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Original article

Abdominal obesity is a modifier of the association between physical activity and metabolic syndrome: a case-control study

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Summary. *Background:* Introduction: The role of physical activity (PA) in metabolic syndrome (MetS) is almost clear; however, the contribution of PA to lower MetS risk in the presence of abdominal obesity remains unknown. Therefore, the present study aimed to assess the role of PA as well as anthropometric indices in MetS among abdominally obese individuals. *Methods:* This age and gender-matched case–control study was conducted on 164 abdominally obese people of North-West of Iran (81 MetS and 83 population-based controls) aged 18-60 years in 2015. The long version of International Physical Activity Questionnaire (IPAQ) was applied to classify participants into three categories: low, moderate, and high level physical activity (PA). MetS was assessed according to Iranian National Obesity Committee criteria. Biochemical and anthropometric parameters were measured. Both bivariate and multivariate binary logistic regression models were used for data analysis. *Results:* The mean level of triglyceride, fasting blood sugar, systolic blood pressure, and diastolic blood pressure was significantly higher in cases than controls ($P<0.05$). The odds of metabolic syndrome was decreased among people with moderate PA, but it was not statistically significant ($P>0.05$). Multivariate binary logistic regression also showed no significant association between PA levels and MetS components among abdominally obese, even after adjusting for confounders ($P>0.05$). Anthropometric indices were not significantly different between the two groups ($P>0.05$). When stratified by BMI, there was no significant association between PA level and MetS incidence. *Conclusion:* Abdominal obesity seems to be an important factor diluting the association of PA with MetS. In other words, waist circumference may play a mediator role in the association of PA level with MetS.

Key words: physical activity, IPAQ, abdominal obesity, metabolic syndrome, waist circumference

Introduction

Metabolic syndrome (MetS) is a collection of interrelated disorders, namely abdominal obesity, dyslipidemia, hyperglycemia and hypertension (1, 2). It is one of the major risk factors for cardiovascular diseases and diabetes (3) considered as the second and the fourth cause of death in the world, respectively (4). A quarter of adults in the world have MetS (5); and its prevalence in the Eastern Mediterranean region and Iran was reported to be 19- 45% (6) and 25- 40% (7), respectively.

Although identifying lifestyle-related risk factors of MetS may help us with prevention and control of the disease, assessing the importance of its components seems to be warranted (8). As the disease criteria indicates waist circumference (WC) is the most important component and association of risk factors with MetS may be diluted when this factor is being controlled; however, such association is not examined yet.

Physical activity (PA) level, as an important factor in the development of MetS, has been examined in several studies (9-13). A cross-sectional research suggested that vigorous PA has a negative association with MetS (12), while in a case-control study, conducted on women aged 30-60 years with and without MetS, no statistical association was found between PA and MetS (13). Association of PA with MetS was previously investigated among US handicapped adolescents within different body mass index (BMI) categories (9). Moreover, the relationship of PA with MetS was assessed within different BMI categories among children (14). A study by Brambilla et al. also showed that PA affects metabolic risk factors within body weight categories(15). However, to the best of our knowledge, the association of PA with MetS has not been assessed in the presence of abdominal obesity. Therefore, this study aimed to assess the role of abdominal obesity in the association of PA level with MetS in North-West of Iran.

Materials and Methods

Design and Participants

In this case-control study, five-hundred volunteers were recruited from general population, after public announcement. After primary screening based on the defined criteria, 142 were excluded due to WC<95 cm or age<18 y and >60y; 26 were pregnant or lactating, 16 were athlete, 138 had diabetes, kidney diseases, thyroid problems or cardiovascular diseases or stroke history. Finally, 178 people entered the study. All participants gave written informed consent before data collection. After taking blood samples and anthropometric measurements, 14 of them were excluded due to FBS ≥ 126 mg/d, leaving 164 people (82 men, 82 women) to conduct the study. The study was approved by Ethics committee of Tabriz University of Medical Sciences.

Inclusion and exclusion criteria

People aged 18-60 years and WC≥ 95 cm were included in the study. Pregnant or lactating women and those with physical conditions affecting PA, including clinically diagnosed diabetes, self-reported stroke, cardiovascular and kidney diseases, thyroid problems, severe mental disorders and malignancies were excluded.

Cases and controls

According to the Iranian National Committee of Obesity, MetS was defined as presence of at least three of the disorders including WC≥95 cm for both sexes according to the Iranian cut point; triglyceride (TG) >150 mg / dL (7.1 mmol / L); High Density Lipoprotein (HDL) <40 mg/dL (1 mmol/L) in men and <50 mg/dL (1 mmol/L) in women); Blood Pressure (BP)>130/85 mmHg; and Fasting Blood Sugar (FBS) >100 mg / dL (16).

Eighty-one people had ≥3 criteria for MetS and formed the case group (MetS) and 83 people had no or less than 2 criteria and formed the control group (No MetS). Cases and controls were matched for age and gender.

Biochemical assays and Measurements

Fasting blood samples were drawn after an overnight fast of 12 hours. Blood glucose was measured on the day of blood collection by enzymatic colorimetric method using glucose oxidase. Serum total triglyceride concentrations were measured by commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran). HDL-cholesterol (HDLC) was measured after precipitation of the apolipoprotein B containing lipoproteins with phosphotungistic acid.

All anthropometric indices were measured by a trained researcher. Height (without shoes in standard situation with precision of 0.1 cm and with an inelastic measuring tape) and weight (with Seca scale, light cloth and precision of 0.1 kg) were measured and BMI was calculated as the weight in kg divided by the square of the height in meters (17). WC was measured using a non-stretchable fiber measuring tape. The subjects were asked to stand erect in relaxed position with both feet together on flat surface; one layer of clothing was accepted. WC was measured as the smallest horizontal girth between the costal and iliac crests at minimal respiration. Hip circumference was taken as the greatest circumference at the level of greater trochanters (the widest portion of the hip) on both sides. Waist to hip ratio (WHR) was calculated by dividing WC (cm) by hip circumference (cm)(18). Blood pressure was recorded in sitting position in the left arm, using the mercury sphygmomanometer Two readings were taken 5 min apart and mean of the two was taken as the blood pressure (19).

Physical activity (PA)

The long-form International physical activity questionnaire (IPAQ) was used for this study. The validity and reliability of IPAQ has been approved by several studies (20, 21). This questionnaire was translated into Persian and its validity and reliability were previously confirmed (22). The participants were classified into three categories based on the guidelines for data processing and analysis of the IPAQ in which individuals lower than <600, 600-3000 and 3000 or higher Metabolic equivalents (MET)-min/week were considered low, moderate, and high PA, respectively (23).

Statistical analysis and sample size

The independent samples t-test was used to compare the means of normally distributed variables between the two groups. The Mann–Whitney U test was used as a nonparametric analog to the independent samples t-test when the normality assumption didn't hold and in such conditions, median (interquartile range (IQR)) was reported. In order to assess the association of two categorical variables, Chi-square test was applied. The Fisher's exact test was used when one or more of the cells had an expected frequency of five or less. Crude odds ratios were calculated and their 95% confidence intervals were reported using Logistic Regression. All the variables were adjusted in multivariate logistic regression analysis to detect the role of confounders, if any. The ORs were calculated against the reference group being the low PA level. Statistical significance was set p-value<0.05 (two tailed test). A sample size of 80 per group was calculated to fulfill a minimum statistical power of 80% and 95% confidence level. Statistical analyses were performed using Stata statistical software package (Release 9. College station, TX: StataCorp LP.).

Ethical considerations

All protocols were approved by regional ethics committee of Tabriz University of Medical Sciences (Ethical code: TBZMED.REC.1394.313). Research was carried out in compliance with the Helsinki Declaration. Data from participants were only collected with informed consent.

Results

Males comprised 49.4% of cases and 50.6% of controls in the present study. The mean (±SD) age of cases and controls was 38.23±8.52 and 37.13±8.64 years, respectively. About 84% of the individuals were married and nearly half of them held Diploma and Associate degree in both groups. About 70% of cases and 60% of controls were obese (p=0.144). Detailed characteristics of the two groups are shown in Table 1.

The mean level of TG, FBS, SBP and DBP was significantly higher in cases than controls (p<0.05). However, anthropometric indices showed no significant differences between the two groups (Table 2). Approximately half of the individuals in the case and control groups had high and moderate PA levels, respectively (Figure 1).

The results of logistic regression test showed that the odd of having MetS was not statistically significant among different PA levels. The adjusted final model confirmed the crude model as well (Table 3).

For further analysis, we examined the association of PA level with MetS incidence stratified by BMI. The subgroup analysis indicated that there was no significant association within each BMI category (Table 4). Logistic regression analysis also showed that PA

Table 1. Baseline Characteristics of the two groups

Variables	MetS (n=81)	No MetS (n=83)	*p*
Age (year) †	38.23 (8.52)	37.13 (8.64)	0.41ᵾ
Sex (male) ‡	40 (49.4)	42 (50.6)	0.87ᶓ
Marital status			
single	13 (16)	68 (84)	0.94
married	13 (15.7)	70 (84.3)	
Education level			
<diploma	20 (24.7)	21(25.3)	0.99
Diploma and Associate	37 (45.7)	38 (45.8)	
≥Bachelor	24 (29.6)	24 (28.9)	
Job			
Householder	28 (34.6)	27 (32.5)	0.59
Free	31 (38.3)	26 (31.3)	
Student	4 (4.90)	4 (4.80)	
Employee	18 (22.2)	26 (31.3)	
BMI (kg/m²)			
<25	4 (4.90)	4(4.80)	0.29
25-30	20 (24.7)	30 (36.1)	
30-35	35 (43.2)	32 (38.6)	
≥35	**22 (27.2)**	**17 (20.5)**	

† Variables with normal numeric scales are reported as Mean (standard deviation); ‡ Variables with categorical scales are reported as Number (%); ᵾ Independent Samples t-test; ᶓ Chi- Square Test; PA, Physical Activity; BMI, Body Mass Index

Table 2. Anthropometric indices and MetS components between the two groups

Variables	MetS (n=81)	No MetS (n=83)	*p*
Weight (Kg) ¥	85 (21)	82 (19.5)	0.18ᵾ
Height (cm) †	165.09 (11.56)	164.56 (10.59)	0.76ᶓ
Waist circumference (cm) †	106.02 (8.30)	105.07 (8.63)	0.47ᶓ
Hip circumference (cm) †	110.9 (6.92)	111.31 (8.26)	0.73ᶓ
Waist to hip ratio (cm) ¥	0.95 (0.07)	0.95 (0.06)	0.22ᵾ
BMI (Kg/m²) †	32.16 (4.25)	31.35 (4.12)	0.21ᶓ
HDL-C (mg/dL) †	39.53 (6.65)	46.44 (9.19)	<0.001ᶓ
TG (mg/dL) ¥	193(84)	112 (58)	<0.001ᵾ
FBS (mg/dL) ¥	94 (13)	87 (8)	<0.001ᵾ
SBP (mg/dL) ¥	112.5(25)	110 (20)	0.01ᵾ
DBP (mg/dL) ¥	80(15)	70(15)	0.008ᵾ

† Variables with normal numeric scales are reported as Mean (standard deviation); ¥ Variables with non-normal numeric scales are reported as Median (interquartile range (IQR)); ᵾ Mann- Whitney U test; ᶓ Independent Samples T- test; MetS, Metabolic Syndrome; BMI, Body Mass Index; HDL-C, High-Density Lipoprotein Cholesterol; TG, Triglyceride; FBS, Fasting Blood Sugar; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure

levels had no significant association with MetS components among abdominally obese patients (Table 5).

Discussion

This paper assessed the association of PA and anthropometric indices with MetS and its components among abdominally obese (i.e. WC≥95 cm) individuals in North-west of Iran. Overall, PA level was not significantly associated with MetS or its components in the present study. In line with our results, the study by Azizi *et al.* found no statistical association between PA and MetS in Iranian adult women (13). Another research on obese adolescents indicated that PA levels of those with MetS was lower than of those without

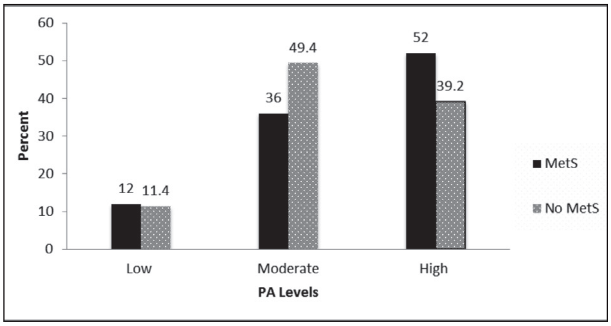

Figure 1. PA level among abdominally obese population with and without MetS (p: non-significant, using Chi Square test) PA, Physical Activity; MetS, Metabolic Syndrome

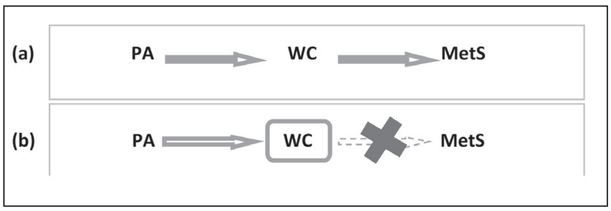

Figure 2. Schematic representation of association between the exposure(PA) and outcome(MetS) before (a) and after (b) adjusting for mediator variable.

this syndrome; but this difference was not statistically significant (24). However, most of the studies have reported negative significant associations between PA and Mets (12, 25). It is notable that none of the aforementioned studies were carried out among abdominally obese people. In fact, the present PA findings confirmed our hypothesis that the association between PA and MetS is not independent of WC and will be disappeared when WC is restricted/ matched. In fact, when people WC>95 was recruited in the present study, their PA level would be close to each other which leads to the non-significant observed associations. In other words, the probability of engaging in PA was relatively high in these subjects as indicated in Figure 1. Therefore, it is clarified for the first time that WC as the most important component of MetS, may play a mediating role in the associations of PA with MetS (Figure 2).

It has been suggested that PA and adiposity have relevant roles on the development of MetS risk factors, but it is not clear if these traits act independently or in conjunction (26, 27). Regarding PA, a recent review by Guinhouya et al. (28) reported that the impact of PA on MetS appeared to be either independent of other factors, or mediated by adiposity in youth.

Table 3. Association of physical activity (PA) level with MetS incidence

variables	moderate PA	high PA
Crude OR(95% CI)	0.69 (0.24, 1.97)	1.25 (0.44, 3.55)
p¥	0.49	0.66
Adjusted OR(95% CI)	0.62(0.20, 1.87)	1.19(0.40,3.53)
p†	0.40	0.75

Low PA was considered as reference category; ¥Logistic Regression Model; †Adjusted for job and education level

Table 4. Association of PA level with MetS incidence stratified by BMI

Variables		moderate PA	high PA
BMI: 25-30 kg/m²	Crude OR (95% CI)	0.46 (0.05,3.92)	0.53 (0.06,4.66)
	Adjusted OR (95% CI)	1.07 (0.09,12.44)	0.94 (0.24,3.66)
BMI: 30- 35 kg/m²	Crude OR (95% CI)	1.14 (0.20,6.41)	1.71 (0.31,9.29)
	Adjusted OR (95% CI)	0.53 (0.09,2.98)	0.64 (0.21,1.91)
BMI≥ 35 kg/m²	Crude OR (95% CI)	0.42 (0.05,3.60)	3.42 (0.34,34.46)
	Adjusted OR (95% CI)	0.28 (0.02,2.90)	0.11 (0.02,0.69)

Low PA was considered as reference category; ¥Logistic Regression test; PA, Physical Activity; MetS, Metabolic Syndrome; BMI, Body Mass Index

Table 5. Association of PA level with MetS components

Variables		moderate PA	high PA
HTN	Crude OR(95% CI)	1(0.24,4.04)	1.63(0.42,6.33)
	p¥	1	0.47
	Adjusted OR(95% CI)	1.07(0.25,4.58)	1.81(0.44,7.48)
	p†	0.92	0.40
Low HDL-C	Crude OR(95% CI)	1.69(0.59,4.84)	2.11(0.74,6.03)
	p	0.32	0.16
	Adjusted OR(95% CI)	1.46(0.49,4.39)	1.90(0.63,5.69)
	p	0.49	0.24
High TG	Crude OR(95% CI)	0.62(0.22,1.79)	1.006(0.35,2.85)
	p	0.38	0.99
	Adjusted OR(95% CI)	0.71(0.24,2.12)	1.16(0.39,3.42)
	p	0.54	0.78
High FBS	Crude OR(95% CI)	2.68(0.31,22.7)	3.87(0.47,31.81)
	p	0.36	0.20
	Adjusted OR(95% CI)	2.84(0.32,24.87)	4.20(0.49,35.81)
	p	0.34	0.18

Low PA was considered as reference category; MetS components were considered as dichotomous variables; ¥Logistic Regression test; †Adjusted for job and education level; PA, Physical Activity; MetS, Metabolic Syndrome; HTN, hypertension; HDL-C, High-Density Lipoprotein Cholesterol; TG, Triglyceride; FBS, Fasting Blood Sugar

If at one extreme, PA prevents the development of metabolic risk, it sounds obvious that adiposity acts in the opposite way, being a stronger predictor of MetS risk than PA (29, 30). Furthermore, previous researches (31, 32) have also demonstrated that the prevalence of MetS is higher among overweight or obese youth than normal weight individuals, emphasizing the adverse role of adiposity in the development of MetS.

In our study, we did not find a significant association between PA and MetS effect when stratified by BMI. Similar to our results, Gomes *et al.*(11) could not show the effect of PA on standardized MetS score among children, and no difference within their BMI categories. In other words, PA could not attenuate the MetS risk among normal weight children or even among those who were overweight. Few studies have demonstrated that PA can diminish the negative association between adiposity and metabolic risk, where high levels of PA improves the MetS profile among obese subjects (15, 33). Several reasons may justify our PA findings. Firstly, it can ameliorate the idea that adiposity has much stronger correlation with MetS risk than PA. The second possible explanation for this result can be due to non-differential misclassification of the participants into different PA levels. Since the participants might not have answered correctly to the long-form IPAQ due to its time-consuming and boring nature which may have led to diluted associations through misclassification of high PA people into moderate/ low PA category and vice versa. However, the IPAQ questionnaire was filled out by a trained interviewer and it was not self-reported. Thirdly, the non-significant findings may be due to temporality issues; such that increasing PA level, diet therapy and all known preventive measures are being suggested by practitioners to improve health status of those diagnosed with MetS. In fact, PA level is changing dramatically after the diagnosis of MetS. As in our study, 40% of the obese with MetS reported to have "high" level PA, compared to only 20% in the obese without MetS, though it was not significant (Data not shown). Therefore, in a case-control study, like ours, the difference of PA level during the last week will be decreased between people with and without MetS and might lead to such non-significant associations.

Despite the limitations mentioned above, the present study has several important strengths: first, the use of IPAQ, suggested by World Health Organization (WHO) and Centers for Disease Control (CDC) as a reliable assessment tool to estimate PA; secondly, the use of native cut-point for WC; thirdly, no recruitment of MetS patients being on drug therapy for metabolic or other disorders, and finally sufficient power to detect PA differences between the two groups.

Conclusion

Though it seems that PA and anthropometric indices were not independent predictors of Mets in the present study, it is probable that WC may play a mediator role in the associations of MetS with PA. These findings also point out that systematic strategies such as nutritional education and healthy food consumption should be planned to attenuate obesity rate among abdominally obese population.

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