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ERECTILE DYSFUNCTION, HORMONE LEVELS, INFLAMMATION IN MALE PATIENTS WITH METABOLIC SYNDROME

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ABSTRACT

Background and Objective

The overall prevalence of metabolic syndrome (MetS) and obesity in male Taiwanese is very high, but the impacts on MetS, sexuality and sex hormones, inflammation markers in male erectile dysfunction (ED) are not entirely clear in relevance. This study's aim is to investigate males with MetS and its components, sex hormones, inflammatory risk factors, sexuality and ED correlation.

Material and Methods

This was a cross-sectional study of 89 male participants, and data collected included demographic data, biochemistry, sex hormones, inflammatory risk factors and International Index of Erectile Function (IIEF-15) questionnaire. Descriptive analysis, difference analysis, and logistic regression model were used to identify relevant variables that may affect ED.

Result

Among our 89 subjects, 46 had MetS (51.7%) and 31 subjects with MetS had ED (67.4%). The presence of MetS had a significant correlation with lower IIEF-ED scores, lower intercourse satisfaction scores, lower total testosterone (TT) serum level ($p<0.01$) and also presence of MetS had a significant correlation with higher D-dimer, fibrinogen and C-reactive protein (CRP) serum level. The results also showed that the greater the number of MetS components had the higher the prevalence of ED and the higher the abnormal CRP, fibrinogen and D-dimer ($p<0.05$). After adjusting for age, we used sexual desire dysfunction, Met S and TT abnormal to run the logistic regression model for predictors of ED, and the analysis showed that there was a significant difference for sexual desire dysfunction (OR = 8.845, 95% CI=2.203 – 35.516, P = 0.002), Met S (OR = 4.100, 95% CI = 1.343 – 12.520, P = 0.013) and TT abnormal (OR = 3.287, 95% CI = 1.022 – 10.570, P = 0.046).

Conclusion
To prevent the development of ED, we should encourage a change in lifestyle to prevent the development of MetS, and early identification and treatment of MetS risk factors might be helpful to prevent ED and secondary cardiovascular disease, including diet and lifestyle interventions.
Key words: *erectile dysfunction; metabolic syndrome; International Index of Erectile Function; testosterone; inflammatory risk factors*

Erectile dysfunction (ED) is the inability to consistently produce and maintain an erection for sexual intercourse of adequate quality throughout its duration.[1,2] ED is not a disease, but a condition brought on by other primary causes, which can be due to lifestyle, drug side effects, age, systemic diseases, and neurological and psychological disorders.[3] ED is more prevalent as age increases and can be quite common.[4] Certain studies associate the occurrence of ED could be an early detector of the manifestation of vascular disease and is an independent risk factor for cardiovascular incidents, recent data also associate low-grade systemic inflammation as an important element of the connections between ED, coronary artery disease (CAD) and metabolic syndrome (MetS).[5,6] Certain risk factors correlated with ED such as obesity, hypertension, detrimental lipid levels, tobacco addiction, diabetes mellitus (DM), depression, anxiety disorders, substance and alcohol abuse, hypothyroidism, prostate carcinoma, testosterone deficiency, renal, hepatic or neurologic disease, and specific medications, can be managed.[7,8] ED also can be an early indicator for other underlying diseases, mainly coronary heart disease and depression.[9–12]

Chronic inflammation is a significant symptom in ED and the development of cardiovascular risk factors. While metabolic syndrome MetS is related to endothelial dysfunction and higher cardiovascular risk. Chronic inflammation and MetS have shown to be connected in recent studies.[13-15]

MetS is the range of metabolic disorders and patients with MetS show an increased risk factor for developing cardiovascular disease (CVD).[16,17] MetS currently affects about 23% of adults and is a condition that increases the risk of CVD, diabetes, stroke, and diseases related to fatty buildups in artery walls. Mottillo's study connects MetS with a 2-fold increase in cardiovascular outcomes and a 1.5-fold increase in all-cause mortality.[18] The overall occurrence of MetS and obesity in male Taiwanese is very high,[19] however, the effects of obesity and MetS, sexuality and sex hormones, inflammation markers on male ED, is not yet apparent. Various epidemiological studies, found a high percentage of ED in patients with CVD, MetS, and the risk factors of exposure, caused mainly by CVD, to atherosclerosis (atherosclerosis) as the machine turn one, ordinary pathological changes in the process of atherosclerosis and cell damage of vascular endothelial, certain studies also show that atherosclerosis is an obstacle predictor of erectile function. MetS is commonly associated with many chronic diseases and increased risk of CVD and type 2 diabetes.[20–23]

The experts of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP)-III established an operational definition of MetS in 2001. Within the definition, abdominal obesity, high blood pressure (BP), high fasting blood glucose, high triglyceride (TG), and low high-density lipoprotein (HDL) cholesterol are indicated as risk factors of MetS. The presence of any 3 of the five factors is defined as MetS.[24]

MetS is rapidly growing as a public health concern due to its connection with increasing incidences of obesity, overweight, and physical inactivity.[25,26] In Tsou's study, the prevalence of MetS in the elderly was found to be 34.3% (405/1181; 39.3% in females vs. 25.6% in males) in the Taipei metropolis. The study also recognized that the majority of the elderly population in Taiwan presented at minimum 2 risk factors for MetS.[27] Several studies have been able to establish that common CVD risk factors also represent risk factors for ED, such as age, hypertension, diabetes, insulin resistance, smoking, increased body

mass index (BMI), cholesterol, and decreased levels of HDL cholesterol.[28–30]

The objectives sought out by this study were to examine the relationship between ED and sexual function, MetS, systemic inflammation. It is also our aim to investigate the prevalence of ED in patients with MetS along with a control group and to evaluate the relationships between acute phase reactants (CRP, fibrinogen, D-dimer), sexual function and sex hormone levels.

METHODS

This study was a cross-sectional design and was conducted at a subject with MetS men aged over 40 years who took part in our community health examinations. These participants were older adults who came from the local community in southern Taiwan. Participants were eligible if they could read and complete the questionnaire. Inclusion criteria were male patients, between 40 and 70 years of age, with ED as defined by the IIEF, and who were willing to sign informed consent for study participation. Exclusion criteria were the use of any androgen therapy or any ED medications during the previous 3 months (7 months for implantable testosterone); any serious medical (like myocardial infarction or heart failure), psychiatric (like schizophrenia), or neurological conditions (other than mild cognitive impairment) that may affect brain structure or cognition; a history of head trauma with loss of consciousness lasting more than 5 minutes; a current or past history of medication, such as antidepressants, that was likely to affect sexual function (especially affect erectile function); or they were unwilling to complete the forms. Subjects who were sexually inactive were excluded from the study.

Ethical Issues

The study protocol was reviewed and approved by the Ethical Committees for Human Research at Kaohsiung Veterans General Hospital. Before each interview, the interviewer explained the objectives and methodology of the study to each participant and signed the survey document once verbal informed consent was obtained from the participant. Participants were informed that the survey was anonymous. The staff distributed the questionnaire and informed the participants that completion of the questionnaire was voluntary and responses were anonymous.

Procedure

Staff members interviewed the participants individually in a quiet room. Data was collected using self-reported questionnaires and in-person interviews. Participants were asked to complete the questionnaire and were offered a presentation on sexual behavioural terms. Doctors and a research assistant were available to answer any questions. After completing the questionnaire, the participants were asked to place it in the provided envelope and close it.

ASSESSMENT INSTRUMENT

Demographic Questionnaire

The questionnaire included 14 items, predominantly multiple-choice. There were 14 demographic and descriptive items, including the participants' gender, relationship status, age, educational level, religion, smoking and drinking habits, CVD history, awareness of his or her health conditions, their relationship with a partner, and so on.

SCALES TO ASSESS SEXUAL FUNCTION

The IIEF

Erectile dysfunction was defined using the IIEF-15. The IIEF was administered to ensure that men were within the normal range of erectile functioning. The IIEF is a 15-item measure assessing 5 domains of sexual function: erectile function (6 items), orgasmic function (2 items), sexual desire (2 items), intercourse satisfaction (3 items), and overall satisfaction (2 items).[31] The IIEF is the most widely used psychometric index of self-reported erectile function, and demonstrates good psychometric properties. Internal consistency of this measure for the current study was acceptable (Cronbach's $\alpha = .62 – .90$).

Physical Examination and Blood Profiles

Participants' blood profiles were obtained after a 12-hour fast, and were sent for storage in a −70°C refrigerator within 4 hours of collection. Samples were sent to a hospital laboratory for analysis. Total testosterone (TT), D-dimer, fibrinogen, and C-reactive

protein (CRP) were measured using standard laboratory procedures. Biochemical markers such as high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), and fasting plasma glucose (FPG) were analyzed using a biochemical autoanalyzer (Beckman Coluter, Lx-20, USA) at the Clinical Laboratory Department of Ping-tung branch, Kaohsiung Veterans General Hospital. Fasting blood samples were obtained between 8:00 and 10:00 AM to minimize diurnal variation. The serum levels of testosterone were measured with a solid-phase, competitive, chemiluminescent enzyme immunoassay (IMMULITE 2000 Total Testosterone, Diagnostic Products Corporation, Los Angeles, CA, USA) at baseline and at the end of the study. Normal ranges for serum testosterone are 300–1200 ng/ dL.[32] In this study, we used an age group from 40 to 70 years of age as the main sample, so low TT was defined as TT <300 ng/ dL.[33] The Adult Treatment Panel III (ATP III) of the NCEP modified for Asians defined MetS as the presence of 3 or more of the fol-lowing: FPG ≥ 100 mg/dL, serum TG ≥ 150 mg/dL, serum HDL-C <40 mg/dL in men and <50 mg/dL in women, BP ≥ 130/ 85 mmHg, or waist circumference >90 cm in men and >80 cm in women.[34,35] Individuals diagnosed as previously having hypertension, DM, or hyperlipidemia, but were under control with regular medication were also included.

A smoker was defined as a person who smoked ≥10 cigarettes/day and had done so for more than 6 months, and a drinker was defined as someone who consumed alcohol every week and had done so for 6 consecutive months.

STATISTICAL ANALYSIS

Data is presented as mean ± SD if not mentioned otherwise. The difference among groups was considered significant if the P value was less than .05. Continuous variables were reported as mean ± SD and categorical variables were reported as percentage (95% confidence intervals [CI]). The means and percentages comparison of ED and MetS under each categorical demographic variable (for example, age, education, inflammatory risk factors, sex hormone and IIEF total score) was examined using the Kruskal-Wallis H (K-W H) test or chi-square test. The K-WH test was used in case of non-normality. In addition, the K-W H test was used to determine the relationship between participants who were both MetS and with ED, and their educational level, age, TT serum level, sexual satisfaction, and sexual desire. We also used univariate and multivariable analyses of the associations between inflammatory risk factors, sex hormone and components of MetS were conducted with binary logistic regression model. We also used MetS, age, sexual desire dysfunction and abnormal of TT to run the logistic regression model for predictors of ED.

RESULTS

Eighty-nine participants were available for analysis. Eleven participants did not complete the tests and were excluded, leaving 89 samples (89.0%) for analysis. The mean ± SD age of all study participants was 56.58 ± 8.35 years (range 40 to 70 years), and the average educational level was 13.53 ± 3.41 years. Of the 89 participants, 53 (59.6%) were currently obese (WC≥90), 37 (41.6%) had a serum testosterone level below 300ng/dl, 42 (47.2%) had ED, 26 (29.2%) were current smokers, 46 (51.7%) had MetS, 49(55.1%) had hypertension, 45 (51.7%) had DM, 40 (44.9%) had hyperlipidemia, 27 (30.3%) had abnormal HDL, 12 (13.5%) had abnormal CRP, 32 (36%) had orgasmic dysfunction. 66 (74.2%) had sexual desire dysfunction and 74 (83.1%) had intercourse satisfaction dysfunction and 77 (86.5%) had overall satisfaction dysfunction. The percentage of sexual dysfunction for normal control group and MetS group are shown in Figure 1, which presents composite percentage for each of the sexual dysfunction domains. Table 1 shows the socio-demographic and other characteristics of the study subjects. The participants were stratified by relationships between ED, MetS and age, education, BMI, IIEF score, hypertension, smoking, drinking and central obesity using the K-W H test and chi-square test. The participants with ED were significantly older, and participants with MetS had a higher BMI. Although the differences between the groups in terms of age, IIEF score (including erectile function, orgasmic function, sexual desire function, intercourse satisfaction, and

FIG 1. The percentage of sexual dysfunction for normal control group and metabolic syndrome group.

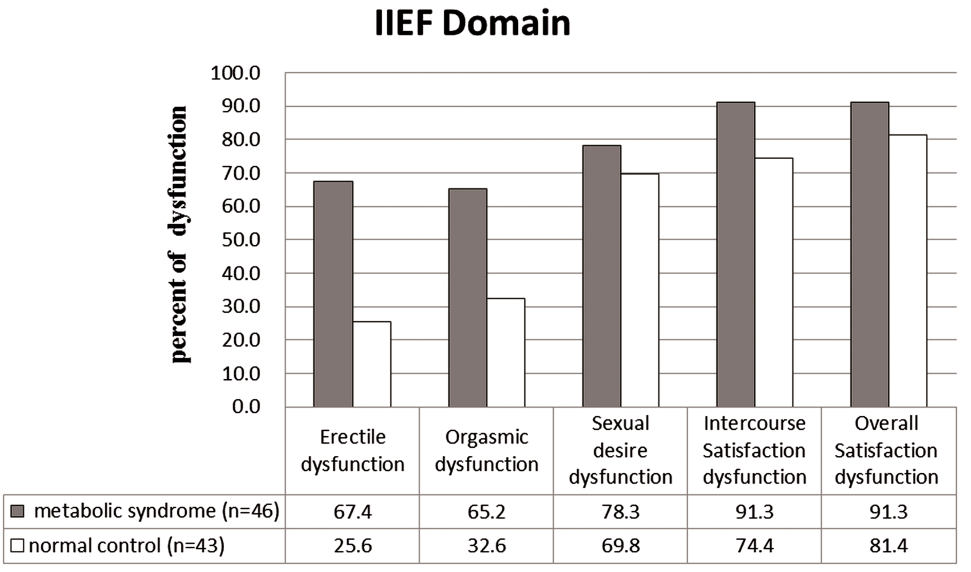


TABLE 1 Socio-demographic and Other Characteristics of the Study Subjects

Characteristic		No MetS		MetS		P value [a]
		No ED n = 32	ED n = 11	No ED n = 15	ED n = 31	
Age		53.69±8.58	60.00±6.51	57.20±6.19	58.06±8.99	0.047*
Education(y)		13.97±3.75	14.36±3.56	13.20±3.10	12.94±3.14	0.190
BMI		24.37±2.70	24.32±3.18	28.28±2.85	28.50±5.04	<0.001*
IIEF score						
Erectile function		28.93±0.98	14.45±7.89	28.53±1.46	14.38±7.47	<0.001*
Orgasmic function		9.56±0.84	3.72±3.58	9.26±1.16	5.10±3.73	<0.001*
Sexual desire function		8.00±1.46	5.45±2.25	8.53±0.64	5.81±2.44	<0.001*
ISF		11.09±2.70	3.27±3.35	10.93±2.59	5.23±4.02	<0.001*
OSF		7.88±1.43	5.09±2.47	8.20±0.77	6.06±1.95	<0.001*
	total (%)	**(col.%)**	**(col. %)**	**(col. %)**	**(col. %)**	**P value [b]**
Hypertension						
No	40 (44.9)	26 (81.3)	6 (54.5)	5 (33.3)	3 (9.7)	<0.001*
Yes	49 (55.1)	6 (18.7)	5 (45.5)	10 (66.7)	28 (90.3)	$\chi^2 = 33.855$
Smoking						
No	63 (70.8)	22 (68.8)	8 (72.7)	12 (80.0)	21 (67.7)	0.840
Yes	26 (29.2)	10 (31.2)	3 (37.3)	3 (20.0)	10 (32.3)	$\chi^2 = 0.839$

Characteristic		No MetS		MetS		P value [a]
		No ED n = 32	ED n = 11	No ED n = 15	ED n = 31	
Drinking						
No	53 (59.6)	20 (62.5)	5 (45.5)	9 (60.0)	19 (61.3)	0.786
Yes	36 (40.4)	12 (37.5)	6 (54.5)	6 (40.0)	12 (38.7)	$\chi^2 = 1.063$
Central Obesity						
No	36 (40.4)	17 (53.1)	9 (81.8)	4 (26.7)	6 (19.4)	0.001
Yes	53 (59.6)	15 (46.9)	2 (18.2)	11(73.3)	25 (80.6)	$\chi^2 = 16.859$

*[a]Kruskal-Wallis test; [b]Chi-square test; *Significant (*p*-value < 0.05)*
ED = erectile dysfunction; MetS = metabolic syndrome; BMI = body mass index; IIEF = International Index of Erectile Function; ISF = Intercourse Satisfaction Function; OSF = Overall Satisfaction Function

overall satisfaction), hypertension and central obesity were significant, the differences with respect to the education, smoking and drinking were not significant.

Table 2 shows the clinical chemistry of study subjects. The participants were stratified by relationship between ED, MetS and CRP, fibrinogen, D-dimer, HDL, DM, TG and testosterone using the K-W H test and chi-square test. Since the data (CRP, fibrinogen, D-dimer, HDL, DM, TG and testosterone) were not in a normal distribution, we used the non-parametric K-W H test to analyze them. Participants with MetS and ED had significantly lower serum levels of TT, HDL, higher serum levels of fibrinogen, CRP, DM and, TG than those No MetS and without ED.

After divided normal and abnormal, the differences of abnormal percentage between the groups were significant in terms of CRP, HDL, TT, DM, TG, and fibrinogen.

Table 3 also showed participants with ED had significantly lower sexual function (including erectile function, orgasmic function, sexual desire function, intercourse satisfaction, and overall statisfaction) and higher serum atherosclerosis risk factors (D-dimer and fibrinogen) than participants without ED. The data also showed on the relationship between ED and abnormal percentages of testosterone, DM, hypertension, abnormal CRP, and MetS using the chi-square test. The relationships between ED and testosterone ($\chi^2 = 10.551$, p value = 0.001), DM ($\chi^2 = 7.148$, p value=0.008), hypertension ($\chi^2 = 17.773$, p value < 0.001), and MetS ($\chi^2 = 15.589$, p value<0.001) were significant.

Table 4 shows that subjects were grouped in accordance with the number of MetS components they had. The results showed that the greater the number of MetS components, the higher the prevalence of ED and the higher the abnormal serum TT level, (p<0.05). The erectile function scores, testosterone serum levels were significantly decreased and CRP, D-dimer fibrinogen were significantly increased with an increment in the MetS components number (p<0.05).

To evaluate the statistical effect of individual MetS to the components of MetS, serum TT level and serum CRP one by one. We found all of the variables had a significant impact on ED prevalence using univariate analysis (Table 5). After adjusting the ORs of age, the results of multiple logistic regression analysis indicated significant ORs for MetS (OR = 6.012, 95% CI = 2.39- 15.11, P<0.001), DM (OR = 3.222, 95% CI = 1.350 – 7.694, P = 0.008), HT (OR = 7.104, 95% CI=2.741 – 18.415, P<0.001), TT abnormal (OR = 4.289, 95% CI = 1.744 – 10.547, P = 0.002), CRP abnormal (OR=16.323, 95% CI = 2.004 – 132.916, P<0.001), respectively.

TABLE 2. Clinical Chemistry of Study Subjects

Characteristic		No MetS		MetS		P value [a]
		No ED n = 32	ED n = 11	No ED n = 15	ED n = 31	
D-dimer		265.8±115.1	332.7±104.8	567.5±926.4	735.0±1098.5	0.005*
Fibrinogen		282.7±54.6	303.3±43.3	305.2±96.2	347.9±91.8	0.017*
CRP		0.73±0.59	2.15±3.09	1.74±2.37	7.13±12.83	0.070
HDL-C		53.1±13.9	56.0±13.0	38.2±9.2	42.7±11.1	<0.001*
Triglyceride		130.4±66.7	117.1±56.0	189.3±65.6	162.8±65.4	0.006*
Glucose		101.6±30.4	101.2±8.5	124.2±50.3	119.8±42.6	<0.001*
Testosterone		3.92±1.17	5.70±2.15	3.54±1.14	2.63±0.97	<0.001*
	total (%)	**(col. %)**	**(col. %)**	**(col. %)**	**(col. %)**	**P value** [b]
CRP						0.007*
Normal	77 (86.5)	32 (100)	9 (81.8)	14 (93.3)	22 (71.0)	$\chi^2 = 12.218$
Abnormal	12 (13.5)	0 (0)	2 (18.2)	1 (6.7)	9 (29.0)	
HDL						<0.001*
Normal	62 (69.7)	31 (96.9)	10 (90.9)	4 (26.7)	17 (54.8)	$\chi^2 = 29.907$
Abnormal	27 (30.3)	1 (3.1)	1 (9.1)	11 (73.3)	14 (45.2)	
Testosterone						<0.001*
Normal	52 (58.4)	26 (81.3)	10(90.9)	9 (60.0)	7 (22.6)	$\chi^2 = 28.055$
Abnormal	37 (41.6)	6 (18.7)	1(9.1)	6 (40.0)	24 (77.4)	
Glucose						<0.001*
Normal	43 (48.3)	25 (78.1)	7 (63.6)	4 (26.7)	7 (22.6)	$\chi^2 = 23.458$
Abnormal	46 (51.7)	7 (21.9)	4 (36.4)	11 (73.3)	24 (77.4)	
Triglyceride						<0.001*
Normal	49 (55.1)	22 (68.8)	10 (90.9)	2 (13.3)	15 (48.4)	$\chi^2 = 19.249$
Abnormal	40 (44.9)	10 (31.2)	1 (9.1)	13 (86.7)	16 (51.6)	
D-dimer						0.224
Normal	76 (85.4)	30 (93.8)	10 (90.9)	11 (73.3)	25 (80.6)	$\chi^2 = 4.369$
Abnormal	13 (14.6)	2 (6.2)	1 (9.1)	4 (26.7)	6 (19.4)	
Fibrinogen						0.038
Normal	76 (85.4)	30 (93.8)	11 (100.0)	10 (66.7)	25 (80.6)	$\chi^2 = 8.451$
Abnormal	13 (14.6)	2 (6.2)	0 (0.0)	5 (33.3)	6 (19.4)	

*[a]Kruskal-Wallis test; [b]using Chi-square test; *significant (*p*-value < 0.05)*
ED = erectile dysfunction; MetS = metabolic syndrome.

TABLE 3 Relationship of Erectile Dysfunction and Age, Educational Level, Atherosclerosis Risk Factors, Sex Hormone and Metabolic Syndrome Risk Factors

	No ED (n=47)	**ED (n=42)**	**P value** [a]
Age	54.81±7.80	58.57±8.38	0.023*
Education level	13.72±3.54	13.31±3.27	0.418
Erectile function	28.81±1.15	14.40±7.49	<0.001*
Orgasmic function	9.47±0.95	4.74±3.70	<0.001*
Sexual desire function	8.17±1.27	5.71±2.37	<0.001 *
ISF	11.04±2.64	4.71±3.92	<0.001*
OSF	7.98±1.26	5.81±2.11	<0.001*
D-dimer	362.08±538.82	629.62±957.95	0.002*
Fibrinogen	289.85±70.23	336.19±83.78	0.007*
HDL-C	48.36±14.33	46.19±12.94	0.449
Triglyceride	149.21±71.25	150.83±65.60	0.895
	No ED (n = 47)	**ED (n = 42)**	**P value** [b]
Central obesity			
No	21 (44.7)	15 (35.7)	0.39
Yes	26 (55.3)	27 (64.3)	$\chi^2 = 0.740$
Glucose			
Normal	29 (61.7)	14 (33.3)	0.008*
Abnormal	18 (38.3)	28 (66.7)	$\chi^2 = 7.148$
Hypertension			
No	31 (66.0)	9 (21.4)	<0.001*
Yes	16 (34.0)	33 (78.60)	$\chi^2 = 17.773$
CRP			
Normal	47 (97.9	31 (73.8)	= 0.001*
Abnormal	1 (1.1)	11 (26.2)	$\chi^2 = 11.009$
MetS			
Normal	32 (68.1)	11 (26.2)	<0.001*
Abnormal	15 (31.9)	31 (73.8)	$\chi^2 = 15.589$
Testosterone			
Normal	35 (74.5)	17 (40.5)	0.001*
Abnormal	12 (25.5)	25 (59.5)	$\chi^2 = 10.551$

[a]*Mann-Whitney test;* [b]*Chi-square test; *significant* (p-*value < 0.05)*
ED = erectile dysfunction; MetS = metabolic syndrome; ISF = Intercourse Satisfaction Function; OSF = Overall Satisfaction Function

Table 4 The Prevalence of ED, Age, Sexual Desire, Sex Hormones and Atherosclerosis Risk Factors in Relation to the Number of MetS Components

	Number of MetS Components			
	A=0-2 (n=43)	**B=3 (n=23)**	**C=4-5 (n=23)**	**P value [a]**
Age	55.00±8.34	58.52±8.73	57.61±7.75	0.162
Erectile function	24.98±7.57	19.48±8.29	19.00±10.25	<0.001*
Orgasmic function	8.02±3.18	6.83±3.51	6.17±3.96	0.055
Sexual desire function	7.35±2.01	6.35±2.20	7.04±2.58	0.207
ISF	8.98±4.49	7.43±4.33	6.77±4.80	0.169
OSF	7.07±2.07	6.70±2.30	7.00±1.65	0.831
CRP	1.12±1.71	4.47±11.81	6.23±10.04	<0.001*
D-dimer	284.6±115.8	655.5±1054.5	702.1±1045.8	0.019*
Fibrinogen	291.49±51.27	289.39±85.00	371.87±90.63	<0.001*
Testosterone	4.34±1.68	3.06±1.00	2.87±1.26	<0.001*
	A = 0-2 (n = 43)	**B = 3 (n = 23)**	**C = 4-5 (n = 23)**	**P value [b]**
ED				0.002*
No	31 (72.1)	7 (30.4)	9 (39.1)	$\chi^2 = 12.763$
Yes	12 (27.9)	16 (69.6)	14 (60.9)	
Testosterone				<0.001*
Normal	35 (81.4)	8 (34.8)	9 (39.1)	$\chi^2 = 18.159$
Abnormal	8 (18.6)	15 (65.2)	14 (60.9)	

*[a]Kruskal-Wallis test; [b]Chi-square test; *Significant (*p*-value < 0.05)*
ED = erectile dysfunction; MetS = metabolic syndrome; ISF = Intercourse Satisfaction Function; OSF = Overall Satisfaction Function

TABLE 5 Univariate Logistic Regression Analysis of MetS, Sex Hormone and Atherosclerosis Risk Factors for ED

					95% CI for OR	
Variable	**Coefficient**	**S.E.**	**P-value**	**Odds ratio**	**Lower limit**	**Upper limit**
MetS	1.794	0.470	<0.001*	6.012	2.392	15.110
Glucose Abnormal	1.170	0.444	0.008*	3.222	1.350	7.694
Hypertension	1.961	0.486	<0.001*	7.104	2.741	18.415
HDL Abnormal	0.483	0.464	0.299	1.620	0.652	4.026
TT Abnormal	1.456	0.459	0.002*	4.289	1.744	10.547
D-dimer Abnormal	0.312	0.602	0.604	1.367	0.420	4.448
CRP Abnormal	2.793	1.070	0.009*	16.323	2.004	132.916
Fibrinogen Abnormal	−0.049	0.602	0.935	0.952	0.293	3.099

**Significant (*p*-value < 0.05)*
CRP = C-reactive protein; ED = erectile dysfunction; HDL = high-density lipoprotein; MetS = metabolic syndrome; TT = total testosterone.

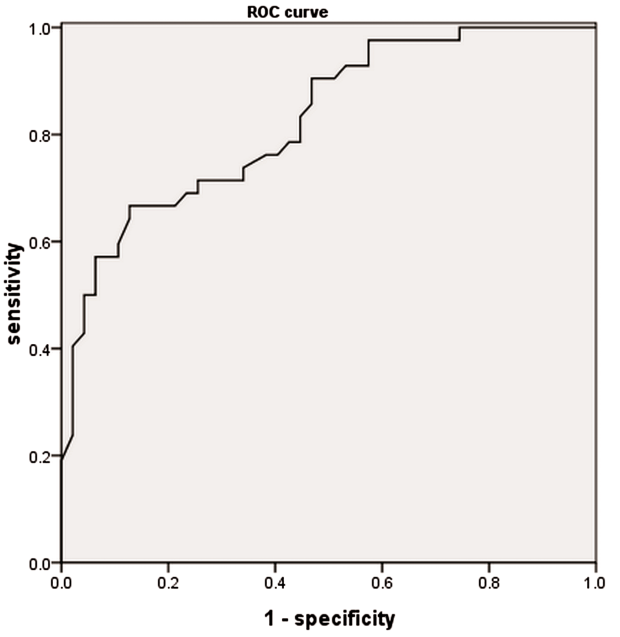
TABLE 6 Multiple Logistic Regression Model of Predictors of ED

Variable	Coefficient	S.E.	P-value	Odds ratio	95% CI for OR	
					Lower limit	Upper limit
Constant	−6.447	2.152	0.003*	0.002		
Age	0.060	0.033	0.073	1.062	0.994	1.134
Sexual desire dysfunction	2.180	0.709	0.002*	8.845	2.203	35.516
MetS	1.411	0.570	0.013*	4.100	1.343	12.520
TT abnormal	1.190	0.596	0.046*	3.287	1.022	10.570

**Significant (*p*-value < 0.05)*
ED = erectile dysfunction; MetS = metabolic syndrome; TT = total testosterone.

Table 6 lists the factors related to ED in multiple logistic regression analysis. After adjusting for age, we used sexual desire dysfunction, Met S and TT abnormal to run the logistic regression model for predictors of ED, and the analysis showed that there was a significant difference for sexual desire dysfunction (OR=8.845, 95% CI = 2.203- 35.516, P = 0.002), Met S (OR = 4.100, 95% CI = 1.343 – 12.520, P = 0.013) and TT abnormal (OR = 3.287, 95% CI = 1.022 – 10.570, P = 0.046). We then used these variables to predict and set the cutoff point for the probability of 0.50, and the correctness of reclassification of 82.6% (Figure 2).

FIG 2. The ROC curve of predicting erectile dysfunction. (AUROC = 0.826±0.043)



DISCUSSION

The MetS is a cluster of metabolic risk factors; the MetS is composed of CVD risk factors including increased body mass index/waist circumference, hypertension, plasma glucose, and TG, as well as decreased HDL-C. This article provides a survey of sexual function, inflammatory and prothrombotic risk factors and sex hormone among patients with MetS in Taiwan. In this study, the research subjects, were divided into 2 groups: those with and without MetS, respectively; we used informatory and prothrombotic risk factors, MetS component factors, and serum testosterone as related indicator risk factors of ED associated with MetS. The average age of the subjects was 56.58 ± 8.35 years, and the mean educational level was 13.53 ± 3.41 years. The results found that 42 sub-jects had ED (47.2%) and 47 did not (52.8%), which is higher than in previous studies,[34,35] and the results also showed that 46 subjects had MetS (46/89, 51.7%) and 67.4% (31/46) had ED in subjects had MetS. Similarly, Heidler and associates reported the prevalence of MetS to be 33.8% for the male population between the ages of 30 and 69 years, with some degree of ED present in 68.4% of the patients with MetS younger than 50 years and in 74.8% of the men with MetS older than 50 years.[36] This study also showed there is significant correlation between the subjects with ED and IIEF-ED score, orgasmic func-tion, sexual desire, intercourse satisfaction and overall satisfaction score (p <0.01). Demir *et al*. observed in

his study that IIEF-5 scores significantly decreased as the number of metabolic risk factors increased ($P< 0.001$).[37] Sanjay' s study also show that presence of the various components of MetS was associated with ED and a decrease IIEF-5 score and this effect was greater than the effect associated with any of the individual components.[38] In our study, we found that the mean IIEF-ED score decreased with an increasing number of MetS components. This finding proved that the ED was associated with an increasing number of metabolic risk factors. The results of this study confirm the association between ED and MetS, similarly previous studies.[39–43] García-Cruz's study showed that ED was found to be associated with severity of MetS, with an increased mean number of MetS components seen as ED severity increased. Multivariable analysis revealed that moderate and severe ED had the vari-ables associated with the highest odds of MetS.[44] In addition, there was a significant correlation between the subjects with ED and atherosclerosis risk factors (D-dimer and fibrinogen), age, serum TT, MetS and MetS components ($p <0.05$). Folsom et al. point out a higher basal plasma D-dimer concentration in the general population is a risk marker for ischemic stroke, especially cardioembolic stroke.[45]

Martinez's study showed that nitrated fibrinogen may serve as a marker of inflammation and oxidative stress in venous thromboembolism.[46] C-reactive protein is an important inflammatory biomarker of subclinical atherosclerosis and was demonstrated as an active molecule with relevance in the process of endothelial dysfunction. Vlachopoulos's study points out that low-grade systemic inflammation could be an important element of the association between metabolic syndrome, ED, and CAD.[47] Our study also showed that the subjects with ED had higher abnormal CRP. In our study, we have observed that patients with ED had higher levels of fibrinogen, D-dimer and abnormal CRP.

We also found that the proportion of participants who had a history of diabetes, hypertension, MetS, abnormal CPR and abnormal TT and these participants who had high prevalence of ED, similarly Hung et al study.[21] Al-Hunayan's study pointed out that ED usually occurs in middle-aged men, especially in those with diabetes, hypertension and MetS,[48] these results are similar to those of this study. Our results also showed that MetS, abnormal TT and CRP were significantly related to erectile function, similar to the Grover et al. finding.[49]

This study has several limitations. First, the number of study participants was relatively small; therefore, the results cannot be generalized. Second, this is not a longitudinal study, and we did not make an initial assessment of participants' sexual dysfunction. Sexual dysfunction is evaluated at only one time point during the assessment of the questionnaire; therefore, causality cannot be determined and the participant's prior sexual functioning cannot be incorporated into our models. Third, bias introduced by underreporting is possible, because sexual behaviour is a sensitive issue, and the topic may be considered socially unacceptable, especially in ethnic Chinese cultural settings. In our study, 11% of the initially enrolled patients refused to answer the questionnaire. After excluding these non-responders, we categorized the participants into an ED group and non-ED group to minimize bias.

CONCLUSION

The results of this study support the idea that MetS, low serum TT and inflammatory risk factors may predict ED in Taiwanese males. To prevent the development of ED, we should encourage a change in lifestyle to prevent the development of MetS, atherosclerosis and other risk factors for CVD. We also found that participants with ED have a higher prevalence of MetS and higher abnormal CRP, so these results support the idea that ED and MS share the same cardiovascular risk factors, and endothelial dysfunction is a common link. The early identification and treatment of MetS risk factors might be helpful to prevent ED and secondary cardiovascular disease, including diet and lifestyle interventions.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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