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ORIGINAL PAPERS: CLINICAL OR BASIC RESEARCH

The prevalence of the metabolic syndrome in a male population with erectile dysfunction

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ABSTRACT

Objectives: *To establish the prevalence and the correlations of metabolic syndrome (MetS) with erectile dysfunction (ED).*

Materials and methods: *A cohort of 1278 men with ages between 27 and 59 years (48,3±6,24), initially evaluated for ED from 2000 to 2005, was retrospectively assessed. Metabolic syndrome was considered according to the IDF Consensus derived from The National Cholesterol Education Program/ Adult Treatment Panel III. For ED assessment, it was used the Sexual Health Inventory for Men (SHIM) questionnaire. The cardiovascular risk (CVR) was assessed by the Systematic Coronary Risk Evaluation (SCORE) diagram. Each element of MetS was correlated with the severity of ED and with the CVR.*

Results: *Organic ED was found in 1068 cases (83,57%), whereas psychological ED in 210 cases (16,42%). Prevalence of MetS was 30,14% (322 cases). ED was correlated with high waist circumference (j=0,884; p<0,001) with hypertension (j=0,601; p<0,08) and hypertriglyceridemia (j=0,392; p<0,05). Relative risk (RR) to induce ED was significant for central obesity: RR=0,85 (0,69-1,39), p<0,001 and for hypertension: RR= 0,72 (0,42-1,15) p<0,001. The severity degree of ED was directly correlated to the incidence of MetS clinical components. Prevalence of severe ED in MetS (39,62%) compare with that in the general population (22%) was significant (p<0,001). Prevalence of the high CVR (SCORE > 15%) in MetS + ED vs. other organic causes of ED was: 24,73% vs. 9,14% (p<0,001).*

Conclusions: *MetS is a frequent cause of ED that increases its severity degree. In people with MetS, ED predicts a highest CVR.*

Keywords: metabolic syndrome, erectile dysfunction, cardiovascular risk

BACKGROUND

The metabolic syndrome (MetS) was strongly considered as a clinical status induced by a negative lifestyle and also having a genetic and familial misbehavior hallmark (1). Joining clinical aspects (central obesity, high blood pressure) and biochemical elements (glycemia and lipid profile modifications) and having insulin resistance with hyperinsulinaemia as principal pathway, MetS can induce damages in the vascular wall, especially endothelial dysfunction. This vassal aggression can create an increased cardiovascular risk (CVR), in coronary but also in many other different vascular territories as well (2).

Before the last decade of the past century, the sexual behavior belonged to the psychological domain, uncommonly described in clinical studies. In the last then years, due to successful new drug therapies, but also due to a

proved predictability of erectile dysfunction (ED) for CVR, the sexual function disturbances and particularly ED management were importantly reconsidered. The induced ED is frequent in some chronic disease: diabetes (over 50%) (3), hypertension and/or arterial ischemia (over 45%) (4) or obesity (over 30%) (5). Epidemiological results show that after the age of 50, 60% of ED cases are related to chronic diseases. That International Society of Impotence Research established that around 60% of ED has organic causes (6), even at the moment of ED evaluation anxiety is added to the rest of initial symptoms (7).

Traditionally considered as a psychological or autonomic nervous disturbance, the main pathway in ED is now ascribed to the endothelial dysfunction. Cavernous endothelium is considered as a faithful marker of alterations produced by reactive oxygen species (ROS) induced by multiple injurious stimuli (oxidized low density lipoprotein particles, advanced glycosylation end products (AGE), abnormal blood pressure, inflammation, etc.) (8). More over, previous studies have already defined ED as a relevant predictor of non clinical expressed vascular disease. In a selected male population with coronary artery disease, 75% had ED, whereas 56% of ED cases presented undiagnosed ischemic heart disease (9). Other results show that men with ED have a 91% high CVR level (10). It is also demonstrated that different risk factors for ED and, among them all the constitutive elements of MetS, are included as potentially depressors of the cavernous endothelial nitric oxide (NO). Known as the most powerful vasodilator substance in the whole vascular field, NO induce smooth muscle relaxation response in the corpora cavernous sincitial tissue, increasing the blood flow insight the erectile system (11, 12).

Considering these data, the relationship between MetS and ED, together with the clinical management of ED, in term to evaluate the CVR and to re-establish the quality of life of the patients with MetS, raises a rational and justified interest. ❑

OBJECTIVES

To evaluate the prevalence of metabolic syndrome and its defining components in a male population with erectile dysfunction. To establish correlations between the MetS components and the cardiovascular risk with the severity degree of ED. ❑

METHODS

Characteristics of the patients

A cohort of 1278 men, randomly attending The Andrology and Sexual Medicine Department of The Clinical Center of Diabetes, Nutrition and Metabolic Disease, was retrospectively assessed by MetS clinical expression. At the moment of the initial ED evaluation, these male persons were unselected by MetS constitutive characters prevalence. The whole study included a period between 2000 and 2005. The mean age of the participants was 48,3±6,24 (27 and 59 years). The patients were divided in five groups: *Group A* = persons with MetS; *Group B* = type 2 diabetes mellitus (T2DM); *Group C*: type 1 diabetes mellitus (T1DM); *Group D*: other clinical (physical) conditions inducing ED; *Group E*: psychogenic ED.

Metabolic syndrome evaluation

For all our patients, MetS was defined according to The International Diabetes Federation (IDF) Consensus (2005) derived from The National Cholesterol Education Program / Adult Treatment Panel III (NCEP/ATP III) criteria: central obesity (waist < 94 cm); high blood pressure (BP ≤ 130/85 mmHg); impaired fasting glucose (fasting glycemia > 100 mg/dl); hypertriglyceridemia (triglycerides serum level > 150 mg/dl); high density lipoproteins (HDL) serum level below 40 mg/dl (13).

Erectile dysfunction evaluation

Erectile dysfunction was evaluated using the methods indicated by guidelines (14): questionnaires, physical examinations, biochemical, endocrine and, in a part of the cases, psychological adequate assessment. The Sexual Health Inventory for Men (SHIM) Questionnaire is now considered to be the most proper instrument in the ED screening and severity degree assessment (15). The 25 points total score of SHIM can be divided as following (16): ≥ 21 points = normal erectile function; 14 – 20 points = mild ED; 7 – 13 points moderate ED; < 7 points = severe ED. We preferred this quantification to

the classical one (≥ 21 = normality; 11 – 20 mild ED; = 10 moderate/severe ED) (17), for a better differentiation of our cases, especially regarding the correlation with CVR. The significant low incidence of nocturnal penile tumescence (NPT), positively correlated with the absence of psychological disturbances was crucial in defining the organic causes of ED. In a few cases endocrine evaluations representing: thyroid (T_3, T_4) gonad (testosterone) pituitary (TSH and prolactine) hormones availability were measured.

CVR evaluation

CVR was evaluated using the SCORE (Systematic Coronary Risk Evaluation) diagram (18). We considered it more faithful because it contains more percentages steps of CVR (very low: <1%; low: 1-3%; mild: 3-5%; moderate: 5-9%; high: 10-14% and very high: ≥15%). Moreover this chart can be differentially applied concerning the risk of cardiovascular disease, or event, in two different categories of countries in Europe: low CVR degree zone (Belgium, France, Greece, Italy, Luxemburg, Spain, Switzerland and Portugal) and high CVR level zone (the rest of European countries, including Romania).

Statistical Analysis

For all the variables, including SHIM, MetS domains, CVR and the correlations between them, survey responses and descriptive statistics (mean and standard deviation) were computed. Significant associations therein were based on related *p* values. All analyses were conducted using SPSS 10.0 for Windows. All *p* values reported below are two-tailed, unless otherwise stated. ❑

RESULTS

From the whole cohort of 1278 retrospective evaluated patients, a number of 1068 persons (83,58%) had organic ED whereas 210 cases (16,42%) presented ED of psychogenic causes (p<0,0001). Demographic characteristics of subjects and of the five groups of participants are described in table 1.

Almost a third of organic induced ED was associated to MetS: 322 cases (30,14%). Another category, associating ED, were persons with diabetes mellitus (type 1 and type 2) representing 317 cases (29,68%). In contrast with other causes, like prostate hypertrophy induced ED for instance, (52 cases; 4,07%) the prevalence of patients with MetS induced ED was highly significant (p<0,0001). An impressive number of 528 ED subjects, associated high blood pressure (HBP) (49,44%) in different comorbidities. A part of them presented ED added just to isolated HBP, without increased waist, glucose intolerance, or modified serum lipids (11,7%) (Table 2).

Characteristics	Group A	Group B	Group C	Group D	Group E	p (OED vs PED)*
Total Nr.	322	211	106	429	210	<0,001
Mean age	49,6±12,7	51,7±10,9	46,7±6,03	46,5±8,81	33,5±4,67	<0,001
Weight (kg)	90,4±18,8	98,3±11,2	78,5±6,9	74,5±6,09	73,1±3,8	<0,05
BMI (kg/m²)	32,4±1,9	31,8±2,2	24,8±1,01	23,9±0,87	22,3±1,75	0,1
Waist (cm)	112,6±19,2	110,5±14,6	89,7±5,6	88,1±7,9	83,3±9,2	0,15
HBP	179 (55,6%)	114 (54.27%)	27 (25,47%)	161 (35,53%)	4 (22.38%)	<0,001
High glucose serum level	276 (85,71%)	100%	100%	0	0	
High cholesterol level	193 (60,01%)	126 (59,52%)	23 (22,34%)	0	26 (12,5%)	<0,001
High triglyce rides level	249 (77,4%)	167 (79,29%)	0	213(49,67%)	41(19,7%)	<0,001
Low HDL – cholesterol	190 (59,12%)	120 (56,89%)	1 (0,96%)	0	0	
Low T level	39 (12,2%)	31 (14,7%)	6 (0,61%)	44 (10,2%)	2 (1,2%)	<0,0001

TABLE 1. Demographic characteristics of the participants
BMI=body mass index; HBP=high blood pressure; HDL=high density lipoprotein; T=serum total testosterone. Data show mean values ± standard deviation and percentages; *calculated significance of the differences between organic ED cases and those with psychogenic cause; OED=organic erectile dysfunction; PED=psychogenic erectile dysfunction.

Diseases	Nr. of cases (%) 1068 (83,58%)		Psychogenic cause 210 (16,43%) p
MetS	322	(30,14)	<0,09
T1DM	106	(9,95)	< 0,05
T2DM	211	(19,75)	NS
Isolated HBP	125	(11,71)	NS
All HBP cases	493	(37,94%)	<0,001
Neurology	26	(2,43)	NS
Pelvic surgery	28	(2,62)	NS
BPH	52	(4,87)	NS
Other (surgery, (trauma, ischemia, etc)	198	(18,53)	NS

TABLE 2. Prevalence of clinical conditions for organic ED vs. the psychogenic cause

MetS=metabolic syndrome; DM=diabetes mellitus; T1DM= type 1 DM; T2DM=type 2 DM; HBP=high blood pressure; BPH=benign prostate hypertrophy.

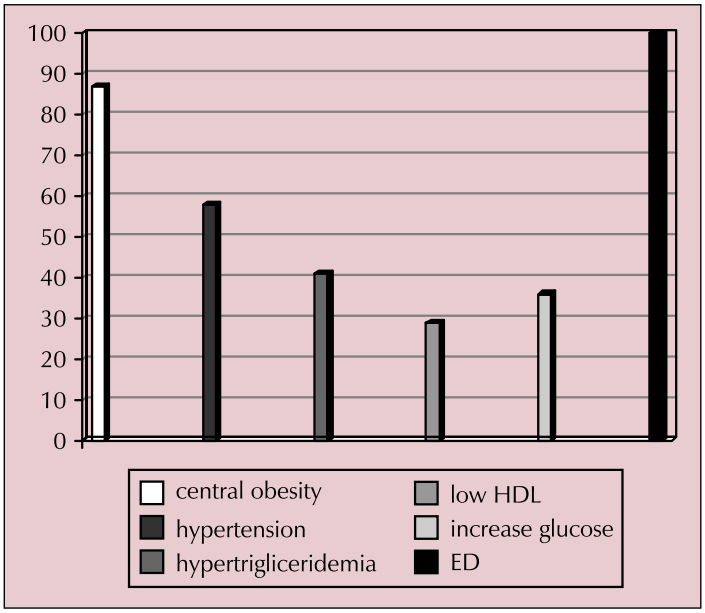

FIGURE 1. Correlation of the incidence of each MetS element with the ED in the studied population

Legend: central obesity = 87%; hypertension = 58%; hypertriglyceridaemia = 41%; Low HDL = 29%; increased glucose level = 36%.

Parameters	RR	(95% CI)	p
Central obesity	0,85	(0,69-1,39)	< 0,001
Glucose ascension	0,57	(0,28-1,35)	0,06
HBP	0,72	(0,42-1,15)	< 0,05
Hypertriglyceridemia	0,69	(0,18-1,81)	0,08

TABLE 3. Relative risk for each MetS clinical element considered as an independent risk factor for inducing ED

This type of comparison showed us in the best way the real involvement and the importance as a risk factor for each clinical condition in the pathway and the onset of ED. Practically significant physical risk for inducing ED, totally different by the psychological causes is represented by the hypertension and the metabolic damages (MetS and DM).

Interesting results were obtained comparing each clinical element of MetS (central obesity, hypertension, hypertriglyceridemia, low HDL cholesterol serum level and increased glucose serum level) with the prevalence of ED (Figure 1).

Usually statistical assessment shows that, in MetS, central obesity is more related to ED then low HDL serum level is ($p<0,001$), whereas triglycerides and increased glycemia, associated to ED, has almost the same prevalence ($p = 0,15$). Using the correlation index for non dichotomise variation parameters (j), significant correlation with ED was obtained for increased visceral adiposity ($j = 0,884$; $p<0,001$), high blood pressure values ($j = 0,601$; $p<0,001$) and for high triglycerides serum levels ($j = 0,392$; $p<0,05$). Continuing statistical evaluation and considering each defining element of MetS as a proved risk factor for ED, the relative risk of each parameter to induce ED is showed in table 3.

It is quite evident that the association of all these risk factors in a distinguished clinical status, as MetS itself really is, represents a bigger danger than each element takes it alone.

Regarding the different severity degree of ED, whereas in the general population previous studies reported a prevalence of severe ED between 17 – 27% (mean value 22%), in our study it was found in 23,82% for the organic ED cases and in 7,6% in psychogenic ED cases. The MetS origin of ED raises the prevalence of severe degree at 39,62%. The difference was significant vs. the general prevalence of severe degree in organic ED ($p<0,05$) and highly significant vs. the prevalence of ED in the general population ($p<0,001$).

In figure 2, the relationships between SHIM score (ED severity evaluation) and the incidence of the elements of MetS was compared. Our results confirm the literature data, that showed that the intensity of symptomatic expression of MetS has a direct influence on the severity degree of ED.

The significance of ED as predictor of the level of RCV, in MetS, known itself as vascular risk factor, is showed in table 4. There is a representative difference between the prevalence of high CVR (>15%) in men with ED associating MetS (24,73%) versus those associating other organic clinical conditions without metabolic disturbance (9,14%): p<0,001. Anyway, it can be observed that ED could be easy considered a marker of moderate to severe CVR for more then 98% in MetS cases and for more than 90% in the rest of the causes of ED.

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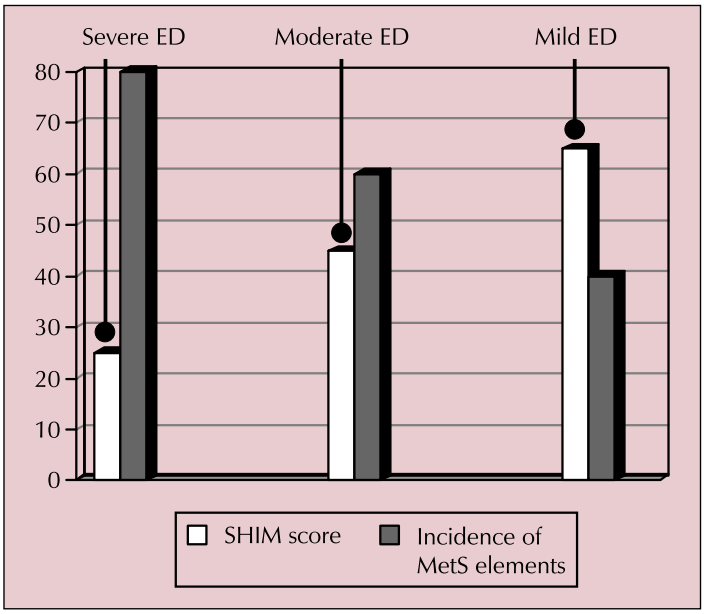

FIGURE 2. Relationship between MetS clinical expression and the severity of ED (SHIM score)

Legend: Dark = MetS elements incidence: A = 4 elem.; B = 3 elem.; C = 2 elem; Light = SHIM score (points): A = 7,6±1,9; B = 12,7±2,4; C = 17,2±2,8.

DISCUSSIONS

This study confirmed on an out stan-ding population, randomly atten-ding our department only for ED management, the high prevalence of physical causes for their erectile system damage (83,58%). Most of them, in the moment of the first evaluation presented more or less degree of anxious status, which was considered by us as over added due to the long evolution of ED (more then one year in the majority of cases), with a progression of the incidence of moments of intercourse failure.

RCV*	Metabolic (MetS±DM) induced ED	Organic (non metabolic) induced ED	p
> 15%	24,73%	9,14%	< 0,001
10 – 14%	42,23%	23,89%	< 0,05
5 – 9%	31,29%	54,31%	< 0,01
< 5%	1,75%	12,66%	< 0,001

TABLE 4. RCV level prediction by ED in metabolic (MetS) vs. non metabolic (HTA, neurological, surgical, urological, etc) induced ED

*Systematic Coronary Risk Evaluation (SCORE).

The most frequent dismetabolic condition correlated to ED was the MetS because it was independently associated to ED in 30,14%. But the most prevalent co-morbidity inducing ED was the association of HBP to different other organic clinical conditions (37,94%). Even the subjects with MetS induced ED had more then a half (55,6%) hypertension. That means that increase sympathetic tone in HBP combined with endothelial dysfunction in MetS, or other organic status, are the most often possible pathway for inducing ED. That is way, it is strongly recommend that male persons with ED to be evaluated in order to investigate his blood pressure and symptomatic unknown MetS elements (or even diabetes).

Metabolic syndrome, with impaired glucose tolerance, was, surprisingly, found in a third of our studied people. Many of them at the first interview for their ED evaluation did not know about their high blood pressure, impaired glucose tolerance or, worse, at moderate diabetic values, or about their lipid profile modifications. Our previous data (19) showed that there is an approximately 8% among newly diabetic male persons which know nothing about their increase serum glucose level and presents as the first sign of metabolic disturbances only the erectile dysfunction symptoms. This kind of data were presented and sustained also by the international literature in very close percentages

(20). The prevalence of the metabolic syndrome among our men with ED (30,14%), is also closely correlated to data performed by the literature (21). In our observations, central (abdominal) obesity was the most frequent element of the metabolic syndrome correlated to ED (87%). If we take into consideration that the excessive abdominal adipose tissue is the most eloquent clinical expression of the insulin resistance syndrome (22), then we are again close to the data presented in the literature (73%) (23).

All our significant correlations of ED with the metabolic syndrome itself and with the majority of its constitutive elements, (especially with the abdominal obesity and the HBP), sustain that the endothelial dysfunction is the more distinguished pathway for all these clinical conditions. It is obvious, however, that there is a close relationship between the intensity of this combination of clinical conditions, and the cardiovascular risk because all of them are obvious expressions of endothelial damages.

In conclusion this study demonstrated that:

1. The metabolic syndrome is a clinical status often correlated to organic erectile dysfunction.
2. Whereas the metabolic syndrome is proved as a risk factor for endothelial damages it could be concluded that metabolic syndrome induced erectile dysfunction could be considered, as well as, a clinical marker for endothelial dysfunction. ❑

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