



Is Epicardial Adipose Tissue, Another Measure of Central Obesity, Correlated with Erectile Dysfunction?

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Background: This study investigated the correlation between epicardial adipose tissue (EAT), a measure of central obesity, and sexual function in males with vasculogenic erectile dysfunction (ED). **Materials and Methods:** The study was a cross-sectional study of selected males with ED aged <75 years who attended the Urology Outpatient Department of Tri-Service General Hospital. Sixty subjects were included in the study, which employed biochemical data, anthropometric indexes, echocardiography, and questionnaires. Biochemical lipid profiles and associated inflammation markers were recorded. The anthropometric indexes included general and central obesity and bioelectrical impedance analysis. Echocardiography results were assessed by a single experienced cardiologist and included epicardial and pericardial fat thickness measurements. Sexual function was evaluated using the International Index of Erectile Function-5 (IIEF-5) score. **Results:** According to the analysis of variance and multivariate logistic regression, only the erectile hardness score (EHS) was statistically positively correlated with the IIEF-5 score. All other anthropometric indexes and echocardiography parameters, including EAT thickness, pericardial adipose tissue thickness, and ejection fraction (EF), were not significantly associated with sexual function. **Conclusions:** Only EHS was statistically associated with sexual function in the male subjects with ED. The anthropometric indexes and EAT thickness, a measure of central obesity, were not significantly correlated with sexual function in the male patients with ED.

Key words: Epicardial fat, pericardial fat, central obesity, erectile dysfunction

INTRODUCTION

Erectile dysfunction (ED) is a common public health problem affecting millions of men worldwide. For many patients, ED is one manifestation of a more generalized pathology. It is a common belief that 50–80% of ED cases are due to multifactorial organic causes. As erectile function is a hemodynamic phenomenon that depends on the integrity of neurological, vascular, and endocrinologic tissue (corpora cavernosa) and psychological factors, changes in any one of these components may lead to ED. Strong epidemiological evidence links a subsequent risk of ED to the presence of

well-recognized risk factors for coronary artery disease (CAD), such as increased body mass index (BMI), hypertension, hypertriglyceridemia, and hypercholesterolemia.¹⁻⁴ These comorbidities are common in cohorts of men with ED.⁵ Endothelial dysfunction is a likely pathological mechanism that is common to both these comorbidities and ED. Esposito *et al.*⁶ suggested that in obese men, endothelial dysfunction might contribute to ED because of a reduced blood flow and an abnormal platelet aggregation response.

Specifically, central obesity has been found to be associated with metabolic changes and diabetes mellitus

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EAT is not a direct predictor of ED

and cerebrovascular and ischemic heart disease.⁷ A study of Riedner *et al.* revealed that central obesity is a predictor of ED among men aged 61–81 years without known diabetes mellitus, hypertension, and other comorbidities.⁸ Moreover, a significant association between central obesity and ED was identified among young males without a history of systemic disease.⁹ Several studies have demonstrated a strong association between ED and metabolic syndrome (MS).^{10–12} On the other hand, Kupelian *et al.*¹³ indicated that the occurrence of ED is a predictor of the development of MS, especially among men with a BMI lower than 25, a group not usually considered at risk of cardiovascular disease (CVD) or diabetes mellitus. Although our subjects did not fit the criteria of MS, possible MS development should be considered. The pathogenesis of ED is likely multifactorial and may not be explained by endothelial dysfunction alone.¹⁴ Hypogonadism contributing to sexual dysfunction has been identified in obese males.¹⁵ A recent meta-analysis by Liu *et al.*¹⁶ indicated that MS was associated with an increased incidence of ED, with significant evidence of heterogeneity among ten studies of 4092 participants. Another large-scale meta-analysis of 12,067 subjects by Besiroglu *et al.*¹⁷ identified a 2.6-fold increase in the incidence of ED in patients with MS; all individual components of MS, with the exception of high-density lipoprotein (HDL), were also found to be correlated with an increased prevalence of ED. Meanwhile, evidence has shown that epicardial adipose tissue (EAT) has a significant effect on MS.^{18,19} Whether obesity is coupled with ED independently or through cardiovascular risk factors or hypogonadism, it is evident that obese men have a high incidence of ED that affects their sexual life and fertility. However, whether or not EAT, another vesical adipose tissue, or central obesity is associated with ED is yet to be explored.

Therefore, we identified urology outpatient department ED patients and examined related characteristics and echocardiographs to study the association or trend between EAT related to central obesity and ED among this population.

MATERIALS AND METHODS

Patients

A cross-sectional study was performed in an unselected consecutive sample of sixty males aged from 40 to 75 years, without a history of diabetes, hypertension, or other systemic disease, who had the habit of smoking or did not smoke. All subjects were required to undergo a general physical examination, including blood pressure, BMI, waist circumference (WC), waist-to-hip ratio (WHR), neck circumference (NC), bioelectrical impedance analysis, and erectile hardness score (EHS). Fasting glucose and lipid profiles were examined by serum testing, including total cholesterol,

triglyceride, HDL, and low-density lipoprotein; inflammation markers enclosing homocysteine, high-sensitivity C-reactive protein (CRP), apolipoprotein A1, and apolipoprotein B; and endocrine levels recruiting testosterone, prolactin, estradiol, follicle-stimulating hormone, and luteinizing hormone. Subjects who had a medical disease history, such as hypertension, CVD, diabetes mellitus, dyslipidemia, or psychiatric problems, were excluded from the study on account of ED confounders to analyze the association with EAT, and use of drugs or alcohol abuse was recorded and analyzed in the study. Written informed consent was obtained from all subjects, and the study protocol was approved by the ethics committees of the institutions involved in the study.

Assessment of erectile function

Erectile function was assessed using a questionnaire consisting of five questions based on the International Index of Erectile Function-5 (IIEF-5),²⁰ which is a multidimensional questionnaire; all five questions were similarly styled. The five questions asked were (i) How often are you able to get an erection during sexual activity?; (ii) When you have erections upon sexual stimulation, how often are your erections hard enough for penetration?; (iii) When you attempt sexual intercourse, how often are you able to penetrate (enter) your partner?; (iv) During sexual intercourse, how often are you able to maintain your erection after you have penetrated (entered) your partner?; and (v) During sexual intercourse, how difficult is it to maintain your erection for completion of intercourse? The IIEF-5 score represents the sum of the scores of questions 1–5, with a maximum score of 25; a score of 21 or less indicated ED. Herein, ED severity was classified as moderate to severe (score 6–11), mild to moderate (score 12–16), mild (score 17–21), or no ED (score >21). Penile Doppler ultrasound was used to document the presence of vasculogenic ED, which was defined as a peak systolic velocity <25 cm/s in either cavernosal artery 15 min following injection of a vasodilator.

Data collection

BMI was calculated from the formula weight in kilograms divided by height in meters squared. WC was obtained from the midpoint between the iliac crest and costal margin. HC was measured at the widest point around the greater trochanter. WHR was calculated as WC divided by hip circumference. NC was identified at between the mid-cervical spine and mid-anterior neck just below the laryngeal prominence with the head in the Frankfurt plane.²¹ Illustrations of echocardiography including the short, long axis of the EAT thickness and the short, long axis of the pericardial adipose tissue (PAT) thickness were recorded. To illustrate the real association between sexual function and obesity, all subjects were categorized by quartiles

according to each anthropometric index, analyzing the severity of ED according to the IIEF-5 score in relation to increasing obesity.

Statistical analysis

The data are expressed as mean $\pm$ standard deviation. Student's *t*-test was conducted to compare the ED and non-ED groups. Analysis of variance (ANOVA) was used to analyze the association between IIEF-5 score and obesity. Multivariate logistic regression was applied to demonstrate the impact of an individual factor on the development of moderate to severe ED (IIEF-5 <17). $P < 0.05$ was considered statistically significant. All analyses were conducted using SPSS statistical software (version 13.0, SPSS Inc, Chicago, IL, USA).

RESULTS

Clinically, sixty subjects completed the questionnaire to obtain an IIEF-5 score and underwent other anthropometric studies, among whom the prevalence of moderate to severe (IIEF-5: 6–11), mild to moderate (IIEF-5: 12–16), and mild ED (IIEF-5: 17–21) was 56.7%, 23.3%, and 20.0%, respectively. All the participants underwent comprehensive echocardiographic study, including EAT thickness (mean of the short axis and long axis), PAT thickness (mean of the short axis and long axis), and ejection fraction (EF).

To address the association between sexual function and smoking, 41 subjects were identified as smokers and the other 19 as nonsmokers in the study. There was no statistical difference in the IIEF-5 score between the smoking and nonsmoking groups (IIEF-5 = 12.30 and 12.49, respectively; Student's *t*-test, $P = 0.422$). In addition, we compared the variables between each category of ED severity, including age, anthropometric indexes, echocardiographic characteristics, lipid profiles, and endocrine levels [Table 1]. According to ANOVA, only age, HDL, and EHS had statistically significant correlations with the IIEF-5 score ($P = 0.002$, $P = 0.004$, $P < 0.001$); [Table 1]. Synergic relationships of HDL and EHS, and a reverse association of age, were noted with sexual function in our study. An inverse trend was observed between the lipid metabolism and sexual function (lipoprotein B/A1, $P = 0.072$; cholesterol, $P = 0.092$). No statistically significant relationships were found between any of the anthropometric indexes and clinical sexual function, except that the indexes of central obesity, including WC, WHR, and NC, had reverse trends. No significant associations were identified between EAT, PAT, EF, and sexual function [Table 2].

To adjust confounding factors relating to ED, the multivariate logistic regression method was applied to analyze the odd ratios for the development of moderate to severe

ED among the risk factors. Only the EHS demonstrated a statistically significant role in the development of moderate to severe ED (odds ratio = 0.01, 95% confidence interval = 0.0003–0.43; $P = 0.016$), [Table 3]. No significant trends among the other risk factors were identified in relation to the development of moderate to severe ED.

DISCUSSION

Obesity is the most common risk factor for CVDs in industrial countries. It is now clear that adipose tissue secretes various bioactive substances, conceptualized as adipocytokines and that dysregulation of adipocytokines directly contributes

Table 1: Results of comparisons between erectile dysfunction severity groups (moderate to severe erectile dysfunction [International Index of Erectile Function-5: 6–11], mild to moderate erectile dysfunction [International Index of Erectile Function-5: 12–16], mild erectile dysfunction [International Index of Erectile Function-5: 17–21], nonerectile dysfunction [International Index of Erectile Function-5 >21] [analysis of variance, *t*-test])

Variables Mean (SD)	Moderate to severe ED (n=34)	Mild to moderate ED (n=14)	Mild ED (n=12)
Age (year)	65.07 (8.02)	60.18 (10.58)	50.92 (9.97)
BMI (kg/m ²)	25.63 (3.71)	24.82 (1.96)	26.34 (2.64)
WC (cm)	93.35 (9.59)	91.43 (6.28)	91.63 (9.39)
WHR	0.927 (0.059)	0.910 (0.042)	0.909 (0.048)
NC (cm)	39.94 (2.73)	39.75 (2.86)	39.58 (2.64)
BFP (%)	24.78 (5.27)	24.83 (1.89)	25.49 (2.64)
HDL (mg/dL)	45.17 (10.58)	51.30 (14.02)	58.85 (14.67)
LDL (mg/dL)	134.10 (27.68)	124.79 (31.55)	121.09 (27.23)
Triglyceride (mg/dL)	171.79 (30.66)	182.57 (27.21)	171.80 (35.26)
Cholesterol (mg/dL)	200.83 (27.42)	197.91 (29.70)	180.67 (32.69)
Apolipoprotein B/A1	0.75 (0.11)	0.72 (0.22)	0.71 (0.13)
Homocysteine (μ mol/L)	12.06 (5.41)	14.55 (3.25)	14.05 (5.22)
hs-CRP (mg/dL)	0.16 (0.36)	0.11 (0.17)	0.16 (0.21)
Testosterone (ng/dL)	383.18 (54.14)	478.31 (92.17)	371.10 (58.07)
EAT (mm)	4.61 (1.39)	4.36 (1.10)	4.70 (0.71)
PAT (mm)	5.54 (1.60)	5.42 (1.26)	6.08 (0.77)
EF (%)	67.54 (7.41)	66.35 (8.35)	69.10 (4.15)
EHS	1.76 (0.49)	2.43 (0.51)	2.83 (0.72)

The results of comparisons of all variables revealed no statistical significance ($P > 0.05$), with the exceptions of age ($P = 0.002$), HDL ($P = 0.004$) and EHS ($P < 0.001$). BMI = Body mass index; WC = Waist circumference; WHR = Waist-to-hip ratio; NC = Neck circumference; BFP = Body fat percentage; HDL = High-density lipoprotein; LDL = Low-density lipoprotein; hs-CRP = High sensitivity-C reactive protein; EHS = Erectile hardness score; SD = Standard deviation; ED = Erectile dysfunction

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Table 2: Mean International Index of Erectile Function-5 scores in each quartile category of three echocardiography characteristics

Anthropometric index	Quartile category	IIEF-5 (mean±SD)	F	P ^a
EAT (mm)	Q1<3.89	9.36±5.22	0.22	0.80
	3.89≤ Q2<4.72	13.54±5.52		
	4.72≤ Q3<5.56	9.27±3.69		
	5.56≤ Q4	12.44±6.06		
PAT (mm)	Q1<5.00	9.08±4.89	0.64	0.53
	5.00≤ Q2<5.56	12.36±5.61		
	5.56≤ Q3<6.25	12.33±4.61		
	6.25≤ Q4	11.64±6.10		
EF (%)	Q1 <64.0	9.46±5.24	0.39	0.67
	64.0≤ Q2<67.5	12.10±5.26		
	67.5≤ Q3<73.0	13.00±5.35		
	73.0≤ Q4	10.30±5.74		

^aANOVA. EAT = Epicardial adipose tissue; PAT = Pericardial adipose tissue; EF = Ejection fraction; IIEF-5 = International Index of Erectile Function-5; ANOVA = Analysis of variance; SD = Standard deviation; ED = Erectile dysfunction

Table 3: The prevalence of each erectile dysfunction category in different quartiles of epicardial adipose tissue thickness

Variables	OR	95% CI	P ^b
Age (years)	1.06	0.91-1.24	0.438
HDL (mg/dL)	0.99	0.88-1.11	0.849
EHS	0.01	0.0003-0.43	0.016
Mean EAT (mm)	1.68	0.32-8.88	0.540
Mean PAT (mm)	0.18	0.03-1.18	0.074
EF (%)	1.09	0.87-1.38	0.457

^bMultivariate logistic regression. OR = Odds ratio; CI = Confidence interval; HDL = High-density lipoprotein; EHS = Erectile hardness score; EAT = Epicardial adipose tissue; PAT = Pericardial adipose tissue; EF = Ejection fraction

to obesity-related diseases. The enlargement of fat cells during the development of obesity has been previously hypothesized to be a triggering factor for the proliferation of new fat cells.²²

ED is defined as the persistent or recurrent inability to achieve or maintain an erection sufficient for satisfactory sexual intercourse. In men reporting symptoms of ED, 79% of subjects are found to be overweight or obese.⁴ In a survey of health professionals, obesity was found to be associated with a 1.3-fold relatively increased risk of ED.²³ In a prospective study of risk factors for ED, obesity and smoking were found to be positively associated and physical activity was inversely associated with the risk of development of ED during the 14-year follow-up period.²⁴

Obesity might be at a pro-inflammatory stage and results in the process of inflammation, then inducing endocrine and

endothelial dysfunction. A further hypothesis presented in these kinds of studies was that weight loss in obese patients reduces the serum concentrations of markers (CRP, interleukin [IL-6], and IL-8) and leads to improved endothelial function.²⁵ Obese men participating in weight loss programs with dietary modification and increased physical activity experienced reduced oxidative stress associated with improved nitric oxide availability.²⁶ Another study of Esposito *et al.*⁶ demonstrated that lifestyle changes by means of reducing body weight and increasing physical activity induce amelioration of erectile and endothelial function in obese men. The results of the study showed that the intervention group with weight loss exhibited significantly improved erectile function and a better response to L-arginine. The effects of lifestyle changes caused not only decreases in biometric indicators (BMI and WHR) but also lowering of the levels of biochemical factors including IL-6, IL-8, and CRP.

Recently, studies and evidence have demonstrated that EAT is significantly associated with MS.²⁷⁻²⁹ Moreover, meta-analyses have indicated that epicardial fat has a determinant role in MS.^{18,19} However, no study has explored the association between EAT and ED to date. To our knowledge, the present study was the first to explore the associations between central obesity, epicardial or pericardial fat, and ED. Although our subjects did not fit the criteria of metabolic syndrome, possible MS development should be considered. The pathogenesis of ED is likely multifactorial, and may not be explained by endothelial dysfunction alone.¹⁴ Hypogonadism contributing to sexual dysfunction has been found in obese males.¹⁵ Whether obesity is coupled with ED independently or through cardiovascular risk factors or hypogonadism, it is evident that obese men have a high incidence of ED that affects their sexual life and fertility.

According to the results of our study, no significant differences were noted between smokers and nonsmokers. Only the EHS showed a statistically positive association with sexual function in the male adult population. No significant associations were identified between EAT or PAT and the other anthropometric indexes recorded in our study, which was in accordance with the meta-analysis results of Pierdomenico *et al.*³⁰ The echocardiographic EAT thickness has been found to be significantly higher in patients with metabolic syndrome than those without, but differences exist according to ethnicity;³⁰ the Asian population owned poorer predictive ability of MS even ED. Besides, the other possible explanation that ED presented of endothelial dysfunction would take place EAT accumulation through a period of time.

The limitations of our study included that this was a cross-sectional study of a small sample without a time-series association between obesity and sexual function, which could

explain why the anthropometric indexes of central obesity only exhibited inverse trends without statistical significance. Owing to underlying CAD or atherosclerosis being highly correlated with EAT or PAT,^{29,31} further study focusing on whether CAD or atherosclerosis disease with or without ED group variations should be performed to explore the detailed mechanism. Meanwhile, vessel quality should be assessed among enrolled ED males as it is important to clarify its relationship with ED. Moreover, obesity-related infertility could also be taken into consideration in future studies.

CONCLUSION

Only EHS was statistically positively correlated with sexual function in the males with ED enrolled in this study, and our results showed that all the measured echocardiographic characteristics, including EAT and PAT thickness, exhibited no significant correlation with sexual function in males with ED.

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Nil.

Conflicts of interest

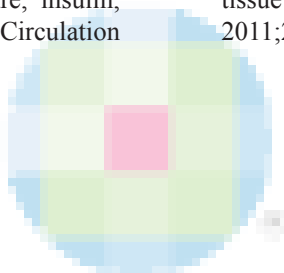
There are no conflicts of interest.

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