Flaccid Penile Acceleration as a Marker of Cardiovascular Risk in Men without Classical Risk Factors

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ABSTRACT

Introduction. Conventional cardiovascular (CV) risk factors identify only half of subjects with incident major adverse CV events (MACE). Hence new markers are needed in high CV risk subjects, as those with erectile dysfunction (ED). A role for dynamic peak systolic velocity (D-PSV) at penile color Doppler ultrasound (PCDU) has been suggested, but it is operator dependent and time consuming. Flaccid penile acceleration (FPA) is a PCDU parameter that reflects PSV, the systolic rise time (SRT), and end diastolic velocity (EDV), arithmetically defined as (PSV–EDV)/SRT.

Aim. The study aims to verify, in a large series of ED patients, whether FPA has a role in predicting MACE.

Methods. A selected series of 1,903 patients (aged 54.6 ± 11.7) with a suspected organic component for ED was retrospectively studied from January 2000 until July 2012. A subset of this sample (n = 622) was enrolled in a longitudinal study that ended in December 2007.

Main Outcome Measures. Several clinical, biochemical, and instrumental (PCDU) parameters were studied.

Results. Decreased FPA levels were associated with worse metabolic profile and sexual symptoms. In addition, FPA was positively associated with both total and calculated free testosterone. In the longitudinal study, unadjusted incidence of MACE was significantly associated with lower baseline FPA. When FPA was introduced in a multivariate model, along with D-PSV, after adjusting for age and Chronic Disease Score, lower FPA, but not D-PSV, was associated with incident MACE in lower-risk—i.e., younger (HR = 0.48 [0.23–0.99]), nonhypertensive (HR = 0.59 [0.38–0.92]), nonobese (HR = 0.68 [0.49–0.96]), or nondiabetic (HR = 0.67 [0.49–0.96] subjects; all $P < 0.05$—but not in higher-risk ones. FPA demonstrated a threshold effect in predicting MACE at a value <1.17 m/s^2 which showed a threefold increase in incidence of MACE in apparently lower-risk individuals.

Conclusions. FPA is an easily obtained PCDU parameter and capable of identifying adverse metabolic and CV profiles, particularly in apparently lower-risk individuals with ED. **Rastrelli G, Corona G, Lotti F, Aversa A, Bartolini M, Mancini M, Mannucci E, and Maggi M. Flaccid penile acceleration as a marker of cardiovascular risk in men without classical risk factors. J Sex Med 2014;11:173–186.**

Key Words. Penile Doppler Parameters; Cardiovascular Risk; Flaccid Acceleration; Sexual Dysfunction; Residual Risk

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Introduction

An adequate cavernosal blood inflow is the fuel of penile erection, a necessary step for allowing successful male fertility and sexuality. The penile architecture can be easily visualized by the combined application of Doppler effect to B-mode sonography, introduced by Lue et al. [1,2], that firstly evaluated penile blood flows in flaccid condition and after intracavernous injection of papaverine both in healthy volunteers and in subjects with erectile dysfunction (ED). Since then, the use of penile color Doppler ultrasound (PCDU) has became more and more relevant and nowadays is considered as the gold standard for studying penile vasculature, giving information on diameter of the penile (cavernous) artery, peak systolic velocity (PSV), degree of arterial dilatation, and waveform shape. PSV, measured 5–20 minutes after the injection of a vasodilating agent (dynamic PCDU; D-PCDU), such as prostaglandin E1 (PGE_1; 10 μg), is the usual parameter for the evaluation of penile circulation [3–5]. Dynamic PSV (D-PSV) of the cavernosal arteries has been demonstrated to discriminate accurately normal from abnormal cavernosography [3,6]. In particular, a D-PSV <25 cm/s has a sensitivity and specificity ≥95% for detecting impaired cavernosal blood flow at angiography, whereas a D-PSV ≥35 cm/s is associated with normal vasculature [3,6]. Besides PSV, the following parameters, commonly used in vascular diagnostics for blood-flow quantification, can describe the waveform derived from D-PCDU: acceleration time or systolic rise time (SRT), end-diastolic velocity (EDV), and resistive index (RI) [3,7]. All these parameters give insights on different aspects of penile hemodynamics. Whereas PSV reflects the greatest flow velocity detectable in the cavernosal artery throughout the systole, SRT is the time measured from the start of the systolic peak velocity to the maximum value, whereas EDV and RI provide information on penile veno-occlusive mechanisms. Despite these evidence-based advantages and the relatively low invasiveness, D-PCDU is not routinely used for the evaluation of ED, primarily because it is time consuming [7] and it carries the risk of priapism [7]. In addition, D-PCDU is operator dependent [7], and it may result in an incorrect diagnosis because of anxiety and its related sympathetic stimulation [8,9] or as a consequence of the high prevalence of arterial anatomical variants [10]. Hence, standardization of D-PCDU is cumbersome and the major urological societies [11,12] and The International Society of Sexual Medicine (ISSM) [7] do not recommend its routine use in the screening of ED, limiting its application to cases in which information on vascular supply is needed as, for example, in the choice of surgical treatment. In contrast, a growing amount of evidence has shown that ED is an early marker of cardiovascular (CV) disease (CVD) ([13,14], see for review ref. [15]). Hence, recognizing an arteriogenic component of ED is pivotal for identifying patients that can benefit from changing lifestyle, both for their sexual and CV health [16]. Hence, finding a simple parameter that can give insight into penile vascular health without carrying the inconvenience of priapism and with limited costs in terms of time and money is an ideal goal for both sexual and CV medicine.

We previously demonstrated, in a large population of ED subjects, that D-PSV lower than 25 cm/s was associated with a doubled risk of forthcoming major adverse CV event (MACE) [13], but we also found that PSV in the flaccid state can provide additional information on penile and overall CV status [13,17–19]. In particular, flaccid PSV <13 cm/s was capable of detecting subjects with inducible myocardial ischemia [17], and of predicting incident MACE [13]. Also, SRT has demonstrated its usefulness in reflecting vessel health, in fact its increase has previously been shown to reflect proximal arterial disease in the lower limbs [20,21]. Oates et al. [22] showed that SRT after pharmacological stimulation is a good discriminant of penile arteriopathy, as confirmed by pudendal arteriography (data confirmed also by other authors [23–25]). Acceleration is a dimension that recapitulates all the previously mentioned Doppler parameters, because it reflects both PSV and the time elapsed to reach it. It is calculated as ([PSV – EDV]/SRT, m/s^2) and represents the slope of the tangent of the systolic rise waveform [7]. Moreover, acceleration is not affected by other parameters such as heart rate which can affect the SRT. In earlier studies, waveform acceleration was even superior to D-PSV in detecting arteriography-documented penile abnormalities [26].

Aim

The aim of this study is to evaluate the clinical correlates of flaccid penile acceleration (FPA) in a large series of patients consulting for ED and with a suspected organic component for ED, and to verify the role of this parameter—relatively