Metabolic syndrome and hormone profile in patients with erectile dysfunction∗


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Abstract
Objectives: To demonstrate the existence of relation between metabolic syndrome and erectile dysfunction (ED) and to analyze the hormone profile of these patients regarding a healthy population group.

Material and methods: A case–control study was designed with 65 men divided into 2 groups according to presence or non-presence of ED. Group A was made up of 37 men with ED and group B for 28 healthy men without ED. Ages ranged from 40 to 65 years. The presence of metabolic syndrome according to the ATP III definition, performance of physical exercise, smoking habit, body mass index (BMI) and complete hormone profile including testosterone (total, free and bioavailable) was studied.

Results: Greater presence of metabolic syndrome was detected among men of group A (72.9%) vs. those of group B (17.8%) (p = 0.0001). Among the parameters that make up the metabolic syndrome, there are differences between both groups in systolic and diastolic blood pressure, fast blood sugar and abdominal circumference, all these differences being significant. After performing multivariate analysis between the metabolic syndrome and ED adjusted for age, BMI, International Index for Erectile Function (IIEF), physical exercise and smoking habit, we have observed an independent significant relation between the metabolic syndrome and ED. We have not found differences between both groups in any hormone parameter.

Conclusion: A relationship is found between metabolic syndrome and ED. Thus, it seems recommendable to perform the metabolic profile and cardiovascular risk study in these patients.

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Introduction

ED is defined as the persistent or repeated inability to achieve and maintain an erection of sufficient rigidity to perform satisfactory sexual intercourse.\(^1\) There is a well-known and internationally accepted test (IIEF) which makes it possible to objectify and classify the ED into mild, moderate, or severe depending on the scores obtained. It consists of 15 questions, among which 6 assess the erectile function and help to classify the patients according to their severity.\(^2\) The causes involved in the ED can be multiple and pose a health problem for the patient because they have been linked to other syndromes and diseases. Two of these syndromes most strongly associated with the ED are the metabolic syndrome, and the androgen deficiency syndrome, mainly testosterone.\(^3\) The metabolic syndrome is defined by a series of clinical and analytical factors that increase the cardiovascular risk and these are hypertension, insulin resistance with hyperglycemia, hypertriglyceridemia, low HDL cholesterol levels, and abdominal obesity. There are several classifications of different scientific societies that define some criteria to diagnose it.\(^4\)\(^5\) The syndrome of androgen deficiency, mainly testosterone, is characterized by the gradual decline with age in serum testosterone, and the consequences that this entails in relation to sexual behavior and erectile function.\(^6\)\(^7\) The main action of testosterone is to regulate the erection time in relation to sexual desire and coordinate the erection with sex. If there is a drop in serum testosterone, these functions will not be performed correctly, and hormone dysfunction will occur in regulating the erection.\(^8\)

The insulin resistance, abdominal obesity, and chronic inflammation are key elements of the metabolic syndrome, and associated they lead to endothelial damage, which at the level of the penile arteries could justify the ED.

The aim of this work is to study the presence of metabolic syndrome and hormonal profile in relatively young patients (40–65 years) with clinically diagnosed ED compared to a control group without ED, to determine whether the ED acts as a marker of metabolic syndrome in these patients and analyze the possible underlying hormonal abnormalities.

Material and methods

We designed a case–control study including a total of 65 men aged between 40 and 65, who were divided into two groups based on the results of the IIEF questionnaire completed by each of them: 37 men with ED (group A) and 28 men without ED (group B). The participants in group A come from the Urology department of the hospital and those in group B are healthy outpatient controls. Informed consent was obtained in all cases.

Exclusion criteria were considered for the study: men under 40 or over 65 years, males treated with drugs that cause ED, decrease libido, or alter sexual behavior (beta blockers, antidepressants, LHRH analogues, antiandrogens, etc.), and presence of clinically demonstrable cardiovascular disease.

The metabolic syndrome was defined according to the criteria of the ATP III (three or more of the following criteria): systolic/diastolic blood pressure ≥130/85 mm Hg, abdominal perimeter ≥102 cm, triglycerides ≥150 mg/dl, HDL cholesterol <40 mg/dl, glucose ≥110 mg/dl. The patients taking treatment for hypertension or dyslipidemia were considered to meet the criteria for metabolic syndrome.

The variables analyzed were: systolic and diastolic blood pressure (mm Hg) after 5 min rest, and again 10 min later, physical exercise, smoking, weight (kg), height (m), BMI (kg/m\(^2\)), serum glucose levels (mg/dl), triglycerides (mg/dl), HDL cholesterol (mg/dl), albumin (g/dl), sex hormone binding globulin (SHBG) (nmol/l), serum hormone profile including follicle stimulating hormone (FSH) (mUI/ml), luteinizing hormone (LH) (mUI/ml), estradiol (pg/ml), progesterone (ng/ml), total testosterone (ng/ml), free testosterone (ng/ml), bioavailable...
testosterone (ng/ml), thyroid stimulating hormone (TSH) (µUI/ml), and prolactin (ng/ml).

The statistical study was performed using the SPSS/PC software (version 15.0 for Windows). Student’s “t”-test was applied for analyzing and comparing the means of the variables studied between the two groups, after verification of normality using the Shapiro–Wilk test and Levene’s test for analysis of variance. In the case of non-standard variables, the Mann–Whitney U test was applied. The qualitative variables were analyzed and compared with each other using the Chi-square test. The correlation between variables was studied using Pearson’s correlation coefficient and exponential regression techniques. Binary logistic regression was performed to measure the association between ED and metabolic syndrome in multivariate analysis. \( p \leq 0.05 \) was considered statistical significance level.

Results

The mean age of the men in group A was 55.8 ± 7.7 years, and 52.5 ± 4.8 years \((p = 0.06)\) for men in group B. The mean score in the IIEF test in the group of patients was 9.70 ± 7.2 and 29.76 ± 0.52 \((p = 0.0001)\) in the control group. The weight was higher in the participants from group A \(88.5 \pm 10.4 \text{ kg}\) compared to group B \(78.8 \pm 7.8 \text{ kg}\), finding statistically significant differences \((p = 0.04)\). The BMI was 29.8 ± 4.4 kg/m² in group A vs. 26.9 ± 4.6 kg/m² in group B, this difference being also statistically significant \((p = 0.01)\). There were no differences in the two groups in smoking or physical exercise \((p > 0.05)\).

If we analyze individually each of the parameters and criteria that comprise the metabolic syndrome, we observe that there are statistically significant differences between the two groups with regard to systolic blood pressure: 151 ± 22 mm Hg in group A vs. 128 ± 13 mm Hg in group B \((p = 0.0001)\), with diastolic blood pressure: 88 ± 10 mm Hg in group A vs. 78 ± 7 mm Hg in group B \((p = 0.0001)\), with abdominal perimeter: 106.6 ± 11.2 cm in group A vs. 94.2 ± 11.3 cm in group B \((p = 0.0001)\) and with blood glucose: 115.7 ± 28 mg/dl in group A vs. 102.90 ± 29 mg/dl in group B \((p = 0.05)\). Regarding the other two parameters of metabolic syndrome, there are no statistically significant differences for HDL cholesterol or triglycerides levels (Table 1). After verifying and applying the definition of metabolic syndrome, we observed that 72.9% of the patients in group A met at least three criteria vs. 17.8% of the patients in group B (OR: 11.2; CI 95%: 3.41–37.28; \(p = 0.0001)\).

Regarding the hormonal profile analyzed, we found no statistically significant differences between groups A and B in terms of total testosterone \((4.9 \pm 2.2 \text{ ng/ml} \text{ vs. } 5.2 \pm 1.9 \text{ ng/ml}, \text{ respectively, } p = 0.7)\), free testosterone \((0.09 \pm 0.03 \text{ ng/ml} \text{ vs. } 0.14 \pm 0.22 \text{ ng/ml}, \text{ respectively, } p = 0.2)\), and bioavailable testosterone \((2.3 \pm 0.8 \text{ ng/ml} \text{ vs. } 2.2 \pm 0.6 \text{ ng/ml}, \text{ respectively, } p = 0.7)\). In the other hormonal parameters analyzed, there have not been statistically significant differences (Table 2). The patients with ED and metabolic syndrome did not show lower mean values of total, free, or bioavailable testosterone \((p = 0.17, p = 0.67, \text{ and } p = 0.63, \text{ respectively)\).

We performed a linear correlation study between the parameter that quantifies and diagnoses ED (IIEF test score) and the parameters of metabolic syndrome and hormonal profile studied, finding a statistically significant negative linear relation between IIEF score with systolic blood pressure \((R = -0.549; p = 0.0001)\), diastolic blood pressure \((R = -0.434; p = 0.0001)\), with weight \((R = -0.255; p = 0.04)\), with BMI \((R = -0.316; p = 0.01)\), with abdominal perimeter \((R = -0.438; p = 0.0001)\), and blood glucose levels \((R = -0.250; p = 0.05)\), that is, the lower the score on the IIEF scale, the greater the values of these parameters included in the criteria for metabolic syndrome. No linear correlation was found between the levels of total, free, or bioavailable testosterone and the values of the IIEF.

Binary logistic regression (Table 3) showed the association between the metabolic syndrome and the ED after controlling for several variables that could act as confounders, among which age, BMI, IIEF, smoking, or physical exercise are included (OR: 14.07; CI: 95%: 2.3–24.6; \(p = 0.004)\).

Discussion

The ED is the second most frequent alteration after premature ejaculation in the sexual function in men, affecting about 25% of men between 40 and 70 years, 10% of them with complete absence of erection. There are different causes involved in the pathophysiology of the ED (vascular, endocrinological, neurological, psychological), with the vascular ones due to alteration of the endothelium being the most frequent, while the endocrinological ones regarding androgen deficiency are less common. It has also been observed in humans that surgical or pharmacological castration does not necessarily produce an alteration in erectile capacity. Although hypogonadism often occurs in men over the years, it is independent of the ED according to some studies. \(^{10–12}\) In our study, we observed that the patients with ED have no hypogonadism or lower levels of total, free, or bioavailable testosterone than the control group, which is based on the theory of previous works, in which testosterone does not have to be lowered in ED, but rather the testosterone deficiency syndrome is related to the age of the patient and may result in ED in accordance with other causes, mainly vascular. However, some studies have supported in recent years the association between low testosterone levels, ED, and metabolic syndrome. \(^9,13,14\) It is even routinely recommended in patients diagnosed with ED requesting screening not only of parameters of metabolic syndrome, but also of testosterone. \(^9\) Based on our results, we can only recommend requesting an androgen hormone study if there are, besides the ED, other symptoms that make us suspect a late-onset hypogonadism, and we could not check that the patients with ED and metabolic syndrome had lower plasma levels of total, free, or bioavailable testosterone.

For its part, the metabolic syndrome was significantly associated with the presence of ED of vascular cause, so the diagnosis of ED in a relatively young patient rules out the presence of associated metabolic syndrome. The diagnosis of the risk factors comprising the metabolic syndrome, and which have been able to go unnoticed, is essential to establish an early treatment and prevent the future...
development of cardiovascular disease.\textsuperscript{16,17} Recent studies have shown that the patients with metabolic syndrome have a decrease in the IIEF score, and the score of the erectile function decreases more significantly with the increasing number of metabolic risk factors.\textsuperscript{18,19} The metabolic syndrome factors which are more strongly associated with the presence of ED are diabetes mellitus or elevated levels of blood glucose (hydrocarbon intolerance), abdominal perimeter, and hypertension.\textsuperscript{16,20}

In our work, we observed that the metabolic syndrome is present in the patients with ED in a much more prevalent, statistically significant way compared to the control group. Besides, the factors of this syndrome that are negatively correlated are the levels of blood glucose, the blood pressure, and abdominal perimeter figures. When blood glucose, blood pressure, or abdominal perimeter increased, we observed a linear decrease in the IIEF test score, which means there is a relation between these factors and the presentation of ED. In addition, another factor associated and related with the ED and IIEF score is the BMI, since the higher the BMI, the lower the IIEF score, a result present in some studies published in the literature.\textsuperscript{21} Therefore, it is shown that there is a strong association between the metabolic syndrome and ED, and there is a strong relation between some of the criteria of the metabolic syndrome and the severity of the ED. It is also important to note that the patients who meet criteria for metabolic syndrome are at increased cardiovascular risk,\textsuperscript{22-25} and with a greater likelihood they are going to present ED, so the latter can be considered an early marker of cardiovascular disease risk.

In fact, it was shown that the ED precedes in a time which can range from months to about 10 years, at the occurrence of cardiovascular events.\textsuperscript{26,27} The vascular changes that occur in the penile arteries are a reflection of the coronary arteries, having shown that in patients with established cardiovascular disease, the prevalence of ED is very

### Table 1  Parameters that constitute the metabolic syndrome between groups A and B.

<table>
<thead>
<tr>
<th></th>
<th>Group A (ED)</th>
<th>Group B (control)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic AP (mm Hg)</td>
<td>151 ± 22</td>
<td>128 ± 13</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diastolic AP (mm Hg)</td>
<td>88 ± 10</td>
<td>78 ± 7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Abdominal perimeter (cm)</td>
<td>106.6 ± 11.2</td>
<td>94.2 ± 11.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>47.2 ± 9.4</td>
<td>54.1 ± 11.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>146.5 ± 72.4</td>
<td>155.1 ± 91.6</td>
<td>0.71</td>
</tr>
<tr>
<td>Blood glucose (mg/dl)</td>
<td>115.7 ± 28.1</td>
<td>102.9 ± 29.7</td>
<td>0.05</td>
</tr>
</tbody>
</table>

### Table 2  Serum hormone profile between groups A and B.

<table>
<thead>
<tr>
<th></th>
<th>Group A (ED)</th>
<th>Group B (control)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dl)</td>
<td>4.5 ± 0.2</td>
<td>4.6 ± 0.2</td>
<td>0.12</td>
</tr>
<tr>
<td>SHBG (nmol/l)</td>
<td>38.5 ± 19.5</td>
<td>46.7 ± 28.7</td>
<td>0.24</td>
</tr>
<tr>
<td>Total testosterone (ng/ml)</td>
<td>4.9 ± 2.2</td>
<td>5.2 ± 1.9</td>
<td>0.71</td>
</tr>
<tr>
<td>Free testosterone (ng/ml)</td>
<td>0.09 ± 0.03</td>
<td>0.14 ± 0.22</td>
<td>0.24</td>
</tr>
<tr>
<td>Bioavailable testosterone (ng/ml)</td>
<td>2.3 ± 0.8</td>
<td>2.2 ± 0.6</td>
<td>0.75</td>
</tr>
<tr>
<td>FSH (mUI/ml)</td>
<td>6.1 ± 3.6</td>
<td>4.9 ± 1.7</td>
<td>0.23</td>
</tr>
<tr>
<td>LH (mUI/ml)</td>
<td>4.9 ± 2.7</td>
<td>3.9 ± 1.3</td>
<td>0.07</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>17.7 ± 4.2</td>
<td>10.7 ± 3.7</td>
<td>0.60</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>0.4 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>0.43</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>32.2 ± 12.4</td>
<td>27.6 ± 13.8</td>
<td>0.22</td>
</tr>
<tr>
<td>TSH (µUI/ml)</td>
<td>2.7 ± 1.7</td>
<td>2.1 ± 0.9</td>
<td>0.09</td>
</tr>
</tbody>
</table>

### Table 3  Multivariate analysis of binary logistic regression of factors associated with the metabolic syndrome (dependent variable).

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erectile dysfunction (vs. control)</td>
<td>14.07</td>
<td>2.3–24.6</td>
<td>0.004</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.05</td>
<td>0.96–1.16</td>
<td>0.23</td>
</tr>
<tr>
<td>BMI (per unit kg/m²)</td>
<td>1.82</td>
<td>1.67–1.99</td>
<td>0.46</td>
</tr>
<tr>
<td>Smoking (vs. no smoking)</td>
<td>2.15</td>
<td>0.41–11.17</td>
<td>0.36</td>
</tr>
<tr>
<td>Physical exercise (vs. no physical exercise)</td>
<td>1.23</td>
<td>0.47–3.24</td>
<td>0.66</td>
</tr>
<tr>
<td>IIEF (per unit)</td>
<td>1.01</td>
<td>0.91–1.10</td>
<td>0.97</td>
</tr>
</tbody>
</table>
high and can range between 33 and 75%, and it is also related with the degree of severity of the coronary lesions, so that if the injury is acute or of a single vessel, the ED is not serious, and if the coronary condition occurs in several vessels or is chronic, the ED that the patient has is more severe.

Although the sample size in this study is limited, significant results were obtained in line with other recently published observations. Further studies will probably be needed to define the pathogenic factors that justify the relation between cardiovascular disease and ED, and to analyze whether the treatment of the metabolic syndrome might improve the erectile function.

In conclusion, the patients with ED have an increased risk of metabolic syndrome in the multivariate analysis, and there is also a correlation between the severity of the ED measured by the IIEF and abdominal obesity, blood glucose, and hypertension. No association between the levels of total, free or bioavailable testosterone with the metabolic syndrome or the ED has been shown. Screening for cardiovascular risk factors in young patients with ED could be critical to establish an early diagnosis and treatment.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgement

To the Department of Urology of the Hospital Universitario San Cecilio.

References
