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Vascular and Chronological Age in Men With Erectile Dysfunction: A Longitudinal Study

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ABSTRACT

Introduction: Impaired penile color Doppler ultrasound predicts major adverse cardiovascular (CV) events (MACE), particularly in men at low-risk. However, penile color Doppler ultrasound is not recommended in routine clinical checkups.

Aim: To evaluate whether the difference between vascular and chronological age (Δage), as derived from the SCORE algorithm, is a predictor of MACE in subjects consulting for erectile dysfunction (ED) independently from other CV risk factors, including penile color Doppler ultrasound parameters.

Methods: A consecutive series of 1687 male patients attending the Outpatient Clinic for ED for the first time was retrospectively studied. Among them, the SCORE was applicable in 49.9% (n = 841) men, of whom 87.9% (n = 739) were free from previous MACE and were analyzed.

Main Outcome Measures: Vascular age was derived from the SCORE algorithm and the Δage was considered. Information on MACE was obtained through the City of Florence Registry Office. MACE were identified using the International Classification of Diseases, and fatal and nonfatal MACE were coded as 410−414 (ischemic heart disease), 420−429 (other heart diseases), or 798−799 (sudden death from cardiac diseases), 430−434 or 436−438 (cerebrovascular disease), and 440 (peripheral arterial disease).

Results: Δage was associated with incident MACE. When dividing the population according to the median age (56 years), family history of CV diseases, and the presence of metabolic syndrome, the association between Δage and MACE was maintained only in low-risk subjects, even after adjusting for confounders [HR = 1.09(1.03−1.16), 1.05(1.01−1.10) and 1.08(1.01−1.16) for younger men, without CV family history or metabolic syndrome, respectively, all $P < .05$], including penile color Doppler ultrasound parameters.

Conclusion: In subjects consulting for ED, Δage is associated with incident MACE, in particular in low-risk men. The prediction of MACE by Δage is independent from other risk factors including penile color Doppler ultrasound parameters, so it can be used as a costless and safe surrogate marker of penile vascular damage.

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Key Words: Erectile Dysfunction; Vascular Age; Cardiovascular Risk; SCORE Algorithm; Penile Color Doppler Ultrasound

INTRODUCTION

Erectile dysfunction (ED) shares several risk factors with cardiovascular (CV) diseases (CVD), such as aging,[1] smoking,[2] hypertension,[3] diabetes,[4,5] dyslipidemia,[3] obesity,[4] and sedentary lifestyle,[2] along with low testosterone (T).[6,7] ED is now considered 1 of the multiple expressions of endothelial dysfunction and atherosclerosis. In fact, arteriogenic ED, usually assessed through penile color Doppler ultrasound, is associated with a relevant increase in the risk of CVD; as such, it can be used as a factor for the identification of subjects at high CV risk.[8−11] The impact of arteriogenic ED on CV risk is particularly evident in younger subjects, as shown by the Olmsted County Study[12] and from the results of a recent meta-analysis.[13]

The SCORE project is a study based on a large pool of representative data sets from 12 European countries and is aimed at creating a scoring system for use in the clinical management of CV risk in European clinical practice. On the basis the results of the SCORE project, an algorithm—taking into account age, smoking habits, systolic blood pressure, and total cholesterol—was

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produced for estimating the 10-year CV risk.[14] Considering that the same 10-year risk corresponds to different combinations and extent of the risk factors, the concept of vascular age was introduced. In fact, the vascular age of a subject with a certain risk profile is equal to the chronological age of a subject with the same estimated CV risk, but whose risk is attributable only to age, as none of the considered modifiable risk factors (smoking, systolic blood pressure >140 mmHg, and total cholesterol >230 mg/dL) are present.[15,16] Vascular age easily explains the high relative risk of CVD that a young person, by definition at low absolute risk, is exposed to when appropriate measures for prevention or correction of risk factors are not adopted. The calculation of estimated vascular age was originally based on the CV risk tables derived from the Framingham Heart Study[15] and then applied also to the SCORE (Systematic COronary Risk Evaluation)[15] project scales, thus allowing the determination of vascular age in Southern European countries, including Italy, where the Framingham algorithm would overestimate the risk.[17–19]

There is no agreement on what vascular age represents and on its clinical utility.[20] At present, the European guidelines on CVD prevention[21] recommend its use as a support to communication on CV risk, especially with younger people with a low absolute risk but a high relative risk, but not as a basis for treatment decisions. The concept of risk associated with modifiable risk factors is further stressed by the use of the difference between vascular and chronological age (Δage). In fact, according to the SCORE project algorithm, a 40-year-old man, smoker, with a systolic blood pressure of 180 mmHg and a total cholesterol of 310 mg/dL has the same estimated 10-year risk as a 61-year-old man, non-smoker, with a systolic blood pressure of 120 mmHg and a total cholesterol of 230 mg/dL. Hence, using the concept of vascular age, we communicate to the 40-year-man that he has a vascular age of 61 years and a Δage of 21 years, whereas the 61-year man has a vascular age of 61 and a null Δage. Considering vascular age these men are equal; however, whereas the 40-year-old man can reduce his own risk by improving his lifestyle, the 61-year-old man cannot change his estimated CV risk. This difference is captured by the concept of Δage. Few studies have been published evaluating the clinical correlates of Δage. In a huge sample of men consulting for ED, we recently investigated the clinical correlates of Δage.[22] In that study we found that Δage was associated with an adverse metabolic profile, identifying subjects with a high-risk CV profile. In addition, it showed a high correlation with penile color Doppler ultrasound parameters, suggesting that Δage can be a surrogate marker of penile artery disease, but easier to obtain, costless, and free from adverse events, such as priapism. Whereas penile color Doppler ultrasound parameters have already demonstrated their role in predicting major adverse CV events (MACE) in ED men,[9–11] so far no study has evaluated the association between Δage and the incidence of MACE.

The aim of the present study is to evaluate, in a population of subjects seeking medical care for ED and free from previous MACE, whether the difference between vascular age, as derived from the SCORE project scale, and chronological age (Δage) can predict incident MACE independently from other risk factors, including the penile color Doppler ultrasound parameters, thus providing an alternative and simpler method for taking into account arterial damage in ED-related CV risk.

METHODS

Data from a consecutive series of 1687 patients attending the Outpatient Clinic for ED for the first time between 2000 and 2007 were retrospectively collected and data concerning CV events as well as mortality and causes of death were acquired. This sample is a subset of 1 previously described that was used for the cross-sectional survey for whom information on MACE was collected.[22] Men involved in the study were referred to the Outpatient Clinic of Sexual Medicine and Andrology Unit of the University of Florence by their general practitioner, according to Italian regulation of access to public healthcare services. All patients enrolled underwent the usual diagnostic protocol applied to newly referred subjects at the Outpatient Clinic. All the data provided were collected as part of the routine clinical procedure. An informed consent for the study was obtained from all patients. Among these subjects, only those who had all the parameters for calculating the SCORE algorithm (N = 841) were considered. According to the applicability of the SCORE,[14] men who had a previous CV event (n = 102) were excluded from the analysis, leaving 739 men in the analysis sample. The sociodemographic and clinical characteristics of the sample studied (ie, having all the parameters for calculating SCORE and free from previous CV events) are reported in Table 1. All the data on their medical history, including medications, were collected during the first visit, before any specific diagnostic procedure or therapy. Patients were asked to report their family history, noting diseases of their first-degree relatives. CV events such as ischemic heart disease, other heart diseases, sudden death from cardiac diseases, cerebrovascular disease, and peripheral arterial disease were considered relevant and were collected. For descriptive purposes, hypertension and diabetes mellitus were defined as previously known diagnosis and/or when patients reported to take medications specific for these conditions. Chronic Diseases Score, an index of concomitant morbidities, was used for adjustments in the statistical models to control the analyses for several comorbid conditions together without the concern of overfitting. The Chronic Diseases score is an aggregate comorbidity measure based on current medication use.[23,24] It was originally created by a panel of health professionals by using a pharmaceutical database to reach consensus decisions as to which classes of medications should be included in the score and how they should be weighted to correspond to disease complexity and severity. The Chronic Diseases Score was originally validated for use as a predictor of physician-rated diseases status, self-rated health status, hospitalization, and mortality.[23,24] It is calculated as the algebraic sum of scores derived from the use of a large set of medications, each one