Metabolic Syndrome and Erectile Dysfunction

The ultrasound evaluation of cavernosal atherosclerosis

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.
Metabolic syndrome and erectile dysfunction

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           | 28.5 ± 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     | 91.8 ± 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 ± 0.10                             | 0.49 ± 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 CVRFs; 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.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

M.S. researched and analyzed data and wrote and reviewed the manuscript. N.C. researched and analyzed data, contributed to discussion, and reviewed the manuscript. P.P. and R.S. researched data. A.F. reviewed and edited the manuscript. C.F. edited the manuscript.

References
1. Foresta C, Caretta N, Corona G, et al. Clinical and metabolic evaluation of subjects with erectile dysfunction: a review with a proposal flowchart. Int J Androl 2009;32: 198–211.
2. Müller A, Mulhall JP. Cardiovascular disease, metabolic syndrome and erectile dysfunction. Curr Opin Urol 2006;16: 435–443
3. Vlachopoulos C, Rokkas K, Ioakeimidis N, Stefanadis C. Inflammation, metabolic syndrome, erectile dysfunction, and coronary artery disease: common links. Eur Urol 2007;52: 1590–1600
4. Heidler S, Temml C, Broesnner C, et al. Is the metabolic syndrome an independent risk factor for erectile dysfunction? J Urol 2007;177: 651–654
5. Grundy SM, Cleeman JJ, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart
Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735–2752 [erratum in Circulation 2005;112]

6. Caretta N, Palego P, Ferlin A, et al. Resumption of spontaneous erections in selected patients affected by erectile dysfunction and various degrees of carotid wall alteration: role of tadalafil. Eur Urol 2005; 48:326–331

7. Caretta N, Palego P, Roverato A, Selice R, Ferlin A, Foresta C. Age-matched cavernous peak systolic velocity: a highly sensitive parameter in the diagnosis of arteriogenic erectile dysfunction. Int J Impot Res 2006; 18:306–310

8. Foresta C, Palego P, Schipilliti M, Selice R, Ferlin A, Caretta N. Asymmetric development of peripheral atherosclerosis in patients with erectile dysfunction: an ultrasonographic study. Atherosclerosis 2008;197:889–895

9. Jackson G, Montorsi P, Adams MA, et al. Cardiovascular aspects of sexual medicine. J Sex Med 2010;7:1608–1626

10. Caretta N, Palego P, Schipilliti M, Ferlin A, Di Mambro A, Foresta C. Cavernous artery intima-media thickness: a new parameter in the diagnosis of vascular erectile dysfunction. J Sex Med 2009;6:1117–1126

11. Chew KK, Finn J, Stuckey B, et al. Erectile dysfunction as a predictor for subsequent atherosclerotic cardiovascular events: findings from a linked-data study. J Sex Med 2010;7:192–202

12. Demir O, Demir T, Kefi A, et al. Penile vascular impairment in erectile dysfunction patients with metabolic syndrome: penile Doppler ultrasound findings. Urol Int 2009;82:175–178

13. Chatterjee R, Palla K, Kottaridis PD. Cavernosal arterial insufficiency and metabolic syndrome probably represent a common pathology of endothelial dysfunction in recipients of high-dose therapy and stem-cell transplantation. J Clin Oncol 2004;22:2253–2254

14. Baldassarre D, Werba JP, Castelnuovo S, et al. The metabolic syndrome predicts carotid intima-media thickness no better than the sum of individual risk factors in a lipid clinic population. Atherosclerosis 2010;210:214–219

15. Scuteri A, Najjar SS, Morrell CH, Lakatta EG; Cardiovascular Health Study. The metabolic syndrome in older individuals: prevalence and prediction of cardiovascular events: the Cardiovascular Health Study. Diabetes Care 2005;28:882–887