High Proportions of Erectile Dysfunction in Men With the Metabolic Syndrome

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Erectile dysfunction is an important cause of decreased quality of life in men (1,2). Strong epidemiological evidence links the subsequent risk of erectile dysfunction to the presence of well-recognized risk factors for coronary heart disease, such as increased body weight, hypertension, and dyslipidemia (3,4). Some have suggested that a diagnosis of erectile dysfunction is a sentinel event that should prompt investigation for coronary heart disease in asymptomatic men (5). We postulated an association between erectile dysfunction and the metabolic syndrome because four of the five components of the metabolic syndrome are risk factors for erectile dysfunction and are also characterized by abnormal endothelial function (6).

RESEARCH DESIGN AND METHODS

— Men were recruited among those attending the outpatient department for metabolic diseases of the teaching hospital at the second University of Naples, Naples, Italy. To be enrolled in the study, subjects had to have three or more of the criteria to meet the diagnosis of the metabolic syndrome, as recommended by the Adult Treatment Panel (7). Exclusion criteria were diabetes or impaired glucose tolerance, impaired renal function, pelvic trauma, prostatic disease, peripheral or autonomic neuropathy, hypertension (blood pressure >140/90 mmHg), cardiovascular disease, psychiatric problems, use of drugs or alcohol abuse, and smoking (both present and past smoking). Endocrine causes of erectile dysfunction were also excluded. A total of 50 men, matched for age and body weight, served as the control group. The study was approved by the institutional committee of ethical practice of our institution, and all of the study subjects gave written informed consent.

Erectile function was assessed by completing questions one through five of the International Index of Erectile Function (IIEF), which is a multidimensional questionnaire for assessing erectile dysfunction (8). The erectile function score represents the sum of questions one through five of the IIEF questionnaire, with a maximum score of 25; a score ≤21 indicates erectile dysfunction.

Endothelial function was assessed with the L-arginine test, as previously described (9). We developed a score in which the blood pressure and platelet aggregation responses to L-Arginine (3 g i.v.) were summed. This gives a score ranging from 0 points, indicating maximal impairment of endothelial function, to 10 points, indicating normal function of the endothelium (10).

Assays for serum total and HDL cholesterol, triglyceride, and glucose levels were performed in the hospital's chemistry laboratory. High-sensitivity C-reactive protein (CRP) was assayed by immunonephelometry on a Behring Nephelometer 2 (Dade Behring, Marburg, Germany).

Data are presented as the mean ± SD unless otherwise indicated. We compared baseline data using a *t* test for continuous variables and Wilcoxon's test for CRP. We classified all study patients as having three, four, or five components of the metabolic syndrome and assessed for evidence of a relationship among erectile dysfunction, median CRP level, and endothelial function score across these groups using the Jonckheere-Terpstra test. The χ^2 test was used for comparing proportions of subjects with erectile dysfunction. Spearman's rank correlation coefficients were used to quantify the relationship among IIEF score, endothelial function score, and CRP level. All analyses were conducted using SPSS version 9.0 (SPSS, Chicago, IL).

RESULTS

— Men with the metabolic syndrome (n = 100) were matched with men of the control group for age (38.4 ± 3.3 vs. 37.9 ± 2.9 years) and BMI (26.9 ± 1.9 vs. 26.6 ± 2.1 kg/m^2). Compared with the control group, patients with the metabolic syndrome had an increased prevalence of erectile dysfunction (26.7 vs. 13%, P = 0.03), reduced endothelial function score (6.3 ± 0.9 vs. 9.5 ± 0.3, P = 0.01), and higher circulating concentrations of CRP (median [interquartile range] 1.7 [0.6–3.8] vs. 0.6 [0.2–2.7] mg/l).

Erectile dysfunction prevalence (IIEF <21) and CRP level increased as the number of components of the metabolic syndrome increased (Fig. 1); by contrast, there was an inverse relationship between the number of components of the metabolic syndrome and the endothelial function score (P for trend <0.01).

The IIEF score was positively associated with the endothelial function score (r = 0.24, P = 0.04) and negatively associated with CRP (r = 0.27, P = 0.03). These correlations were little affected by adjustment for age.

CONCLUSIONS

— Erectile dysfunction is present in up to 30 million men in the U.S. and ~100 million men world-

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Abbreviations: CRP, C-reactive protein; IIEF, International Index of Erectile Function.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

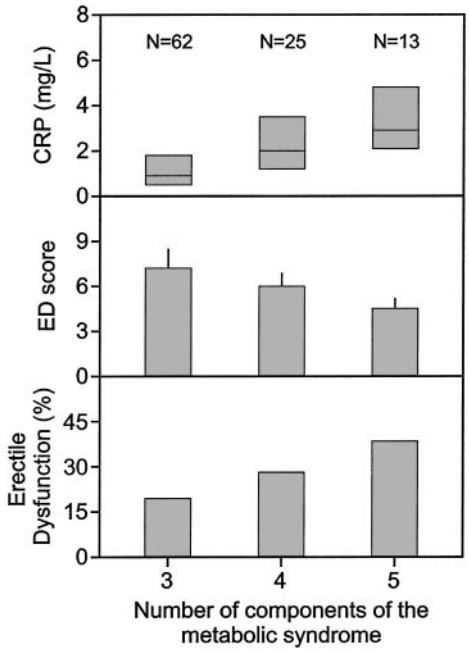

Figure 1—*Distribution of erectile dysfunction (IIEF <21), endothelial function score, and CRP level among patients by the presence of three, four, and five components of the metabolic syndrome.*

wide (11) and affects up to 52% of men between the ages of 40 and 70 years (2). Our results show a linear increment in the prevalence of erectile dysfunction that is associated with a linear increase in CRP level and a linear impairment of endothelial function score as the number of components of the metabolic syndrome increased. Moreover, the association we found between IEEF and endothelial function score supports the presence of some common vascular pathways underlying both conditions. A defective nitric oxide (NO) activity, linked to reduced NO availability, could provide a unifying explanation for this association. In particular, in isolated corpus cavernosum strips from patients with erectile dysfunction, both neurogenic- and endothelium-dependent relaxation are impaired (12). Moreover, erectile dysfunction in diabetic men correlates with endothelial dysfunction and endothelial activation (13). Lastly, CRP, at concentrations known to predict diverse vascular insults, profoundly quenches NO synthesis, while augmenting the release of endothelin-1 and upregulating adhesion molecules and chemoattractant chemokines, uncovering a proinflammatory and proatherosclerotic phenotype (14). Interestingly enough, Kaiser et al. (15) recently reported that subjects with erectile dysfunction but without evidence of clinical cardiovascular disease and free of traditional cardiovascular risk factors present widespread abnormality of endothelial function, as has been seen in patients with cardiovascular risk factors (7). Thus, many patients with erectile dysfunction seem to have a vascular mechanism similar to that seen in atherosclerosis.

The metabolic syndrome is highly prevalent in the U.S. population (16). Thus, a large group of people are at increased risk for developing diabetes and cardiovascular disease. Although the greater prevalence of erectile dysfunction in men with the metabolic syndrome needs to be confirmed in larger epidemiological studies, the linear relationship we found between the number of components of the syndrome and erectile dysfunction is suggestive for a progressive burden of raising cardiovascular risk on erectile function. In any case, the adoption of a healthy lifestyle is strongly recommended in order to reduce the prevalence of the metabolic syndrome (10) and hence the burden of erectile dysfunction.

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