Evaluation of Microalbuminuria in Patients with Erectile Dysfunction

Alessandra Barassi, MD,* Raffaele Pezzilli, MD,† Antonio Maria Morselli-Labate, MD,† Wanda Porreca, MD,‡ Guido Piediferro, MD,§ Francesco Ciociola,§ Giovanni Colpi, MD,§ and GianVico Melzi d’Eril, MD*

*Università degli Studi di Milano—Dipartimento di Medicina, Chirurgia e Odontoiatria, Milano, Italy; †Ospedale S.Orsola-Malpighi—Dipartimento di Medicina Interna e Gastroenterologia, Università degli Studi di Bologna, Bologna, Italy; ‡Ospedale San Paolo—Laboratorio di Analisi, Milano, Italy; §Ospedale San Paolo—Uo de Urologia Andrologica, Milano, Italy

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ABSTRACT

Introduction. The recent sophisticated diagnostic procedures aimed at identifying the exact cause of erectile dysfunction (ED) are often complicated in clinical application, invasive, or highly expensive. Microalbuminuria, a test easy to perform and of low cost, is a marker of extensive endothelial dysfunction, and it has been suggested to be linked to ED.

Aim. The aim of this study was to investigate the eventual role of microalbuminuria in differentiating patients with arteriogenic and non arteriogenic ED.

Methods. The diagnosis of ED was based on the International Index of Erectile Function 5-questionnaire, and patients were classified as arteriogenic (N = 29) and non-arteriogenic (N = 49) in relation to the results of echo-color-doppler examination of cavernosal arteries in basal conditions and after intracavernous injection of 10 μg prostaglandin E1.

Main Outcome Measures. The microalbuminuria of 78 males without the most common atherosclerotic risks and with ED was measured.

Results. Microalbuminuria, defined as urinary albumin/creatinine ratio, was not significantly (P > 0.05) different between patients of the two groups.


Key Words. Erectile Dysfunction; Microalbuminuria; Endothelial Function; Cardiovascular Risk for Erectile Dysfunction

Introduction

Erectile dysfunction (ED) has been defined by the National Institute of Health as the inability to achieve and/or to maintain penile erection of sufficient quality to allow a satisfactory sexual intercourse [1]. It has been estimated to affect 20 million to 30 million men in the United States, and that approximately 5–20% of men, complain of moderate to severe ED [2]. Although penile erection is the result of a complex and coordinated series of events involving vascular response, neuronal pathways, and psychosomatic stimulation, the proper function of the vascular endothelium is...
The coincidence of microalbuminuria and extrarenal vascular damage in diabetic patients led to the hypothesis that albuminuria does not only reflect a state of glomerular, but also generalized endothelial dysfunction [21]. Many recent studies [22] demonstrate the usefulness of microalbuminuria as a valuable and clinically relevant tool for the identification of individual patients at risk for the development of end-organ damage, for example, systemic cardiovascular disease. Therefore, the endothelium appears to be the link between metabolic changes and physiological dysfunction. In accordance with the aforementioned data, we hypothesized that microalbuminuria could be a marker of vascular ED in a population free of the most common atherosclerotic risks. The benefits of using microalbuminuria to screen for endothelial injury are that it is inexpensive and the results are available rapidly.

The aim of this study was to investigate the relationship between arteriogenic ED and microalbuminuria, as a marker of endothelial dysfunction, in a group of patients without known clinical risk factors for vascular pathology.

**Materials and Methods**

Erectile function was assessed on an appropriate clinical work-up study and by using the abridged five-item version of the International Index of Erectile Function questionnaire (IIEF-5), a validated, self-administered questionnaire [23,24]. Seventy-eight men (mean age 44.1 years, range 24–62 years) underwent echo-color-doppler examination of cavernosal arteries in basal conditions and after intracavernous injection of 10 µg prostaglandin E1, and the peak systolic velocity (PSV) and end-diastolic velocity (EDV) were recorded 5, 10, 15, 20, and 25 minutes after the drug injection into the proximal portion of the penis. PSV and EDV are reported as the mean of the values measured in both cavernosal arteries. Patients were classified as non-arteriogenic when their PSV was \( \geq 35 \text{ cm/sec} \), or \( <35 \text{ cm/sec} \) but \( >25 \text{ cm/sec} \) with concomitant EDV \( \leq 0 \text{ cm/sec} \), and arteriogenic when their PSV was \( \leq 20 \text{ cm/sec} \) [25]. Resistance index (RI) >0.80 is considered normal. The erection quality was estimated 20 minutes after each injection. If a patient appeared stressed, he was given a second injection of the same dose of prostaglandin E1 and all measurements were repeated. The procedure was repeated in one non-arteriogenic and two arteriogenic patients without changing the outcomes.
None of the patients had clinical evidence of coronary artery disease, diabetes mellitus, hypertension, malignancy, renal failure, congestive heart failure, systemic inflammatory disease, or arrhythmias. In all patients, we measured the testosterone and prolactin serum levels, and only patients without endocrine risk factors were considered in the present study. In accordance with Helsinki Declaration II, the design and execution of the experiment were explained thoroughly to the participants, and informed consent was obtained. The Mann-Whitney and the Fisher’s exact tests were applied to analyze data by running the SPSS (Version 12.0 for Windows) statistical package. Urinary microalbumin concentration was measured in duplicate in the morning samples on a Behring Nephelometer II analyzer (Dade Behring). The within-run (N = 40) and the between-run coefficient of variation (CV) (N = 15) of the determination were 4.1% and 5.0% at 49.2 g/L, respectively. The detection limit was 11 mg/L. Urinary creatinine in the same morning samples was measured in duplicate by a modified Jaffe’s reaction (Crea, Roche) on a Modular analyzer (Roche) and the within-run (N = 40) and the between-run CV (N = 15) of the determination were 1.2 and 2.3% at 0.6 g/L, respectively. The detection limit was 0.040 g/L. Both determinations were performed on the same day of the sample collection. The UACR (mg/g) was calculated by dividing the mean of the urinary albumin values by the mean of the urinary creatinine concentration. The body mass index (BMI) of all patients has been calculated because the population with higher muscle mass have higher levels of creatinine excretion [26].

Results

The characteristics of the arteriogenic and non-arteriogenic ED patients are summarized in Table 1. Out of the 78 males, based on the echocolor-doppler examination results, 29 patients had arteriogenic ED (mean age 42.1 years, range 26–62 years; mean BMI 23.4 Kg/m², range 20.9–25.6 Kg/m²) and 49 patients had non-arteriogenic ED (mean age 45.0 years, range 24–61 years; mean BMI 23.0 Kg/m², range 20.2–25.5 Kg/m²). The age and the BMI of the two groups were not significantly different (P = 0.213 and P = 0.312, respectively). Mean PSV was 16.2 cm/sec (range 9–19 cm/sec) and 46.4 cm/sec (range 32–79 cm/sec) in patients with arteriogenic and with non-arteriogenic ED (P = 0.001), respectively. Mean EDV was 4.11 cm/sec (range 0–6 cm/sec) and 2.18 cm/sec (range from –6 to +12 cm/sec) in patients with arteriogenic and with non-arteriogenic ED (P = 0.002), respectively. Mean RI was 0.72 (range 0.63–0.79) and 0.95 (range 0.73–1.2) in patients with arteriogenic and with non-arteriogenic ED (P = 0.001), respectively. In the first group, IIEF values were: mean 11.20 (range 0–22); in the second group the respective figures were 12.9 (range 0–21). There were no significant differences between the two groups (P = 0.289). Undetectable levels of albuminuria in at least one of the two determination were present in 20 (69.0%) patients with arteriogenic ED and in 40 (81.6%) of those with non-arteriogenic ED (P = 0.267). In the 18 patients with detectable UACR concentrations, the mean ± SD UACR was 38.6 ± 27.9 mg/g (range 8–95 mg/g) and 52.2 ± 41.8 mg/g (range 10–143 mg/g) in the first (9 patients) and in the second (9 patients) group, respectively. UACR of arteriogenic ED patients were not significantly different from UACR of non-arteriogenic ED patients (P = 0.429). Even in the patients with detectable UACR concentrations, there was no correlation with IIEF scores in both groups (P = 0.05).

Discussion

The small diameter of the cavernosal arteries and the high content of endothelium and smooth muscle on a per-gram tissue basis (compared with
other organs) may make the penile vascular bed a sensitive indicator of systemic vascular disease [27]. A normal erectile function requires a healthy endothelial function [28]. Endothelial dysfunction, which is associated with impaired release and activity of NO, therefore, can be a cause of vascular ED [29,30]; through the same system, endothelial dysfunction is the physiologic connection between ED and systemic vascular disease [31,32]. As previously mentioned, microalbuminuria is considered as a marker of extensive endothelial dysfunction. In the Steno hypothesis put forward by Deckert [21], albumin leakage into the urine is a reflection of widespread vascular damage. In a sense, the kidney is the window of the vasculature. In view of these considerations, endothelial function and chronic inflammation have been suggested as possible candidates to explain the association between microalbuminuria and cardiovascular diseases [33,34]. However, other studies indicate that although microalbuminuria, endothelial dysfunction, and low-grade inflammation are linked, they all are independently associated with risk for cardiovascular death [35,36].

In our present search for a sensitive marker of endothelial dysfunction in ED patients, the aim of our study was to check if a simple examination like microalbuminuria could replace the dynamic echo-color-doppler evaluation of the cavernosal arteries in discriminating the arteriogenic from the non-arteriogenic ED subjects. Our results do not support a role of microalbuminuria as a screening method. In line with this evidence, recently conducted studies that measured early markers of cardiovascular diseases and endothelial dysfunction (flow mediated-vasodilation and soluble P-selectine), demonstrated that damage to the penile vascular bed occurs before systemic vascular illness becomes clinically apparent [37–39].

Conclusion

Our study shows that in ED patients without clinical evidence of atherosclerotic diseases, and free of the common risk factors associated with generalized penile arterial insufficiency, the cavernosal arteries damage, as assessed by dynamic echo-color-doppler, may be independent on or may precede extensive endothelial dysfunction. In addition, in this kind of ED patients microalbuminuria expressed as UACR cannot be predictive of pure penile arteriogenic etiology, at least in our experimental conditions. In general, no relation-ship was shown between ED and microalbuminuria in patients without any other known clinical pathology.

This preliminary study shows that urinary microalbumin expressed as UACR would be unsatisfactory for the prediction of ED of arteriogenic etiology, at least in our experimental conditions.

Corresponding Author: Alessandra Barassi, MD, University of Milan, Via Di Rudinì, Milan, 20142, Italy. Tel: +393923325300; Fax: +90281844027; E-mail: alessandra.barassi@unimi.it

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Statement of Authorship

Category 1
(a) Conception and Design
Alessandra Barassi; GianVico Melzi d’Eril; Raffaele Pezzilli
(b) Acquisition of Data
Antonio Maria Morselli-Labate; Wanda Porreca; Guido Piediferro; Alessandra Barassi; Giovanni Colpi
(c) Analysis and Interpretation of Data
Guido Piediferro; Francesco Ciociola; Giovanni Colpi; Alessandra Barassi; GianVico Melzi d’Eril

Category 2
(a) Drafting the Article
Alessandra Barassi; GianVico Melzi d’Eril; Wanda Porreca; Raffaele Pezzilli; Antonio Maria Morselli-Labate
(b) Revising It for Intellectual Content
Alessandra Barassi; GianVico Melzi d’Eril; Raffaele Pezzilli; Francesco Ciociola; Giovanni Colpi; Guido Piediferro

Category 3
(a) Final Approval of the Completed Article
Alessandra Barassi; Raffaele Pezzilli; Antonio Maria Morselli-Labate; Wanda Porreca; Guido Piediferro; Francesco Ciociola; Giovanni Colpi; GianVico Melzi d’Eril

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