Metabolic Syndrome and Erectile Dysfunction

The ultrasound evaluation of cavernosal atherosclerosis

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OBJECTIVE—To study the relation between metabolic syndrome (MS), cavernosal morphological vasculopathy, and peripheral vascular alterations (carotid and femoral wall) in patients with erectile dysfunction.

RESEARCH DESIGN AND METHODS—A total of 207 patients and 50 control subjects were evaluated for cardiovascular risk factors, physical examination, reproductive hormones, ultrasound analysis of cavernosal, carotid and femoral arteries (intima-media thickness), and cavernosal flow measurement (peak systolic velocity).

RESULTS—A total of 28% of patients had MS, and they presented with a high prevalence of cavernosal alterations (70.3%) and systemic vascular impairment (59.3%), whereas patients with cavernosal alterations (44%) showed the higher prevalence of MS (48.9%). The number of MS components was related to the prevalence of penile vasculopathy. However, multivariate analysis showed that MS is not an independent predictor for cavernosal vasculopathy.

CONCLUSIONS—Patients with cavernosal vasculopathy have an increased cardiometabolic risk, and screening for MS components might identify individuals with a higher risk for cavernosal and systemic atherosclerosis.

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Erectile dysfunction (ED) is linked to cardiovascular risk factors (CVRFs) included in the metabolic syndrome (MS) and vascular alterations (1). A total of 79–96.5% of patients with MS present with ED, and 29.4–66% of patients with ED have MS (2–4), but the relations between penile vascular alterations and MS were poorly studied.

RESEARCH DESIGN AND METHODS

—A total of 207 consecutive patients (age 52.9 ± 11.5 years) with ED and 50 control subjects with induratio penis plastica, recurvatum penis, or erectile pain were recruited. ED (the consistent inability to achieve or maintain a penile erection of sufficient quality for satisfactory sexual intercourse for at least 6 months [2]) was assessed by the International Index of Erectile Function (IIEF) and included six questions of IIEF-15 (n.1,2,3,4,5,15). Scores <26 were considered diagnostic. Subjects were asked about smoking, diet, physical activity, and drugs, and waist circumference, BMI, arterial pressure, fasting glucose, HDL cholesterol, triglycerides, prolactin, total testosterone, and psychosexual evaluation were assessed, together with dysautonomia in diabetic patients. CVRF screening included treatment for diabetes, arterial hypertension, or dyslipidemia. Exclusion criteria were as follows: hyperprolactinemia, pelvic surgical interventions, psychiatric diseases, and drug/alcohol abuse. No subjects had taken phosphodiesterase type 5 (PDE5) inhibitors. MS diagnosis was based on the National Cholesterol Education Program–Adult Treatment Plan III (NCEP-ATPIII) modified guidelines (5).

Penile echocolordoppler ultrasonography was performed at a high resolution (iU22; Philips, Best, the Netherlands) after intracavernosal injection of 10 μg alprostadil (6). Cavernosal peak systolic velocity (PSV) and intima-media thickness (IMT) were measured, and penile vasculopathy was classified (7). Carotid and femoral arterial IMT was calculated (8). The study was approved by the hospital ethics committee.

Absolute data were expressed as mean ± SD and categorical variables as percentage. Comparison between two groups was performed by Student *t* test for continuous data. The number of subjects in every group was higher than the minimum to test effectiveness, with $\alpha = 0.05$ (confidence level 95%) and $\beta = 10\%$. Univariate analysis was applied and variables with statistical significance were included in a multivariate model by stepwise logistic regression to identify independent predictors. *P* values < 0.05 were considered statistically significant. Statistical analysis was performed using Statistica 7.1 software (Copyright StatSoft, Tulsa, OK).

RESULTS

—A total of 28% of patients (58/207) had MS, and 44% (92/207) showed an impairment in cavernosal arteries, with a higher prevalence than in control subjects ($P < 0.05$). Patients also presented higher prevalence of CVRFs than control subjects (data not shown): diabetes 19.1%, fasting altered glycemia 11.9%, hypertriglyceridemia 32.5%, low HDL 21.4%, and arterial hypertension 40.1%. They showed regular physical activity (half an hour walking/day) and adequate lifestyle (no drug misuse, controlled diet and sleep-wake rhythm). Table 1 shows the main findings, with the higher prevalence of MS (48.9%) in patients with penile vasculopathy, who also showed the worse IIEF score. Diabetic patients showed a higher prevalence of MS (68.4 vs. 19.4%, $P < 0.05$) and higher cavernosal IMT (0.31 ± 0.07 vs. 0.21 ± 0.08 mm, $P < 0.05$) with higher prevalence of penile vasculopathy when compared with individuals without diabetes

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Table 1—*Clinical and ultrasound parameters in patients and control subjects*

	Control subjects	ED patients without penile vasculopathy	ED patients with penile vasculopathy
n	50	115	92
Age (years)	48.2 ± 14.6	49.4 ± 12.5	58.3 ± 8.35*
IIEF score	28.3 ± 1.2	19.8 ± 2.3	17.6 ± 1.6*
BMI	24.7 ± 2.3	26.5 ± 3.3	27.9 ± 3.6
Waist circumference (cm)	87.0 ± 5.6	98.1 ± 10.7	110.6 ± 6.2*
Glycemia (mg/dL)	88.6 ± 11.2	89.7 ± 25.6	114.5 ± 58.6*
HDL (mg/dL)	47.6 ± 8.9	50.6 ± 12.2	43.7 ± 13.3*
Triglycerides (mg/dL)	138.7 ± 47.6	114.8 ± 54.4	159.8 ± 122.9*
Arterial hypertension (%)	14.3	23.4	61.2*
Metabolic syndrome (%)	10.7	13.9	48.9*
Testosterone (nmol/L)	15.6 ± 2.4	16.5 ± 5.6	14.0 ± 5.6
Diabetes or glycemia >100 mg/dL (%)	2.3	4.9	34.3*
HDL <40 mg/dL (%)	12.9	15.6	30.7*
Triglycerides >150 mg/dL (%)	23.7	25.2	45.2*
Smoking (%)	27.1	28.0	31.8
PSV (cm/s)	62.7 ± 19.3	56.4 ± 16.0	45.8 ± 18.0*
IMT cavernosal (mm)	0.17 ± 0.04	0.17 ± 0.05	0.31 ± 0.03*
IMT carotid (mm)	0.62 ± 0.16	0.63 ± 0.19	0.79 ± 0.27*
Carotid vasculopathy (%)	14.3	15.4	52.0*
IMT femoral (mm)	0.64 ± 0.21	0.74 ± 0.34	0.93 ± 0.34*
Femoral vasculopathy (%)	12.1	19.6	70.3*
Carotid plus femoral vasculopathy (%)	3.2	9.3	45.7*

*$P < 0.05$.

(81.6 vs. 34.6%, $P < 0.05$). Vascular findings were confirmed also considering only patients with MS (data not shown) and patients with MS and diabetes with respect to patients with MS without diabetes (0.31 ± 0.07 vs. 0.26 ± 0.06 mm, $P < 0.05$). Dysautonomia, diabetes duration and treatment, and glycemic control were slowly implicated (mean diabetes duration was 8.3 ± 6.1 years, all patients were treated with metformin, three patients had poor glycemic control, and five dysautonomic diabetic patients in the group had penile vasculopathy).

A multivariate model including CVRFs, MS, and age with respect to penile vasculopathy showed that diabetes, hypertension, low HDL, and age were significantly independent predictors. The prevalence of penile vasculopathy was higher, increasing the number of MS components (15.2% = no CVRF; 32.7% = 1 CVRF; 50% = 2 CVRFs; 68.2% = 3 CVRFs; 75% = ≥4 CVFRs; $P < 0.05$).

Patients with MS had a higher prevalence of cavernosal vasculopathy (70.3 vs. 28.6%, $P < 0.05$) and cavernosal plaques (41.9 vs. 11.6%, $P < 0.05$) than individuals without MS and had higher cavernosal IMT (0.31 ± 0.03 vs. 0.17 ± 0.05 mm, $P < 0.05$). The patients showed higher prevalence of peripheral vasculopathy with higher carotid and femoral IMTs (data not shown) and higher prevalence of concomitant vascular damage at the cavernosal, carotid, and femoral districts (59.3 vs. 27.4%, $P < 0.05$).

CONCLUSIONS—ED and MS share the same CVRFs, and endothelial dysfunction is a common link. Penile vascular impairment, the predominant cause of ED (9), is diagnosed by PSV and cavernosal arterial morphology (IMT ≥0.3 mm or plaque presence). The latter shows a positive relation with peripheral vasculopathy and the number of CVRFs (10,11). Previous reports showed only lower PSV values in patients with MS (12,13) and a progressive decline of PSV with increasing number of MS components (3). A lower PSV in patients with ED and MS may still be in the normal range because cavernosal impairment can occur earlier than PSV alterations, and it could be a sensitive predictor also for systemic atherosclerosis (10).

Seventy point three percent of patients with MS and ED have penile vasculopathy, while the frequency of cavernosal alterations is higher increasing with the number of MS components and in diabetic patients. Nevertheless, MS does not independently predict penile vasculopathy. Similar results were found regarding carotid (14) and coronary (15) atherosclerosis, showing also in patients with ED that MS could be only a cluster of different CVRFs. Interestingly, patients with MS and ED showed a more advanced systemic vascular impairment, whereas we did not find differences in penile vasculopathy related to diabetes duration and treatment, possibly because of the low number of patients. Moreover, findings may not be generalizable because of the special penile pathologies of the population studied. Limitations involve difficulties in the recruitment of control subjects. In fact, the administration of alprostadil only for study purpose in subjects without ED could be detrimental, and we did not find cavernosal wall alterations in the absence of ED (7). An early screening for MS in patients with ED might identify individuals with higher risk for cavernosal and systemic atherosclerosis. We recommend the cavernosal morphological examination in patients with ED and multiple CVRFs or MS. Possible differences among diabetic patients and in responsiveness to PDE5 inhibitors need further protocols.

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