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Glyco-metabolic profile among type 2 diabetic patients with erectile dysfunction

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Abstract. The aim of this study was to evaluate the glyco-metabolic profile among type 2 diabetic patients with erectile dysfunction (ED). We evaluated 88 type 2 diabetic males, aged 62.78±9.26 years. We administered patients the IIEF (International Index of Erectile Function) questionnaire to assess erectile function, organ function, sexual desire, and satisfaction level during and after the sexual intercourse and the SAS (self-rating anxiety scale) and SDS (self-rating depression scale) questionnaires to evaluate anxiety and depression. We evaluated: BMI, abdominal circumference, glycated hemoglobin (HbA_{1c}), fasting plasma glucose (FPG), fasting plasma insulin (FPI), HOMA index, lipid profile, testosterone, free testosterone, dihydrotestosterone, and sex hormone binding globulin (SHBG). The IIEF questionnaire showed that in the examined sample there were 50 patients (56.8%) affected by ED, and 38 patients (43.2%) without ED. Comparing the two groups, 57.9% of patients without ED, and 70.0% of patients with ED were smokers, and the difference between the two groups was significant ($p<0.05$). Furthermore, 23.7% of patients without ED, and 38.0% of patients with ED had a history of chronic ischemic heart disease ($p<0.05$ between the two groups). Patients with ED were older, and, surprisingly, had lower levels of HbA_{1c}. Furthermore, patients with ED had higher levels of FPI, and lower levels of testosterone and dihydrotestosterone. The prevalence of ED in Italian type 2 diabetic males with mean age of 62 years is about 56% and it is linked to higher levels of FPI, but lower levels of HbA_{1c}, free testosterone and dihydrotestosterone.

Key words: Erectile dysfunction, Type 2 diabetes mellitus, Hyperinsulinemia, Testosterone, International Index of Erectile Function (IIEF)

ERECTILE DYSFUNCTION (ED), defined as the inability to produce or maintain an erection for the sexual intercourse, is a common public health problem that affects millions of men throughout the world, and has a significant impact on quality of life. Erectile dysfunction is reported by 1 of 5 men older than 20 years in the United States [1, 2]. It has been well recognized that diabetes is an important component of ED and that in people affected by type 2 diabetes mellitus, ED not only begins 10 to 15 years earlier than in the general population [3], but it is also less responsive to oral pharmacological therapy [4]. In a survey of 2,869 men, Ponholzer *et al.* [5] found that having diabetes increases the odds of having ED. The authors found that patients with diabetes were at the greatest risk for developing ED with an odds ratio (OR) of 3.00 compared to patients having other conditions such as hyperlipidemia (OR 2.29), hypertension (OR 2.05), psychological stress (OR 1.68) or low physical activity (OR 1.35).

Previous studies have also showed that a higher glycated hemoglobin (HbA_{1c}) was significantly associated with an increased risk of ED and that a period of intensive therapy significantly reduced the prevalence of ED among men with type 1 diabetes for 1 to 15 years with non proliferative retinopathy or microalbuminuria [6].

Corona *et al.* [7] evaluated the relationship between the prevalence of hypogonadism in diabetic and non-diabetic patients affected by ED, with diabetics having a significantly greater prevalence of hypogonad-

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ism, especially in the sixth decade of life, compared to non-diabetics.

There are also a lot of observational studies that showed a significant inverse relationship between total testosterone and insulin resistance in men [8-11], with a stronger correlation with free testosterone than with total testosterone [12-14].

The aim of this study was to estimate the prevalence of ED in a sample of male subjects affected by type 2 diabetes mellitus and to evaluate the glyco-metabolic profile among type 2 diabetic patients with ED, observing if there is a correlation between HbA_{1c}, testosterone, and ED in these subjects.

Material and Methods

Study design

This observational study was conducted at the Department of Internal Medicine and Therapeutics, University of Pavia (Pavia, Italy).

The study protocol was conducted in accordance with the Declaration of Helsinki and its amendments, and the Good Clinical Practice Guidelines. It was approved by the local Ethical Committee and all patients provided written informed prior consent to entering the study. TRIAL REGISTRATION: ClinicalTrials.gov NCT01049750.

Patients

We enrolled 88 males affected by type 2 diabetes mellitus, aged ≥18 according to the ESC (European Society of Cardiology) and EASD (European Association for the Study of Diabetes) Guidelines criteria [15]. The mean age was 62.78±9.26 years.

Suitable patients, identified from review of case notes and/or computerized clinic registers, were contacted by the investigators in person or by telephone.

Patients were excluded if they had anatomic abnormalities of the penis (Peyronie's disease), or had undergone gonadectomy. Furthermore, we also excluded patients treated with drugs aimed at treatment of ED.

Patients were taking different medications; the complete list of the various drugs taken is reported in Table 1.

Assessments

All patients underwent an initial screening assessment that included a medical history, physical examination, vital signs, and a 12-lead electrocardiogram. We administered patients the IIEF (International Index of Erectile Function) questionnaire to assess the presence of erectile function, the self-rating anxiety (SAS) questionnaire to assess the presence of anxiety and the self-rating depression scale (SDS) questionnaire for a thorough evaluation of the patient's depression. All questionnaires were validated in Italian. We also evaluated some parameters such as body weight and body mass index (BMI), waist, abdominal, and hip circumferences, HbA_{1c}, fasting plasma glucose (FPG), capillar pre- and post-prandial glycemia; fasting plasma insulin (FPI), homeostasis model assessment insulin resistance index (HOMA-IR), total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein-cholesterol (HDL-C), triglycerides (Tg), systolic blood pressure (SBP), diastolic blood pressure (DBP), testosterone, free testosterone, dihydrotestosterone, sex hormone binding globulin (SHBG).

All plasmatic parameters were determined after a 12-h overnight fast with the exception of capillar postprandial glycemia, determined 2 hours after a standardized meal. Venous blood samples were taken for

Table 1 Therapies regularly taken by patients

	Patients without ED	Patients with ED	*p* values
N (%)	38 (43.2)	50 (56.8)	ns
Oral anti-diabetic drugs, n (%)	33 (86.8)	37 (74.0)	ns
Insulin, n (%)	7 (18.4)	12 (24.0)	ns
Hypocholesterolemic drugs, n (%)	22 (57.9)	32 (64.0)	ns
Vasodilatators, n (%)	6 (15.8)	22 (44.0)	$p<0.01$
Ace-inhibitors, n (%)	28 (73.7)	38 (76.0)	ns
Beta-blockers, n (%)	13 (34.2)	17 (34.0)	ns
Diuretics, n (%)	1 (2.6)	6 (12.0)	ns
Anti-thrombotic drugs, n (%)	26 (68.4)	39 (78.0)	ns

ns, not significant; ED, erectile dysfunction

all patients between 08.00 and 09.00. We used plasma obtained by addition of Na_2-EDTA, 1 mg/mL, and centrifuged at 3000 g for 15 minutes at 4°C. Immediately after centrifugation, the plasma samples were frozen and stored at -80°C for no more than 3 months. All measurements were performed in a central laboratory.

Body mass index was calculated by the investigators as weight in kilograms divided by the square of height in meters.

Blood pressure measurements were obtained from each patient (using the right arm) in the seated position, using a standard mercury sphygmomanometer (Erkameter 3000, ERKA, Bad Tolz, Germany) (Korotkoff I and V) with a cuff of appropriate size. Blood pressure was measured by the same investigator, in the morning, after the patient had rested for ≥10 minutes in a quiet room. Three successive blood pressure readings were obtained at 1-minute intervals, and the mean of the 3 readings was calculated.

Glycated hemoglobin level was measured by a high-performance liquid chromatography (HPLC) method (DIAMAT, Bio-Rad, USA; normal values 4.2-6.2%), with intra- and interassay coefficients of variation (CsV) of <2% [16]. Plasma glucose was assayed by glucose-oxidase method (GOD/PAP, Roche Diagnostics, Mannheim, Germany) with intra- and interassay CsV of <2% [17].

Capillar pre- and post-prandial glycemia were measured using the FreeStyle Freedom Lite® Blood Glucose Monitoring System (Abbott Laboratories, Abbott Park, Illinois, U.S.A.).

Plasma insulin was assayed with Phadiaseph insulin radioimmunassay (RIA) (Pharmacia, Uppsala, Sweden) by using a second antibody to separate the free and antibody-bound 125 I-insulin (intra- and interassay CsV 4.6 and 7.3%, respectively) [18].

The HOMA-IR index was calculated as the product of basal glucose (mmol/L) and insulin levels (μU/mL) divided by 22.5 [19, 20].

Total cholesterol and Tg levels were determined using fully enzymatic techniques [21, 22] on a clinical chemistry analyzer (HITACHI 737; Hitachi, Tokyo, Japan); the intra- and interassay CsV were 1.0 and 2.1 for TC measurement, and 0.9 and 2.4 for Tg measurement, respectively. High density lipoprotein-cholesterol level was measured after precipitation of plasma apo B-containing lipoproteins with phosphotungstic acid [23]; the intra- and interassay CsV were 1.0 and 1.9, respectively; LDL-C level was calculated by the Friedewald formula [24].

Testosterone levels were determined by enzyme immunoassay (ELISA) according to the instructions of the manufacturer of the kit (Diagnostics Biochem Canada Inc., Ontario, Canada); the intra- and interassay CsV were 6.6% and 7.3%, respectively [25].

Dihydrotestosterone was measured using ELISA, according to the manufacturer of the kit (Diagnostics Biochem Canada Inc., Ontario, Canada); the intra- and interassay CsV were 3.9% and 5.9%, respectively [26].

Sex hormone binding globulin value was measured by a commercially available ELISA kit (Diagnostics Biochem Canada Inc., Ontario, Canada); the intra- and interassay CsV were 5.3% and 7.2%, respectively [27].

Questionnaires

The IIEF questionnaire consists of 15 items grouped in 5 domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. IIEF is a psychometrically valid and reliable instrument that was developed through consultations with an international panel of experts for use in determining efficacy of treatment in controlled clinical trials [28]. The IIEF has high sensitivity and specificity for detecting real treatment effects or the lack of treatment effects in patients with ED of broad spectrum etiology [28]. In the IIEF questionnaire the score for each item ranges from five for normal erection to one for no erection. IIEF rates erectile function as absence of ED (score 21-25), mild ED (score 16-20), moderate ED (score 11-15), and severe (score 5-10).

The SAS questionnaire was designed by Zung *et al.* [29] in 1964 to quantify the level of anxiety. SAS is a validated 20 item self report assessment device which include measures of state and trait anxiety. Each question is scored on a scale of 1-4 (based on these replies: "none or a little of the time," "some of the time," "good part of the time," "most of the time"). SAS rates anxiety as absence of anxiety (score 20-44), mild to moderate anxiety (score 45-59), marked to severe anxiety (score 60-74), extreme anxiety (score 75-80).

The SDS questionnaire was also designed by Zung to assess the level of depression for patients diagnosed with depressive disorder [30] to quantify the degree of depression of a patient. There are 20 items on the scale that rate the four common characteristics of depression: the pervasive effect, the physiological equivalents, other disturbances, and psychomotor activities. Each question is scored on a scale of 1 through 4 (based on

these replies: “a little of the time,” “some of the time,” “good part of the time,” “most of the time”). SDS rates depression as absence of depression (score 20-49), mild depression (score 50-59), moderate depression (score 60-69), severe depression (score 70-80).

Statistical Analysis

Quantitative data were expressed as median [interquartile range]; the qualitative variables were described as counts and percentages. The comparison of quantitative variables between two groups was performed with the Student t test for independent data, the chi-square test (or Fisher exact test if expected frequencies of less than 5) was, instead, used for comparisons between qualitative variables. Correlations were analyzed using the Pearson correlation coefficient *r*. All tests were two-tailed and the limit of significance chosen was 5% ($p<0.05$). Results were adjusted for potential confounders, such as age. Analysis were made using the software STATA (vers: 9; STATA Corporation, College Station, 2008, Texas, USA) [31].

Results

IIEF questionnaire

The IIEF questionnaire showed that, in the examined sample, there were 50 patients (56.82%) affected by ED, and 38 patients (43.18%) without ED. Between patients with ED, 22 (44%) suffered of mild ED, 13 (26%) of moderate ED, and 15 (30%) of severe ED.

Self-rating anxiety questionnaire

According to the SAS questionnaire, there were 44 (88%) patients with ED and 37 (97%) patients without ED affected by some degrees of anxiety; the difference between the two groups was statistically significant ($p<0.05$), even if the distribution of the various degrees of anxiety did not change between the two groups (Fig. 1).

Self-rating depression scale

The SDS questionnaire showed that 42 (84%) patients with ED and 36 (95%) patients without ED were also affected by some degrees of depression. Patients with ED have a significantly higher prevalence of depression ($p<0.05$), even if the distribution of the various degrees of depression did not change between the two groups (Fig. 2).

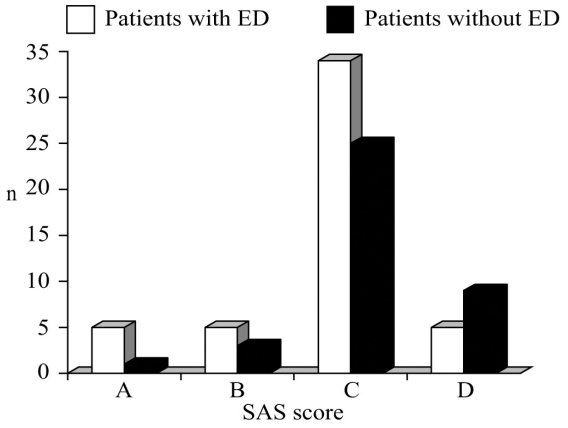

Fig. 1 SAS score distribution in patients with and without ED
A: SAS score between 20-44 (absence of anxiety)
B: SAS score between 45-59 (moderate anxiety)
C: SAS score between 60-74 (severe anxiety)
D: SAS score between 75-80 (extreme anxiety)
p = not statistically significant; ED: erectile dysfunction; SAS: self-rating anxiety questionnaire

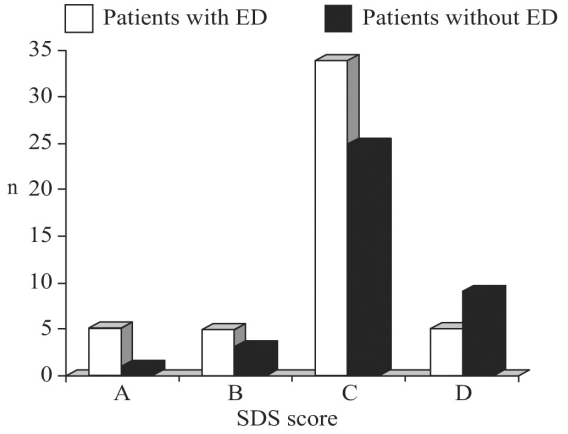

Fig. 2 SDS score distribution in patients with and without ED
A: SDS score between 20-49 (absence of depression)
B: SDS score between 50-59 (mild depression)
C: SDS score between 60-69 (moderate depression)
D: SDS score between 70-80 (severe depression)
p = not statistically significant; ED: erectile dysfunction; SDS: self-rating depression scale questionnaire

Qualitative parameters

Comparing the two groups, 57.9% of patients without ED, and 70.0% of patients with ED were smokers, and the difference between the two groups was significant ($p<0.05$). Furthermore, 23.7% of patients without ED, and 38.0% of patients with ED had a history of chronic ischemic heart disease ($p<0.05$ between the two groups). No statistically significant differences were observed regarding alcohol consumption, hyper-

Table 2 Qualitative variables comparison between the two groups

	Patients without ED	Patients with ED	*p* values
N (%)	38 (43.2)	50 (56.8)	ns
Sm. St., n (%)	22 (57.9)	35 (70.0)	$p<0.05$
Alcohol, n (%)	15 (39.5)	13 (26.0)	ns
Hepatic steatosis, n (%)	21 (55.3)	20 (40.0)	ns
Hypertension, n (%)	21 (55.3)	31 (62.0)	ns
Dyslipidemia, n (%)	16 (42.1)	26 (52.0)	ns
CHD, n (%)	9 (23.7)	19 (38.0)	$p<0.05$
Hyperuricemia, n (%)	5 (13.1)	6 (12.0)	ns
CKD, n (%)	2 (5.3)	3 (6.0)	ns
Retinopathy, n (%)	4 (10.5)	5 (10.0)	ns
Neuropathy, n (%)	2 (5.3)	6 (1.0)	ns
Vasculopathy, n (%)	1 (2.63)	2 (4.0)	ns

ns, not significant; ED, erectile dysfunction; Sm. St, smoking status; CHD, chronic ischemic heart disease; CKD, chronic kidney disease

tension, dyslipidemia, or diabetic complications such as retinopathy, neuropathy and vasculopathy between the two groups (Table 2).

Quantitative parameters

Patients with ED were older (65.0 [62.9-67.7] *vs* 59.2 [57.6-63.0] years, $p<0.01$), and had a higher BMI (30.2 [28.8-31.6] *vs* 28.3 [27-29.7] kg/m^2, $p<0.05$) compared to patients without ED. Moreover patients with ED had higher waist circumference (105.5 [101.4-107.6] *vs* 98.3 [96.1-102.4] cm, $p<0.05$), abdominal circumference (106.4 [104.9-111.9] *vs* 101.0 [99.8-106.2] cm, $p<0.05$), and hip circumference (104.6 [103.6-109.5] *vs* 98.5 [97.6-103.1] cm, $p<0.01$).

Surprisingly, patients with ED had lower levels of HbA_{1c} (6.5 [6.0-7.1] *vs* 7.0 [6.5-7.9] %, $p<0.02$); observing the HbA_{1c} trend in the previous year, 13 (26.0%) patients with ED and 7 (18.4%) patients without ED had HbA_{1c} <7% in all measurements; 16 (32.0%) patients with ED and 11 (28.9%) patients without ED had HbA_{1c} >7% with a frequency between 1 and 30% of the measurements; 14 (28.0%) patients with ED and 11 (28.9%) patients without ED had HbA_{1c} >7% with a frequency between 31 and 70% of the measurements, and 7 (14.0%) patients with ED and 9 (23.7%) of patients without ED had HbA_{1c} >7% with a frequency between 71 and 100% of the measurements. The differences in the distribution of HbA_{1c} between the two groups were not statistically significant (Fig. 3). Patients without ED were younger at the time of type 2 diabetes mellitus diagnosis (52.1 [50.1-56.2] years) compared to patients with ED (58.6 [54.6-60.5] years), and the difference between the two groups was significant ($p<0.05$).

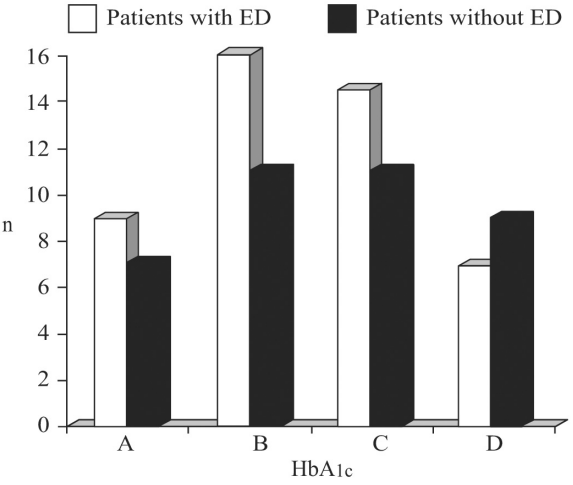

Fig. 3 HbA_{1c} distribution in patients with and without ED
A: patients with HbA_{1c} <7% in all measurements
B: patients with HbA_{1c} >7% with a frequency between 1 and 30% of the measurements
C: patients with HbA_{1c} >7% with a frequency between 31 and 70% of the measurements
D: patients with HbA_{1c} >7% with a frequency between 71 and 100% of the measurements
p = not statistically significant; ED: erectile dysfunction

Patients with ED had higher levels of FPI (11.4 [6.7-21.9] *vs* 7.5 [5-12.5] µU/mL, $p<0.05$), and HOMA IR (3.4 [1.8-7.5] *vs* 2.8 [1.5-4.2], $p<0.05$), and lower levels of free testosterone (1.01 [0.7-1.4] *vs* 1.55 [0.9-2.0] pg/mL, $p<0.01$), and dihydrotestosterone (139.2 [124.3-194.8] *vs* 171.6 [131.8-234.3] pg/mL, $p<0.05$) (Table 3).

No significant differences were observed between the two groups regarding, FPG, capillar pre- and post-prandial glycemia, TC, LDL-C, HDL-C, Tg.

Correlations

There was a significant inverse correlation between IIEF score and age (r=-0.3318 and p=0.0054), and between IIEF score and age at the moment of type 2 diabetes mellitus diagnosis (r=-0.2756 and p=0.0219). A significant inverse correlation between IIEF score and free testosterone levels (r=-0.2570, and p=0.0358), such as between IIEF score and the numbers of time HbA_{1c} was >7.0% (r=-0.30, and p=0.0400) were recorded.

Discussion

Previous studies showed that the etiology of ED is often multi-factorial, with psychological, neurological, endocrine, vascular, traumatic or iatrogenic causes involved [32]. One of the most frequent cause is surely linked to the psychological sphere; in nervous men increased sympathetic tone and raised circulating catecholamine concentrations may interfere with the mechanisms of smooth muscle relaxation underlying erection. The problem is self perpetuating: each failure increases the anxiety and depression associated with subsequent attempts at erection [33]. In our study we observed that, in term of absolute numbers, anxiety and depression were more common in patient with ED,

Table 3 Quantitative variables comparison between the two groups.

	Patients without ED	Patients with ED	*p* values
N (%)	38 (43.18)	50 (56.82)	ns
Age (years)	59.2 [57.6-63.0]	65.0 [62.9-67.7]	$p<0.01$
Age at diagnosis of DM (years)	52.1 [50.1-56.2]	58.6 [54.6-60.5]	$p<0.05$
Duration of DM (years)	5 [3-9]	5 [2-11]	ns
Weight (Kg)	78.5 [74.0-90.0]	[77.5-97.5]	$p<0.05$
Height (cm)	170 [165-173]	170 [167-172]	ns
BMI (kg/m^2)	28.3 [27-29.7]	30.2 [28.8-31.6]	$p<0.05$
Waist circumf. (cm)	98.3 [96.1-102.4]	105.5 [101.4-107.6]	$p<0.05$
Abd. circumf. (cm)	101.0 [99.8-106.2]	106.4 [104.9-111.9]	$p<0.05$
Hip circumf. (cm)	98.5 [97.6-103.1]	104.6 [103.6-109.5]	$p<0.01$
HbA_{1c} (%)	7.0 [6.5-7.9]	6.5 [6.0-7.1]	$p<0.02$
FPG (mg/dL)	132.5 [113-159]	124.5 [101-141]	ns
Cap. pre-prandial glyc. (mg/dL)	121.0 [110-136]	120.0 [102-139]	ns
Cap. post-prandial glyc.(mg/dL)	139.0 [117-165]	139.5 [123-153]	ns
SBP (mmHg)	135 [120-140]	130 [120-145]	ns
DBP (mmHg)	80 [80-87]	80 [80-90]	ns
FPI (μU/mL)	7.5 [5-12.5]	11.4 [6.7-21.9]	$p<0.05$
HOMA-IR	2.8 [1.5-4.2]	3.4 [1.8-7.5]	$p<0.05$
TC (mg/dL)	147.5 [142-167]	163 [146-176]	ns
LDL-C (mg/dL)	84.7 [65.6-93]	87.0 [73.8-98.6]	ns
HDL-C (mg/dL)	41.5 [37-47]	43.5 [38-51]	ns
Tg (mg/dL)	112 [88-140]	134 [90-185]	ns
Testosterone (pg/mL)	1.3 [1.1-1.5]	1.2 [1.0-1.4]	ns
Dihydrotestosterone (pg/mL)	171.6 [131.8-234.3]	139.2 [124.3-194.8]	$p<0.05$
Free testosterone (pg/mL)	1.55 [0.9-2.0]	1.01 [0.7-1.4]	$p<0.01$
SHBG (mmol/L)	33.0 [24.6-41.9]	32.1[22.3-49.7]	ns

Data are expressed as median [interquartile range]. ED, erectile dysfunction; ns, not statistically significant; Abd. Circumf., abdominal circumference; HbA_{1c}, glycated hemoglobin; FPG, fasting plasma glucose; Cap. pre-prandial glyc., capillar pre-prandial glycemia; Cap. post-prandial glyc., capillar post-prandial glycemia; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPI, fasting plasma insulin; HOMA-IR, homeostasis model assessment insulin resistance index; TC, total cholesterol; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; Tg, triglycerides; SHBG, sex hormone binding globulin

even if the distribution of the various degrees of these diseases, assessed throughout the SAS and SDS questionnaire scores, were similar in patients with or without ED, and no correlations were observed, suggesting that anxiety and depression are more a consequence than a cause of ED. However, the main causes of ED are vascular diseases: in older patients a reduced flow of blood into the penis due to atherosclerotic lesions of the internal iliac, pudendal, and cavernosal arteries is the most common cause [34]. Risk factors for vascular disease include a family history, hypertension, alcoholism, smoking, diabetes, and hyperlipidemia [32]. In our study we observed that patients affected by type 2 diabetes and smokers have a higher prevalence of ED confirming what already reported by Austoni *et al.* [35] that observed that the risk of ED is influenced by smoking with a dose and duration response effect. On the other side we did not record a major prevalence of alcoholism in patients with ED.

Moreover, we did not record any difference between patients with or without ED regarding the prevalence of hypertension, differently from what observed by Burchardt *et al.* [36]; he observed that ED is more prevalent in patients with hypertension than in an age matched general population, and that patients treated with diuretics and β-blockers had the highest incidence and those treated with α-blockers had the lowest incidence of ED. This difference is probably due to the fact that the patients enrolled in our study were already in treatment for hypertension, and no differences between the therapy taken were observed with the exception of vasodilatators, more used in patients affected by ED.

The same thing can be said about hyperlipidemia, differently from what previously reported [37], we did not identify hyperlipidemia as a risk factor for ED, probably because patients were already in treatment with hypocholesterolemic drugs.

Regarding the prevalence of ED, we recorded a prevalence of ED of 56% in patients with type 2 diabetes, this is in line with what already reported in literature: ED occurs in 32% of type 1 and 46% of type 2 diabetic men; in particular between the ages of 30 to 34 years, ED is present in 15% of diabetics, this number increases to 55% by the age of 60 years that is the mean age of our sample [38]. This is probably linked to the fact that free serum testosterone concentrations fall progressively with age because the testes produce less testosterone and more androgens are removed from the blood by rising concentrations of SHBG. Falling testosterone concentrations are associated with a loss of libido and reduced frequency of erections [32]. We confirmed those data: patients affected by ED have lower levels of free testosterone and dihydrotestosterone, and slightly higher levels of SHBG, even if the latter did not reach statistically significance. This trend is probably linked to the fact that, in our sample, patients with ED were significantly older than patients without ED, confirming that older people have lower levels of testosterone.

However, an apparently surprising result of our study is that patients with lower HbA_{1c} seem to have a higher prevalence of ED; this is in contrast with what already published in literature in Italian population by Fedele *et al.* [39]: they observed that, in comparison with men with good metabolic control, the ORs for ED were 1.7 and 2.3 in men with fair and poor control, respectively. We think that this difference is probably linked to the fact that in our sample patients with ED had also a higher BMI, and higher abdominal circumference compared to patients without ED. Obesity, and in particular visceral obesity, is strictly related to insulin resistance [40], and insulin resistance proved to be a risk factor for ED [41]. We have also to consider the relatively new diagnosis of diabetes (mean duration 7.3 years), our patients still have a good insulin reserve, so they are still able to balance insulin resistance with a major insulin secretion; having higher levels of insulin, they have a better glycemic control, but a higher prevalence of ED. This is proven by the fact that when we analyzed the variation of HbA_{1c} during the previous year, and not the mean $HbA_{1c,}$ there was a significantly inverse correlation between IIEF score and the number of times HbA_{1c} was higher than 7%.

A limitation of this study is the relatively small samples of subjects involved that can limit the generalizability of the study, another limitation is that we simply studied the prevalence of ED between type 2 diabetic patients, without starting any treatment when diagnosis was done. However, at the best of our knowledge, we are the firsts to observe a correlation between ED and insulin resistance.

Conclusions

Our study showed that the prevalence of ED in Italian males with type 2 diabetes mellitus with mean age of 62 years, is about 56% and it is linked to higher levels of FPI, but lower levels of HbA_{1c}, and lower levels of free testosterone and dihydrotestosterone.

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