PREVALENCE OF INTERNAL PUDENDAL ARTERY DISEASE IN DIABETIC PATIENTS WITH ERECTILE DYSFUNCTION AND ANGIOGRAPHICALLY DOCUMENTED MULTI-VESSEL CORONARY ARTERY DISEASE

Hossam Zaki, Wail Nammas, Ahmed Shawky *, Ayman Mortada, Tarek Zaki

Cardiology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Received 27 September 2012; accepted 23 November 2012
Available online 18 January 2013

KEYWORDS
Diabetes mellitus; Coronary artery disease; Erectile dysfunction; Internal pudendal artery

Abstract
Objectives: We set out to explore the prevalence of significant atherosclerotic disease of the internal pudendal arteries (IPA) in diabetic men with erectile dysfunction (ED) and angiographically documented multi-vessel coronary artery disease (CAD).

Background: ED shares common risk factors of CAD, and is increasingly recognized as a well established risk factor for future cardiovascular events.

Methods: We enrolled 30 consecutive diabetic patients with ED undergoing elective coronary catheterization. Erectile function was evaluated using the abbreviated 5-item questionnaire known as the Sexual Health Inventory for Men. Distal aortography was first performed, followed by selective internal iliac arteriography. Significant IPA disease was defined as 50% or more luminal obstruction seen in the projection that best delineates the takeoff of the artery.

Results: The mean age of the whole series was 59.6 ± 8.4 years. The mean duration of diabetes mellitus was 8.1 ± 7.1 years, and the mean duration of ED was 4.3 ± 3.2 years. Significant IPA disease (stenosis/occlusion) was found in 11 (36.7%) patients; unilateral in 6 (20%) patients, and bilateral in 5 (16.7%) ones. Significant internal iliac artery disease (stenosis/occlusion) was found in 6 (20%) patients; unilateral in 4 (13.3%) patients, and bilateral in 2 (6.7%) ones. Significant IPA disease correlated positively with age and negatively with estimated creatinine clearance (p < 0.05 for both).

Conclusions: In diabetic male patients with ED who have angiographically documented multi-vessel CAD, significant IPA obstruction (stenosis/occlusion) is rather frequent, and it correlates positively with age, and negatively with the estimated creatinine clearance.

© 2012 Egyptian Society of Cardiology. Production and hosting by Elsevier B.V. All rights reserved.

1. Introduction

Defined as the repeated inability to achieve and maintain erection sufficient for satisfactory sexual intercourse, erectile dysfunction (ED) affects more than 150 million men all over
the world.\textsuperscript{1,2} Although ED is multifactorial in origin vascular causes are not uncommon, being mostly related to insufficient arterial inflow to the penile arteries, impaired cavernosal smooth muscle relaxation, or veno-occlusive dysfunction.\textsuperscript{3} It was reported that men with ED may have angiographically documented significant atherosclerotic disease of the iliac, internal pudendal, or cavernosal arteries.\textsuperscript{4,6} Interestingly, ED shares common classic risk factors of atherosclerotic coronary artery disease (CAD), such as aging, diabetes mellitus, hypertension, cigarette smoking, and dyslipidemia.\textsuperscript{7–9} Furthermore, artery disease (CAD), such as aging, diabetes mellitus, hypertension, cigarette smoking, and dyslipidemia.\textsuperscript{7–9} Furthermore, ED is increasingly recognized as a well established risk factor for future cardiovascular events.\textsuperscript{10} In this respect, it was demonstrated that nearly 70% of men presenting with new onset angina and angiographically documented CAD had pre-existing ED.\textsuperscript{11}

The mainstay of therapeutic approach to ED is based on identification and treatment of an underlying cause, in addition to administration of phosphodiesterase-5 inhibitors. Nevertheless, inadequate response to therapeutic doses of phosphodiesterase-5 inhibitors was observed in 25–35% of men with ED; the rate of poor responders is even higher (40–50%) in diabetic patients.\textsuperscript{12}

In a single-center prospective study design, we sought to explore the prevalence of significant atherosclerotic disease of the internal pudendal arteries (IPA) in diabetic men with ED and angiographically documented multi-vessel CAD.

2. Materials and methods

2.1. Patient selection

Prospectively, we enrolled 30 consecutive diabetic patients with ED undergoing elective coronary catheterization in our cath lab during the period from November 2010 to May 2011. Patients underwent elective coronary catheterization either for suspected CAD, or for recurrent symptoms despite adequate prior therapy. Patients were considered eligible for enrollment if they had angiographically documented multi-vessel significant CAD, defined as 50% or more luminal obstruction of at least three sizable epicardial coronary arteries (measuring 2.5 mm or more in diameter), seen in 2 different projections, or at least 50% luminal obstruction of the left main coronary artery plus significant disease in a sizable right coronary artery.

Diabetes mellitus was defined according to the diagnostic criteria described by the American Diabetes Association as a fasting plasma glucose $\geq 126$ mg/dl, and/or a 2-h postload glucose $\geq 200$ mg/dl, or specific anti-diabetic drug therapy.\textsuperscript{13} The presence of hypertension was defined as a systolic blood pressure $\geq 140$ mmHg and/or a diastolic blood pressure $\geq 90$ mmHg, previously recorded by repeated noninvasive office measurements, which leads to lifestyle modification or antihypertensive drug therapy. Erectile function was evaluated using the abbreviated 5-item questionnaire known as the Sexual Health Inventory for Men.

These 5 items were scored on a scale of 0–5, and have been shown to discriminate highly between men with and without ED with an optimal cutoff score $\leq 21$ for diagnosis of ED.\textsuperscript{14} We excluded patients with known nonvascular causes of ED such as neurogenic ED due to radiation injury, prior penile trauma, or radical prostatectomy, as well as those with an estimated creatinine clearance $< 60$ mL/min. Before enrollment, an informed written consent was obtained from each patient after full explanation of the study protocol, and the protocol was reviewed and approved by our local Institutional Human Research Committee as it conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as revised in 2002.

2.2. Coronary and pelvic artery angiography

Femoral artery access was adopted, and coronary angiography was performed using the standard technique. If indicated, \textit{ad hoc} percutaneous coronary intervention was carried out in the same session. Pelvic angiography was performed after coronary angiography. Distal aortography was first performed using a pig-tail catheter with its head positioned between the forth and fifth lumbar vertebrae. Automatic pump injection was performed in the anteroposterior projection at a rate of 15 mL/s to define the aorto-iliac bifurcation, common and internal iliac arteries. Then, selective internal iliac arteriography was carried out. The ipsilateral iliac artery was injected from a straight-head catheter placed retrogradely in the common iliac artery. The contralateral iliac artery was injected from a Judkins Right or Williams catheter advanced over a 0.035-inch angled guide wire introduced by the crossover technique. Before angiography, nitroglycerine was injected (200 $\mu$g) intra-arterially to overcome vasconstriction frequently encountered with small and medium-sized arteries. The IPA was seen as a posterior division of the distal internal iliac artery, with the takeoff best seen in the 30–40$^\circ$ ipsilateral oblique view. Angiograms were taken in multiple projections to visualize the entire length of the internal iliac and IPA.

2.3. Quantitative lesion analysis

The outer diameter of a contrast-filled catheter was used for calibration. Reference vessel diameter and the percent diameter stenosis were measured using quantitative vessel angiography (Inturis Allura, Phillips Medical Systems, Netherlands). The lesions were analyzed in multiple projections and stenosis severity measured from the most severe angiographic view. The reference vessel diameter was measured adjacent to the stenosis at the most healthy appearing segment. Significant IPA disease was defined as 50% or more luminal obstruction

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image1a.png}
\caption{Right anterior oblique view with cranial angulation showing 50% stenosis of the right internal pudendal artery.}
\end{figure}
seen in the projection that best delineates the takeoff of the artery (Fig. 1A and B).

2.4. Statistical analysis

Continuous variables were presented as mean ± SD, if they were normally distributed. Data were tested for normal distribution using the Kolmogorov–Smirnov test. Categorical variables were described with absolute and relative (percentage) frequencies. Pearson’s correlation coefficient test was performed to study the correlation between significant IPA disease and various demographic and clinical variables. A probability value of \( p < 0.05 \) was considered statistically significant. Analyses were performed with SPSS version 12.0 statistical package (SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline clinical characteristics

A total of 30 diabetic male patients with ED and angiographically documented multi-vessel CAD were enrolled in the current study. The mean age of the whole series was 59.6 ± 8.4 years. Baseline clinical characteristics are shown in Table 1. The mean duration of diabetes mellitus was 8.1 ± 7.1 years, and the mean duration of ED was 4.3 ± 3.2 years. The body mass index ranged from 20.9 to 44.9; 18 patients (60%) were overweight, 6 (20%) were obese, 1 (3.3%) was morbidly obese.

3.2. Angiographic data

Significant left main coronary artery stenosis was found in 2 (6.7%) patients. Significant IPA disease (stenosis/occlusion) was found in 11 (36.7%) patients; unilateral in 6 (20%) patients, and bilateral in 5 (16.7%) ones. Significant internal iliac artery disease (stenosis/occlusion) was found in 6 (20%) patients; unilateral in 4 (13.3%) patients, and bilateral in 2 (6.7%) ones. Significant IPA disease was positively correlated with age (\( r = 0.428, p = 0.018 \)) (Fig. 2), and negatively correlated with estimated creatinine clearance (\( r = -0.48, p = 0.007 \)) (Fig. 3).

4. Discussion

The current study demonstrated that in diabetic male patients with ED who have angiographically documented multi-vessel CAD, significant IPA obstruction (stenosis/occlusion) is rather frequent (36.7%), and its presence correlates positively with age, and negatively with the estimated creatinine clearance. Moreover, significant internal iliac artery obstruction (stenosis/occlusion) is not infrequent (20%). Both arterial bed affections are mostly the consequence of atherosclerosis, and might probably be implicated in the underlying etiology of ED. The IPA is the chief source of arterial blood supply to the penis; it extends as the straight-line continuation of the distal internal iliac artery. Ultimately, the IPA divides into the dorsal penile, cavernosal, and bulbourethral arteries. The cavernosal arteries provide blood flow to fill the sinusoids of the corpora cavernosa, resulting in normal erection. During arousal, parasympathetic activation induces relaxation of the smooth muscle fibers in the walls of the sinusoids, leading to a near sevenfold increase in blood flow. During full erection, the intracavernosal pressure approaches 100 mmHg, a fact which underscores the importance of adequate arterial inflow pressure. During intercourse, contraction of the ischiocavernosal muscle rigorously augments the intracavernosal pressure to suprasystolic values. Hence, atherosclerotic obstruction (stenosis/occlusion) of the IPA and/or internal iliac artery would sufficiently compromise penile arterial inflow, resulting in ED. Atherosclerosis is a diffuse process that is prone to affect almost every vascular bed. In the presence of diabetes mellitus,
atherosclerotic disease is often more diffuse and extensive with more aggressive complications. Therefore, in diabetic patients with ED, there is good reason to suggest insufficiency of penile arterial inflow (internal iliac artery and IPA) as a possible underlying etiology.

Currently available non-invasive imaging techniques, such as computed tomography and magnetic resonance angiography are inaccurate for the evaluation of the distal segments of the IPA and its branches. Hence, selective contrast angiography is the ‘gold standard’ for diagnosis of atherosclerotic IPA disease, hitherto. For clear ethical reasons, sole invasive imaging of the internal iliac artery and IPA was not incorporated as a part of the routine workup of patients with ED, even when there is a high index of suspicion (diabetes mellitus). Thus, we opted to employ invasive imaging in diabetic patients with ED undergoing invasive evaluation of the coronary arteries. Due to the limited sample size, we hypothesized that exclusive enrollment of patients with multi-vessel CAD (which speaks of more extensive atherosclerosis) would further increase the diagnostic gain of invasive assessment, by increasing the pretest likelihood of having atherosclerotic disease of the pelvic arteries, as well.

The current study enrolled patients with a relatively high-risk profile: all diabetic with a mean duration of 8.1 ± 7.1 years (23.3% insulin-dependent), 40% hypertensive, 43.3% smokers, 83.3% overweight or obese, all with multi-vessel CAD. The relative prevalence of IPA and internal iliac artery disease might bear a strong relationship with the high prevalence of risk factors for atherosclerosis. This might again reiterate the prior observation that ED and CAD share common risk factors, and that ED is a predictor of cardiovascular events and it precedes symptomatic CAD by 2–3 years. To the best of the authors’ knowledge, the current study is among the first ones to report the prevalence of significant atherosclerotic disease of the IPA in diabetic patients with ED undergoing invasive coronary catheterization. However, we postulate that the prevalence would obviously be lower should patients with lower-risk profile or those representative of real-life practice have been enrolled.

4.1. Clinical implications

Current management of ED essentially involves treatment of potentially reversible underlying causes, and most often a trial of phosphodiesterase-5 inhibitor administration. In diabetics, however, a high rate (40–50%) of poor response to these agents was previously reported. Subsequent therapeutic options for poor responders are excessively invasive and uncomfortable, such as vacuum constrictor devices and penile prosthesis. Therefore, invasive diagnostic imaging to explore the presence of significant IPA stenosis/occlusion amenable for percutaneous intervention would be greatly justified, especially in diabetic patients with a high index of suspicion (due to widespread diffuse atherosclerosis affecting various vascular beds) and a high rate of poor response to conventional therapy with phosphodiesterase-5 inhibitors. Anecdotal case reports of percutaneous balloon angioplasty of penile inflow arteries (internal iliac artery and IPA) had been already described before the introduction of stents, with initial clinical success. Yet, the major limitation was recurrence, most probably due to restenosis. A late-breaking report described 3 cases of ED not responsive to phosphodiesterase-5 inhibitors who were treated with percutaneous balloon angioplasty in the IPA, and who experienced a significant improvement of erectile function following revascularization. Since it extends as a straight-line continuation of the internal iliac artery, percutaneous access to the IPA can be easily achieved through the contralateral femoral (crossover) approach. Hence, we recommend invasive imaging of the penile inflow arteries (internal iliac artery and IPA) in patients with ED, undergoing elective coronary catheterization, who are poor responders to phosphodiesterase-5 inhibitors, especially those with a high index of suspicion: diabetics and those with multi-vessel CAD.

5. Conclusion

In diabetic male patients with ED who have angiographically documented multivessel CAD, significant IPA obstruction (stenosis/occlusion) is rather frequent, and it correlates positively with age, and negatively with the estimated creatinine clearance.

6. Limitations of the study

Our findings are based on a single center study with a relatively small sample size of the cohort. Moreover, the current study has not evaluated the response of patients with ED to phosphodiesterase-5 inhibitors. Similarly, measurement and replacement of testosterone was not performed. Furthermore, penile vascular duplex was not performed to exclude cavernosal arterial or tissue disease, or venous leak as possible underlying causes of ED. Finally, the exclusive enrollment of patients with multi-vessel CAD limits the generalization of the findings to all diabetic patients with ED undergoing elective catheterization in real-world practice.

References


