% high risk). Thistool uses a composite CVD end-point including ischemic heart disease,ischemic stroke, heart failure and peripheral artery disease. Thevariables included in the score are age, gender, diabetes duration,HbA1c, systolic blood pressure, LDL-cholesterol, albuminuria, glomerularfiltration rate, smoking habit and regular exercise (≥ 3.5 h/wk.).

Statistical analysis:

Data are expressed as mean ± standard deviation (SD)or proportion (%). Normal distribution ofcontinuous variables was evaluated with the Kolmogorov-Smirnovtest. To compare continuous variables,an independent samples t test was performed. The Chisquare test was used to analyse categorical data. A *p* value < 0.05 was considered significant. The Statisticalanalysis was performed using SPSS v.25 (IBM SPSS Statistics 25).

Results

A total of 312 T1D patients were included (51,6 % females', mean age of 31 ± 12 years and 19 ± 11 years of diabetes duration).The main clinical and metabolic characteristics of thestudy population are shown in Table 1. There were 138 (44, 2%) subjects with normal ABI, 112 (35, 9%) with PAD and 62 (19, 9%) with AC. AC were more frequent in men than in women (p = 0,006). A family history of stroke were frequent in both PAD and AC groups (p = 0,042 and p = 0,046 respectively). Patients with AC were more frequently older (36 ± 13 vs. 30 ± 12; P = .012), had a longer diabetes duration (20 ± 11 vs. 14 ± 9; P < 0,001), a higher prevalence of hypertension (25,8 % vs. 14,5 %, P = 0,05), a higher prevalence of smoking (19,3 % vs. 9,4 %, P = 0,046), a lower estimated glomerular filtration rate (egger) (81 ± 30 vs. 92 ± 28, P = 0,014) and have more DR (50 % vs. 22,4 %, P <0,001) and pain neuropathy (22,6 % vs. 6,5 %, P = 0,001) than those with normal ABI. Patients with PAD had a higher SBP (131 ± 16 vs. 127 ± 19; P = 0,006), MBP (98 ± 10 vs. 95 ± 12; P = 0, 03) and a lower estimated glomerular filtration rate (egger) (84 ± 24 vs. 92 ± 28, P = 0,017) than those with normal ABI. The Steno-Risk score was directly associated with AC objective at ankle brachial index (Table 2). Thus, there were more subjects with AC in the Steno-Risk 10–20% and in the Steno-Risk ≥20% than in the Steno-Risk <10 % (37, 5 vs. 15, 5; 29 vs. 15, 5 p = 0, 0106) respectively. However, there were a bit more subjects with PAD in the Steno-Risk ≥20% than in the Steno-Risk <10 % (38, 7 vs. 36, 4) and less subjects with PAD in the Steno-Risk 10–20% than in the Steno-Risk <10 % (22, 5 vs. 36, 4).

TABLE 1 Clinical and laboratory characteristics of the patients enrolled in the study

Clinical and laboratory characteristics	Total population = 312	Normal ABI n = 138	PAD n = 112	P-value	AC n = 62	P-value
AGE (years)	31 ± 12	30 ± 12	30 ± 12	NS	36 ± 13	0,006
SEX M / F	151/161	58/80	55/57	NS	38/24	0,012
Diabetes duration (years)	19 ± 11	14 ± 9	15 ± 10	NS	20 ± 11	< 0.001
Family history CVD (n)						
Stroke	20	4	10	0,042	6	0,046
PAD	35	13	13	NS	9	NS
MI	38	14	14	NS	10	NS
Smoking (n)	35	13	10	NS	12	0,046
BMI (kg/m2)	24 ± 4	24 ± 4	25 ± 4	NS	25 ± 4	NS

SBP (mm Hg)	127 ± 19	127 ± 19	131 ± 16	0,006	123 ± 21	NS
DBP (mm Hg)	79 ± 10	80 ± 9	81 ± 9	NS	76 ± 12	NS
MBP (mm Hg)	95 ± 12	95 ± 12	98 ± 10	0,03	92 ± 14	0,065
Hypertension (n)	51	20	15	NS	16	0,05
Dyslipidaemia (n)	48	20	16	NS	12	NS
DR (n)	92	31	30	NS	31	< 0,001
eGFR< 60 ml/min	14	3	5	NS	6	0,058
Peripheric Neuropathy (n)	182	79	58	NS	45	NS
DN4 ≥ 4 (n)	35	9	12	NS	14	0,001
ACR (mg/g)	16 ± 31	24 ± 67	48 ± 218	NS	45 ± 160	NS
eGFR	92 ± 28	92 ± 28	84 ± 24	0,017	81 ± 30	0,014
HbA1c (%)	8,4 ± 1,7	8,4 ± 1,4	8,4 ± 1,9	NS	8,7 ± 1,7	NS
Triglycerides (mg/dl)	98 ± 48	87 ± 47	92 ± 46	NS	92 ± 52	NS
Cholesterol (mg/dl)	168 ± 40	167 ± 42	172 ± 39	NS	159 ± 38	NS
HDL Cholesterol (mg/dl)	63 ± 23	61 ± 22	59 ± 21	NS	63 ± 25	NS
LDL Cholesterol (mg/dl)	90 ± 40	88± 37	93 ± 37	NS	77 ± 32	NS

Note; Values expressed as mean ± SD, or number (n) P-value between PAD vs. Normal and between AC vs. Normal is represented.Abbreviations :ABI : ankle brachial index; PAD : peripheral arterial disease ; AC : arterial calcification ; BMI: body mass index ; SBP systolic blood pressure), DBP diastolic blood pressure ; CVD : cardiovascular disease ; MI myocardial ischemia ; MBP : mean blood pressure ; DN4 : score of neuropathic pain ; ACR : albuminuria creatinuria ratio : NS : no significant ; e*GFR*estimated glomerular filtration rate, HDL: high-density lipoprotein; LDL: low-density lipoprotein; DR : diabetic neuropathy.

TABLE 2: Relationship between ABI anomalies and Steno-Risk category

		ABI category			
N (%)	P=0,0106	normal	PAD	AC	Total n (%)
STENO-RISK category	Steno-Risk <10%	99	75	32	206 (74,4)
	Steno-Risk 10–20%	16	9	15	40 (14,4)
	Steno-Risk =20%	10	12	9	31 (11,2)
Total		125	96	56	277 (100)

Abbreviations: ABI: ankle brachial index; PAD: peripheral arterial disease; AC: arterial calcification

Discussion

Ankle-brachial index is indicated as a first-line test for screening and diagnosis of PAD (7). Its sensitivity is poorer in patients with diabetes or end stage CKD because of medial calcification (8). The latter is also considered as a form of arteriopathy in diabetics linked to premature aging of the arteries, which can explain its relationship with the age and duration of diabetes in our group of T1D patients. ABI ≥ 1.30 is also associated with CV risk factors such as male gender, smoking and hypertension. In addition, a very significant association is found between the presence of diabetic retinopathy and painful neuropathy. The correlation between the Steno-risk cardiovascular risk score and the results of the ABI finds a significant relationship between the arterial calcification suspected by a high ABI and the moderate and high steno risk whereas this relationship is not obvious when the ABI is <0.90. A Brazilian study which evaluated the relationship between ABI and the presence of subclinical atherosclerosis on carotid Doppler in a small group of T1D patients found a high frequency of arterial calcification evoked by ABI (66.7%) . they found that over Age >35 years and ankle-brachial index >1.4 showed a good correlation with atherosclerosis (r=0.49, p=0.021; r=0.56, p=0.008, respectively) and a model associating age >35 years and ankle-brachial index >1.4 showed an excellent relationship with atherosclerosis (r=0.59, p=0.004) (9). Another study showed that an ABI >1.4 was an independent cardiovascular risk factor and that there was a U-shaped associationbetween ABI value and cardiovascular mortality in 4393 American Indians (10).

Our study had some limitations. First, due to its cross-sectional design with only a single center.Second, the steno-risk used in this study is not validated in Algerian population. More longitudinal studies are needed to elucidate this result in a larger cohort.

However, ABI which is a simple non-invasive tool and cost-effective, could be proposed as a means of screening for atherosclerosis disease at an early stage in our T1D patients and an ABI > 1.30 can be proposed as suggestive of a moderate or high cardiovascular risk. This will involve further investigation to confirm cardiovascular disease and early action on the cardiovascular risk factors.

Conclusion

Our study shows that ABI > 1, 30 is more frequent in older patient with type 1 diabetes and it is associated with long duration of diabetes, male gender, smoking, hypertension and a family history of stroke. Moreover, ABI > 1,30 which marks the presence of arterial calcification is significantly associated to moderate and high cardiovascular risk evaluated by steno-risk in patient with type 1 diabetes. ABI may be a simple tool to screen atherosclerosis in T1D.

Conflict of interest statement

None of the authors have any conflicts of interests to declare.

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