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Correlation between Mesenteric Fat Thickness and Characteristics of Coronary Artery Disease in Patients with Metabolic Syndrome

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Abstract

Background and aim: Metabolic syndrome (MetS) includes an assembly of conditions; the most important of which is obesity. The pandemic prevalence of obesity worldwide increased the awareness of MetS. Mesenteric fat thickness is linked to higher risk of coronary artery disease (CAD) complications which may lead to death. Although many studies were done on patients with MetS worldwide, studies on Egyptian patients are limited. Thus, here we examined the relationship between mesenteric fat thickness and the severity and prevalence of CAD among Egyptian patients with MetS.

Methods: Sixty-four patients with MetS were recruited in this prospective cohort study. We assessed the mesenteric fat, and carotid intima media thickness using ultrasonography. Moreover, we evaluated the coronary arteries using myocardial perfusion imaging, MSCT, and/or coronary angiography.

Results: Twenty-three patients had a mesenteric fat thickness less than 10 mm, while 41 patients had a mesenteric fat thickness equal to 10 mm or more. Severity and prevalence of CAD were significantly higher in patients with a mesenteric fat thickness of 10 mm or more ($P<0.001$, and 0.007). Moreover, there was a significant positive correlation between carotid intima media thickness and a number of diseased vessels in patients with CAD.

Conclusion: Our results suggest that mesenteric fat thickness and carotid intima media thickness are good indicators of the prevalence and severity of CAD in patients with MetS. More studies on a large number of the population are required to define MetS in Egyptian patients with MetS, especially in those with a higher risk of CAD.

Keywords: Metabolic syndrome (MetS); Mesenteric fat thickness (MFT); Waist circumference (WC); Coronary artery disease (CAD); Cardiovascular diseases (CVD); Obesity

Abbreviations: CAD: Coronary Artery Disease; CHD: Coronary heart disease; CVD: Cardiovascular Diseases; HbA1c: Glycosylated Hemoglobin; HC: Hip Circumference; HDL-c: High Density Lipoprotein Cholesterol; IMT: Intima Media Thickness; LCIMT: Left Carotid Intima Media Thickness; LDL-c: Low Density Lipoprotein Cholesterol; RCIMT: Right Carotid Intima Media Thickness; SAS: Statistical Analysis System; TG: Triglycerides; VAT: Visceral Adipose Tissue; WC: Waist Circumference

Introduction

Obesity represents a major health problem worldwide. Nearly 30% of the world populations suffer from obesity [1,2]. This problem reaches epidemic levels especially in countries where the sedentary life style prevails. A very high rate of obesity was reported among Egyptians, especially among hypertensive women [3]. Obesity was declared as a 'major, modifiable risk factor' for coronary heart disease (CHD) by the American Heart Association (AHA) [4]. Obesity was previously and routinely determined by anthropometric methods such as body mass index (BMI), or waist circumference (WC). Though these methods are successful in determining the overall adiposity, they fail to determine regional fat depot [5-10]. Populations with regional fat depot especially in the central part of the body, whether or not they are within the normal body mass index (BMI) range, are at higher risk of cardiovascular complications which may lead to death [11,12]. Moreover, several studies underlined abdominal visceral adipose tissue (VAT) as a pathogenic factor that was linked to cardiovascular diseases (CVD), and the metabolic syndrome [13,14].

Metabolic syndrome (MetS) is an assemblage of multiple risk factors comprising abdominal obesity, hypertension, atherogenic dyslipidemia, and pro-inflammatory status [15]. The increased prevalence of obesity raised the awareness of the MetS. Mesenteric fat is a useful tool in determining visceral adiposity and thus determining the pathogenesis of metabolic syndrome and cardiovascular diseases (CVD). The accumulation of Mesenteric fat is highly variable between individuals. Many factors affect mesenteric fat accumulation among which are age, gender, sex hormones, genetic factors, ethnicity, nutritional factors, and life-style [16]. Moreover, a study by Liu et al. reported a significant correlation between mesenteric fat thickness and carotid intima-media thickness (IMT) and MetS [17]. The growing global epidemic of MetS represents a serious burden for clinicians and public health officials all over the world. Although MetS syndrome represents a serious problem in Egyptian population, especially because Egypt is among the countries with the highest prevalence of obesity, studies on Egyptian patients with MetS are scarce.

Here, we examined the relationship between mesenteric fat thickness and severity of coronary artery disease among Egyptian patients with metabolic syndrome. Moreover, we examined the prevalence of coronary artery disease in those patients. We used a cutoff mesenteric fat thickness value of 10 mm to identify high-risk subjects for metabolic syndrome and CVD [18]. Our results showed that patients with MFT equal or more than 10 mm had significantly higher prevalence of CAD than those with MFT of less than 10 mm.

Patients and Methods

Patients

In this prospective cohort study, we recruited 64 male and female patients with MetS (mean age of 54.4 ± 6.7 years; male to female ratio of 82.8:17.2 (%). Informed consent form was obtained from all patients prior to their enrollment in the study. Patients were recruited from the Cardiology outpatient clinics of Nasr City Police Hospital, Cairo, Egypt from the period of January 2014 to December 2016. Patients were enrolled in the study if they met the following criteria: being MetS patients according to the National Cholesterol Education Program Adult Treatment Panel III [15], and if they were forty years or older. Patients were excluded from the study if they: had coronary artery disease or any previous percutaneous coronary interventions (PCI) or coronary artery bypass graft (CABG), were less than forty years, or had left ventricular ejection fraction <40%.

A complete history was obtained from all patients including the history of hypertension, Diabetes, smoking, dyslipidemia, and a family history of CAD [19-22]. Then, we performed clinical examination for all patients including examination of; BMI, pulse, blood pressure, arterial and venous pulsation of the head and neck, upper and lower limb for the presence of cyanosis or lower limb edema, chest and heart examination, waist to hip ratio and waist circumference, and skinfold thickness. BMI was calculated for all patients. Patients fell into one of the three categories according to their BMI; normal weight, overweight and obese, or extreme obese [23].

Laboratory tests were then done for all patients including fasting blood sugar, HbA1c, post prandial blood sugar, triglyceride (TG), LDL, HDL, total cholesterol, uric acid, blood urea, and serum-creatinine.

Evaluation of mesenteric fat thickness (MFT) and carotid intima media thickness (IMT)

All patients were then submitted to ultrasonography examination using Esaote Mylab TM X vision ultrasound machine in order to determine the mesenteric fat thickness (MFT). We used a cutoff value of MFT of 10 mm. As it was suggested by Liu et al. that a mesenteric fat thickness of ≥ 10 mm was an optimal cutoff value to identify metabolic syndrome, with a sensitivity of 70% and specificity of 75%. Abdominal fat thickness was measured by a single operator; a complete survey of the para-umbilical area was performed using a CL 6 MHz curvilinear transducer. The mesenteric leaves appeared as elongated structures with highly reflective peritoneal surfaces. The mean of the three thickest mesenteric leaves was used for the analysis [18]. Carotid IMT was measured with an L 12 MHz linear transducer. All measurements of carotid IMT were made by a single operator. Three IMT measurements were made in the plaque-free section, along with the thickest point on the far wall and within 1.5 cm proximal to the flow divider. The mean IMT was calculated by averaging six measurements from both sides [24].

Evaluation of coronary artery disease (CAD) and left ventricular ejection fraction

We performed a transthoracic echocardiographic examination for all patients (Vivid E 9) to determine left ventricular (LV) dimensions and wall thicknesses, and left ventricular ejection fraction (EF) [25].

All patients then were followed up to assess the symptoms of coronary artery disease. Patients were referred for Multi-slice coronary CT angiography (MSCT), Single-photon emission computed tomography (SPECT) [26], and/or coronary angiography according to the investigator decision.

The lesions of coronary arteries were classified into; significant obstructive coronary artery disease ≥ 50%, non-significant ≤ 50% non-obstructive coronary artery.

Statistical analysis

Results are expressed as the mean ± standard deviation for continuous variables, or as percentages in categorical variables (%). Comparison between categorical data was performed using Chi square and Fischer exact tests. Comparison between continuous data was done using one way ANOVA. Correlation analyses were also done to correlate between the number of diseased vessels and mesenteric fat thickness was done using ANOVA and correlation analyses. Univariate logistic regression models were used to estimate the odds ratios and their 95% confidence intervals for the association of CAD and its types with the studied variable. The prevalence of coronary artery disease (CAD) in the studied subjects was calculated with 95% confidence intervals. A two tailed P value less than or equal to 0.05 was considered significant. Statistical Analysis System (SAS) software package was used for data analysis [27].

Results

Patients

A total of 64 MetS patients (100%) were recruited in this study. Patients were then divided into two subgroups according to their MFT: patients with MFT less than 10 mm (group A), and patients with MFT of 10 mm or more (group B). Group A (MFT<10 mm) included 23 patients (35.94%) with a mean age of 54.26 ± 7.03 years and female to male ratio of 5:18. Fifteen patients (65.2%) presented with dyspnea, and eight patients (34.78%) presented with chest pain. Group B (MFT> or=10 mm) included 41 patients (64.06%) with a mean age of 54.65 ± 6.55 years and female to male ratio of 6: 35. Eighteen patients (43.9%) presented with dyspnea, 23 patients (65.09%) presented with chest pain, and four patients (9.75%) with dizziness.

There were no significant differences between the two groups regarding the vital signs (Table 1). However, there was a significant difference between the two groups in the weight, height, and BMI. Patients in group A (MFT<10 mm) had significantly lower weight, height, and BMI with a p value of 0.007, 0.023, and 0.001, respectively. There were no significant differences between the two groups regarding waist circumferences, hip circumferences, waist to hip ratio,

and skin fold thickness. Similarly, there were no significant differences between the two groups regarding risk factors (Table 1).

Groups/Variable	Group A (MFT<10 mm)	Group B (MFT>or=10 mm)	p value
	Mean ± SD/Number and %	Mean ± SD/Number and %	
Patients Demographics			
Age (years)	54.26 ± 7.03	54.65 ± 6.55	0.96
Female to male	5 to 18	6 to 35	0.51
SBP	136.08 ± 17.77	136.34 ± 18.37	0.957
DBP	82.82 ± 10.21	84.21 ± 8.01	0.558
HR	82.74 ± 7.09	79.8 ± 12.06	0.291
Weight (kg)	92.52 ± 22.86	109.58 ± 24.01	0.007*
Height (meters)	1.78 ± 0.08	1.72 ± 0.07	0.023*
BMI	29.41 ± 7.06	36.74 ± 8.05	0.001*
WC (cm)	120.78 ± 12.61	124.29 ± 14.18	0.282
HC (cm)	124.78 ± 15.67	125.92 ± 17.31	0.794
W/H Ratio	0.97 ± 0.07	0.99 ± 0.08	0.297
skin fold T (cm)	29.26 ± 6.51	31.39 ± 7.78	0.271
Patients' Risk Factors			
HTN	20 (85.95%)	39 (95.12%)	0.341
Duration HTN	4.78 ± 3.31	7.34 ± 6.82	0.097
Dyslipidemia	23 (100%)	37 (90.24%)	0.288
Duration Dyslipidemia	3.78 ± 3.39	4.9 ± 4.98	0.342
FH CAD	8 (34.78%)	10 (24.39%)	0.399
smoking	16 (69.56%)	28 (68.29%)	1

Table 1: Patients demographics and risk factors; *Significant value

As regards the laboratory investigations, there were no significant differences between the two groups. Yet, the level of LDL was lower in group A (MFT<10 mm), and HDL was higher than in group B (MFT> or =10 mm) (Table 2).

Groups/ Variable	Group A (MFT<10 mm)	Group B (MFT>or=10 mm)	p value
	Mean ± SD/Number and %	Mean ± SD/Number and %	
Laboratory Investigations			
FBS	156.21 ± 47.88	149.56 ± 56.33	0.228
HbA1C	7.53 ± 1.21	7.58 ± 1.65	0.893
2H PP	178.65 ± 57.20	174.56 ± 56.58	0.783
TG	168.52 ± 57.91	170.75 ± 95.63	0.919
LDL	113.65 ± 41.31	122.87 ± 55.06	0.1
HDL	46.91 ± 7.65	42.39 ± 10.09	0.067
TC	198.04 ± 46.78	197.21 ± 60.84	0.955
UA	5.53 ± 1.33	6.18 ± 1.72	0.125
Urea	25.56 ± 8.08	29.21 ± 8.56	0.1
S.CRT	1.02 ± 0.18	0.98 ± 0.16	0.328
Ultrasonography Investigations			
RCIMT	0.76 ± 0.17	1.007 ± 0.36	<0.001*
LCIMT	0.76 ± 0.17	1.01 ± 0.31	<0.001*
MFT	7.92 ± 1.35	14.35 ± 4.16	<0.001*
CAD investigations			
CAD	11	35	<0.001*

No of diseased Vessels	0.87 ± 1.25	1.83 ± 1.34	0.007*

Table 2: Laboratory investigations, ultrasonography investigations, and CAD investigations; *Significant value

Ultrasonography investigations of MFT, and IMT

Ultrasonography revealed that MFT, right CIMT, and left CIMT were significantly higher in group B (MFT>or=10 mm) than in group A (MFT<10 mm) with a p value of less than 0.001(Table 2).

CAD investigations

The number of patients with CAD was significantly higher in group B (MFT>or=10 mm) with a p value of less than 0.001. Furthermore, the number of diseased vessels was significantly higher in group B with a p value of 0.007 (Table 2).

When we compared the MFT between MetS patients who did not suffer from CAD, and patients with different types of CAD (patients with obstructive arteries, patients with non-obstructive arteries, and patients with both obstructive and non-obstructive arteries); there was no significant difference in the MFT between patients with normal arteries and with non-obstructive arteries, while there was a significant difference between patients with normal arteries, patients with obstructive arteries, and patients with both types (p<0.01) (Table 3 and Figure 1).

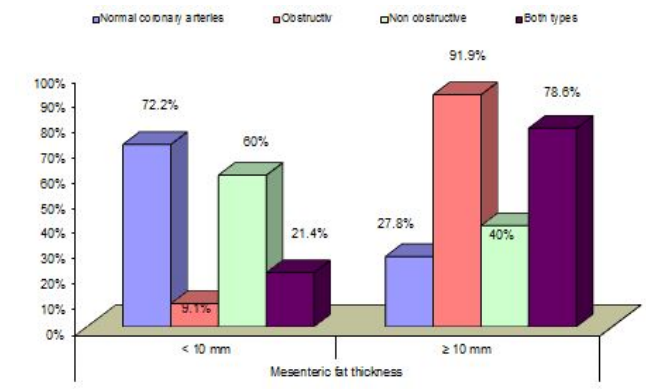

Figure 1: Mesenteric fat thickness of patients with normal vessels and patients with diseased vessels (CAD).

As regards the right carotid intima media thickness, there was no significant difference between patients with normal coronary arteries, patients with obstructive arteries, and patients with non-obstructive arteries. However, there was a significant difference between patients with normal arteries and patients with both obstructive and non-obstructive arteries (p value=0.001). The same results were seen in the left carotid intima (p value =0.002) (Table 3).

Characteristics*	Normal N=18	CAD N=46			P value
		Obstructive	Non obstructive	Both types	
		N=22	N=10	N=14	
MFT (Mean ± SD)	9.5 ± 4.4	13.1 ± 3.4	10.6 ± 3.7	14.5 ± 3.8	0.01*
MFT					
<10 mm	12 (66.66)	2 (9.1)	6 (60.0)	3 (21.4)	<.0001*
≥ 10 mm	6 (33.33)	20 (91.9)	4 (40.0)	11 (78.6)	
RCIMT (Mean ± SD)	0.77 ± 0.20	0.89 ± 0.24	0.80 ± 0.18	1.2 ± 0.45	0.001*
LCIMT (Mean ± SD)	0.80 ± 0.24	0.93 ± 0.25	0.79 ± 0.14	1.15±0.37	0.002*
	Normal N=18	**Non-obstructive N=10**		**OR**	**95% CI**
MFT	18	10		1.07	0.87-1.30
MFT					0.34-8.87
<10 mm	12	6		1	
≥ 10 mm	6	4		1.73	
RCIMT	18	10		2.4	0.04-140.7
LCIMT	18	10		0.75	0.05-6.18
	Normal N=18	**Obstructive N=22**		**OR**	**95% CI**
MFT	18	22		1.35	1.10 -1.70*
MFT					
<10 mm	12	2		1	0.52-192.8
≥ 10 mm	6	20		10.1	
RCIMT	18	22		26	4.4-154.5*
LCIMT	18	22		9	0.60-136.7
	Normal N=18	**Both types N=14**		**OR**	**95% CI**
MFT	18	14		1.25	1.05-1.45*
MFT <10 mm					1.85-49.2*
≥ 10 mm	12	3		1	
	6	11		9.5	
RCIMT	18	14		298.2	5.10 - > 999.9

LCIMT	18	14	296.3	2.31- > 999.9*

Table 3: Association of mesenteric fat thickness and carotid intima media thickness with all studied CAD cases collectively and separately; *Significant value.

Moreover, there was an overall weak positive correlation between the number of diseased vessels and the mesenteric fat thickness (Table 4).

Regarding the left and right carotid media intima thickness, there was a significant positive correlation between the number of diseased vessels and both left and right carotid media intima thickness (Table 4).

CAD (No=46)	
Correlation between the number of diseased vessels and mesenteric fat thickness	All cases (n=46)
Coefficient of correlation (r)	0.1
P value	0.55
Correlation between the number of diseased vessels and right carotid media intima thickness	All cases (n=46)
Coefficient of correlation (r)	0.38
P value	0.02*
correlation between the number of diseased vessels and left carotid media intima thickness	All cases (n=46)
Coefficient of correlation (r)	0.45
P value	0.0003*

Table 4: Correlation between the number of diseases vessels and: mesenteric fat thickness, right carotid media intima thickness, and left carotid media intima thickness; *Significant value.

Discussion

In this prospective cohort study, we examined the interrelationships between mesenteric fat thickness, carotid media intima thickness, and CAD in MetS patients. A total of 64 patients with MetS were recruited and they were classified into two groups; group A with MFT less than 10 mm, and group B with MFT of 10 mm or more.

The mean age of patients whose MFT was less than 10 mm was similar to those with MFT of 10 mm or more. This is consistent with a study carried by Hassanin et al. [28]. This similarity implies that age is not a significant risk factor in patients with MetS. However, more studies are required to compare between patients with different age ranges. In this study, patients were only included if they were 40 years or more.

In our study, the prevalence of MetS was significantly higher in males than in females. This is inconsistent with a study by Beigh et al.; as they concluded that the prevalence of MetS was similar in both genders [29]. This difference in results may result from our small sample size and the fact that we included patients consecutively to eliminate study bias.

Prevalence of CAD was significantly higher in patients with MFT of 10 mm or more. Moreover, the number of diseased vessels was also significantly higher in patients with MFT of 10 mm or more than in those who had MFT less than 10 mm. These results are consistent with studies by Fine et al. [30] and Vijay Kavurma et al. [31].

There was no statistically significant difference between the two groups of patients regarding the waist circumferences, hip circumferences, and skin fold thickness. This is inconsistent with previous studies that showed significant higher WC, HC, and skin fold thickness in patients with MetS [32,33].

However, there were significant differences in BMI, MFT, and carotid intima thickness. Moreover, there was a significant difference in MFT and carotid IMT between patients who did not suffer CAD and those who did suffer from CAD. Moreover, a positive correlation was seen between MFT, CAD, and a number of diseased vessels. Also, a significant positive correlation was seen between carotid intima thickness, CAD, and a number of diseased vessels. These results are similar to previous studies that showed a positive correlation between MFT, carotid intima thickness, and CAD [17,24].

In our study, there was no significant difference between patients regarding the mean FBG, and HbA1c. These results are consistent with a study by Bittencourt et al. [33]. However, all patients had increased HbA1c. Moreover, patients who had CAD with both obstructive and non-obstructive vessels had higher HbA1c levels.

In our study, there was no significant difference between smokers versus non-smokers. This is consistent with Hassanin et al. [28]. However Achari et al. confirmed otherwise [31].

As regards the lipid profile, we did not find any significant differences between the two groups. This is consistent with a study by Hassanin et al. [28] and a study by Bittencourt et al. [33].

Our study indicated that patients with MetS have increased the risk of cardiovascular disease; especially patients with MFT of 10 mm or more. Moreover, carotid intima thickness is positively correlated with increased risk of cardiovascular disease. The mean HBa1c levels were above the normal range, suggesting that hyperglycemia is a major risk factor for cardiovascular disease in patients with MetS. More care should be given to MetS, as it is a pandemic multifactorial problem that requires a complex treatment. Moreover, future studies with large sample size are required to determine the role played by gender, smoking habits, and age.

Ethical Considerations

This prospective study was conducted in accordance with the principles established by the 18th World Medical Assembly (Helsinki, 1964) and all applicable amendments laid down by it, as well as the ICH guidelines for good clinical practice. This study was conducted in compliance with all national and international laws and regulations. All protocols of this study were approved by the Al Azhar University ethics committee. Written informed consent was obtained from all participants in this study.

Addendum

Conceived and designed the study: Wael Wagdy, Ahmed Kmal Motaweih, Mohamad Salem El Baz Performed the Experiments: Wael Wagdy, Mostafa Ateya Mohamad, Wael Refat Abd El Hamed.

Drafted the paper and wrote the paper in final format: Wael Wagdy, Ahmed Kmal Motaweih, Mohamad Salem El Baz.

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