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Peripheral Atherosclerosis in Patients With Erectile Dysfunction: A Population-Based Study

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ABSTRACT

Introduction: The presence of erectile dysfunction (ED) could be a warning of vascular disease in different arterial territories.

Aim: The aim of this study was to investigate the association between ED and the presence of atherosclerosis in 2 different vascular beds: carotid and lower limbs.

Methods: A total of 614 volunteers between 45 and 74 years of age (mean age 61.0 years) were randomly selected from the general population. ED was assessed using the International Index of Erectile Function (IIEF-5). Ankle-brachial index (ABI) measurement and carotid atherosclerosis were evaluated by echo-Doppler.

Main Outcome Measures: Mean carotid intima-media thickness (IMT), prevalence of carotid plaques, mean ABI, and prevalence of ABI < 0.9 were the main outcome measures.

Results: ED was present in 373 subjects (59.7%). Mean carotid IMT was significantly higher in men with ED (0.762 ± 0.151 mm vs 0.718 ± 0.114 mm, $P < .001$). Also the global prevalence of carotid plaques was more frequent in men with ED (63.8% vs 44.8%, $P < .001$), even after adjusting by age, cardiovascular risk factors, and ongoing treatment ($P = .039$). Both the IMT and the prevalence of carotid plaques increased significantly with ED severity (P trend .004 and <.001, respectively). There were no significant differences between groups neither in mean ABI nor in the prevalence of subjects with ABI < 0.9. However, there was a trend to a lower ABI and a higher prevalence of ABI < 0.9 with increasing ED severity.

Conclusion: In the general population, the presence of ED identifies subjects with higher atherosclerosis burden in carotid arteries but not in the lower extremities.

Key Words: Ankle-Brachial Index; Carotid Artery Plaque; Erectile Dysfunction; Intima-Media Thickness

INTRODUCTION

Erectile dysfunction (ED) is defined as the persistent inability to attain or maintain satisfactory erection for intercourse. Its prevalence increases with age, ranging from 5% in men aged 20–39 years to 70% in men aged 70 years and older.[1] The majority of cases have an organic etiology, most commonly vascular disease. Cardiovascular risk factors such as dyslipidemia, hypertension, obesity, and smoking have been shown to increase the risk of ED.[2]

Several meta-analyses have shown that ED significantly increases the risk of cardiovascular disease (CVD), coronary heart disease (CHD), stroke, and all-cause mortality.[3–5] CVD and ED share etiology and pathophysiology, and the degree of ED correlates with severity of CVD.[6] ED often precedes the appearance of clinical CVD,[7] probably because the penile artery has a smaller diameter than coronary arteries and an equally sized atherosclerotic plaque developed in the smaller penile arteries would more likely compromise flow than if the plaque developed in the larger coronary arteries.[6] Therefore, the

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presence of ED could be a warning of vascular disease in different arterial beds.[7]

Measurement of the ankle-brachial index (ABI) is a simple, low-cost, and accurate test for the diagnosis of peripheral artery disease (PAD). The presence of an ABI < 0.9 is accepted as a highly sensitive and specific diagnostic marker of PAD when compared with arteriography, even in patients with no clinical evidence of the disease.[8] A low ABI has been associated with an increased risk of cardiovascular morbidity and mortality.[9,10] Only a few studies have evaluated the association between ED and PAD, and this has been usually done in special populations, such as diabetics[11,12] or subjects with high cardiovascular risk.[13] No previous studies of this relationship have been done in the general population.

B-mode ultrasound of carotid arteries provides measures of intima-media thickness (IMT) and plaque, both widely used as surrogate measures of CVD. Carotid IMT and plaque burden have been shown to be independent predictors of future cardiovascular risk.[14,15] The relationship between carotid atherosclerosis and ED has been investigated in small studies with contradictory results.[16–18] Finally, few studies have simultaneously evaluated the involvement of both vascular beds in patients with ED,[20,21] but never in a population-based study.

The aim of this study was to investigate the association between ED and the presence of atherosclerosis in 2 different vascular beds, carotid and lower limbs, measured by B-mode carotid ultrasound and ABI, respectively, in men between 45 and 74 years randomly selected from the general population.

MATERIAL AND METHODS

The characteristics of the Screening PRE-diabetes and type 2 DIAbetes (SPREDIA-2) study have already been described.[22] In short, the SPREDIA-2 study is a population-based prospective cohort study with baseline screening, in the region of Madrid (Spain). A random sample of urban subjects, between 45 and 74 years living in the northwest metropolitan area of Madrid was selected for the study. Women, subjects with severe chronic or terminal illnesses, institutionalized subjects, or those chronically treated with steroids or antipsychotic drugs were excluded.

Participants were scheduled in the outpatient clinic of the Carlos III Hospital after an overnight fast. Upon arrival, and after signing a consent form, a fasting blood analysis was obtained for measuring the blood levels of glucose, creatinine, HbA1c, lipids, and lipoproteins. Sociodemographic variables, family history of prevalent diseases, cardiovascular risk factors (smoking habit, hypertension, diabetes, hypercholesterolemia), clinical history of CVD, comorbidities, and current treatments were recorded for all individuals. Participants were considered as hypertensive when the arterial pressure was $\geq$ 140/90 mm Hg or were receiving antihypertensive treatment. Hypercholesterolemia was defined has having LDL-cholesterol $\geq$ 100 mg/dL (2.57 mmol/L) and/or receiving hypolipidemic medication. The smoking habit included all who had consumed tobacco over the previous month. A diabetes diagnosis was established when baseline glucose was $\geq$ 7 mmol/L (126 mg/dL) on 2 different occasions, or if the patient was receiving oral hypoglycemic drugs, or insulin. CVD included documented history of coronary heart disease (acute myocardial infarction, angina, coronary revascularization procedure), ischemic or hemorrhagic stroke, and peripheral arterial disease. All participants had a physical examination with determination of height, weight, waist circumference (midway between lowest rib and the iliac crest), and blood pressure.

ED Assessment

ED was assessed using the IIEF-5,[23] Which is designed to be a self-administered measure of ED. The IIEF score ranges from 5 to 25 points, in which a descending score indicates worsening of ED. Erectile dysfunction was classified as normal, mild, mild-moderate, moderate, and severe for IIEFs of $\geq$ 22, 17–21, 12–16, 8–11, and $\leq$ 7, respectively.

Laboratory Methods

Cholesterol and triglycerides were determined by enzymatic assays. Low-density lipoprotein cholesterol (LDL-cholesterol) was calculated according to the Friedewald formula (LDL-cholesterol = total cholesterol − ([high-density lipoprotein cholesterol (HDL-cholesterol) + triglycerides/5]) in subjects with triglycerides below 400 mg/dL. HDL-cholesterol was measured after precipitation of apo-B lipoproteins. Glucose was measured by the glucose oxidase method. HbA1c was measured by a high-performance liquid chromatography (HPLC) method.

ABI Determination

The ABI measurements were performed with a bidirectional portable echo-Doppler of 8 MHz (Minidoppler HADECO ES-100, Kawasaki, Japan) and a calibrated sphygmomanometer. The systolic blood pressure (SBP) was measured in the posterior tibial and pedal arteries of both lower limbs and the brachial artery of both upper limbs. The value of the ABI for each limb was calculated dividing the greater.

SBP obtained in each limb by the SBP of whichever was the higher in the upper limbs. The lowest value obtained was considered the ABI for that individual.

IMT and Carotid Plaque Assessment

An echo-Doppler of both carotids was performed with a 7.5-MHz probe (Sonosite Micromaxx Ultrasound, Sonosite Inc, Bothell, WA, USA). Patients lay in the supine position with the neck rotated to the opposite site of the examination. One centimeter images were obtained from the distal wall of the common carotid artery proximal to the bifurcation, in 3 different angles views. IMT was obtained with an automated software (Sonosite, Sonocalc IMT Software, Sonosite Inc), and the overall mean IMT values for each of the 6 segments analyzed (3 angles