Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 2419–2424

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Variations in the pattern and distribution of non-obese components of metabolic syndrome across different obesity phenotypes among Iranian adults' population

Karimollah Hajian-Tilaki [a,*], Behzad Heidari [b]

[a] Dept of Biostatistics and Epidemiology, Babol University of Medical Sciences, Babol, Iran
[b] Dept of Internal Medicine, Ayatollah Rohani Hospital, Babol University of Medical Sciences, Iran

ARTICLE INFO

Article history:
Received 12 May 2019
Accepted 7 June 2019

Keywords:
Obesity phenotypes
Overweight/obese
Central obese
Metabolic abnormality

ABSTRACT

Aims: To investigate the association of obesity phenotypes with non-obese components of metabolic syndrome (MetS) by considering the presence of general adiposity and central obesity.
Methods: We analyzed the data of population-based cross-sectional study of 981 adults' individuals who were community dwelling in urban population of Babol, the north of Iran. The demographic characteristics and anthropometric measures and hypertension were collected with standard method by trained nurses. The fasting blood sugar, CHL, TG, HDL-C and LDL-C were measured by enzymatic method. The presence of cardiometabolic risk factors were analyzed according to the combination of obesity phenotypes either overweight/obese or central obese. The logistic regression model was used to calculate the adjusted odds ratio (OR) of obesity phenotypes in compared with normal weight not central obese in association of presence of metabolic abnormality.
Results: The 394 (40.6%) individuals were both overweight/obese and central obese and 295 (30.1%) persons were "normal weight not central obese" and the minority 28(2.9%) were normal weight but central obese and the remainder 260 (26.5%) were "overweight/obese not central obese". Overweight/obese not central obese increased significantly the odds of presence of ≥2 non-obese components of metabolic abnormality by 2.17 times (95%CI OR: 1.51, 3.13) but the OR was elevated for the joint phenotypes of overweight/obese and central obese (OR = 4.16 (95%CI: 2.85, 6.06) as compare with normal weight not central obese.
Conclusions: Overweight/obese alone increased the risk of cardiometabolic abnormality but being overweight/obese and central obese a further elevated the risk compared with "normal weight not central obese".

1. Introduction

Obesity is characterized as abnormal or excessive fat accumulation to an extent that it presents a risk for health. It is a key risk factor of cardiovascular diseases, diabetes, hypertension and cancer [1,2]. Comorbidities and disabilities consequent to obesity and overweight provide predominant negative influence on health-related quality of life and a significant economic health burden [3,4]. During the two recent decades, the prevalence of obesity and metabolic syndrome increased dramatically in both developing and industrial countries [5–7]. This led to more attention of health authorities to the issue of obesity and its consequences in the general population [2–4].

The diagnosis of obesity is made by calculation of body mass index (BMI), but in clinical practice the negative influence of abnormally accumulated body fat cannot be predicted based on BMI value alone, because, obesity is a heterogeneous condition, and the association between metabolic complications and obesity is partly dependent to the pattern of body fat distribution. While upper body or visceral fat distribution in obesity is linked with metabolic complications, but the distribution of fat in lower body is a predictive for reduced cardiovascular risk. This indicates a role on the association between metabolic complications and the pattern of adipose tissue distribution [8,9]. At present, there is no gold standard method for assessment of excess body fat in particular

* Corresponding author.
E-mail address: drhajian@yahoo.com (K. Hajian-Tilaki).

https://doi.org/10.1016/j.dsx.2019.06.003
1871-4021/

visceral fat accumulation. Application of imaging technic is costly and is not available to all health centers, hence body adiposity is estimated by anthropometric measures [10–12]. However, estimation of body fat in obese subjects by using BMI has limitation in the differentiation of muscle mass from adipose tissues in the contribution of obesity. Therefore, the diagnosis of obesity based on BMI has limitations in recognizing high risk individuals from those who are at a lower risk of future development of metabolic complications [10–12].

On the other hand, indices of central obesity (abdominal obesity) such as waist circumferences (WC) or waist to height ratio, and waist to hip ratio are better measures to estimate visceral adiposity [13–17].Among the several anthropometric measures,the WCis more important because it is the main measure for screening abdominal fat distribution as well as for the diagnosis of abdominal obesity. The WC is the main componentof metabolic syndrome (MetS) by International Diabetes Federation (IDF), National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), the American Heart Association (AHA)/National Heart, Lung and Blood Institute, and the Iranian National committee of obesity (INCO) [13–17].

Accumulation of adipose tissues in patients with general or abdominal obesity is associated with higher prevalence of cardiometabolic risk factors including non-obese components of MetS and increased risk of cardiovascular diseases, diabetes in which obesity and insulin resistance are the two major underlying risk factors for the development of MetS [18]. Abdominal obesity and other components of metabolic MetS alone or in combination are associated with increased risk of disability and functional dependence in the elderly. In one study the risk of disability was proportional to the number of MetS components [19]. In a study of 8233 adults aged 18–98 in the 2009 nationwide China Health and Nutrition Survey, over 75% of the sample had elevated levels of at least one cardiometabolic risk factor, and only half of young adults were metabolically healthy [20]. In another study of 5248 persons aged ≥15 years old, a significant proportion of non-obese people had abdominal obesity and the presence of abdominal obesity in both overweight and normal weight individuals was significantly associated with high prevalence of cardiometabolic risk factors and diseases [21].In an observational cohort study of approximately 1.3 million adults (aged≥20 years) with overweight or obesity, 32%–60% of the cohort had 4 commonly cardiac risk factors. However, depending on the category of overweight or obesity, the prevalence varied from 27% to 72% and only 14% of the cohort had none of these risk factors. In this study overweight or obesity was associated with greater cardiometabolic risk, but the number and type of cardiac risk factors varied substantially by age, even among participants with life-threatening obesity [22].

The prevalence and distribution of cardiometabolic risk factors or MetS components varies across various population and can be partly attributed to the pattern of obesity or body fat distribution. Identification of high risk individuals particularly among the non-obese population is important for preventive measures since the presence of metabolic abnormalities in normal weight individuals are usually ignored.The capability of anthropometric measures for identification of metabolic abnormalities and high risk individuals varies by obesity phenotypes. The link between metabolic abnormalities, cardiovascular disease and mortality with abdominal obesity is stronger than link with general obesity. This indicates greater capability of WC than BMI [23]. However, superiority of waist circumference (WC), waist to hip ratio and waist/height ratio (WHtR) to BMI have not been observed in other studies [24,25]. Recent studies have suggested that a combination of general obesity and abdominal obesity provide more information in predicting obesity-related outcomes than each of them alone [12,26–30], Depending on the weight, and the presence or absence of abdominal obesity a study population can be classified at least to 4 subgroups including 1)normal weight without central obesity (normal WC), 2)normal weight with central obesity (abnormal WC), 3) overweight/obese without central obesity,4) overweight/obese with central obesity (abnormal WC).

In spite of high prevalence of obesity, abdominal obesity and MetS in the general population as well as in Iranian population especially Iranian women, and its increasing trend in recent decades [6,22–24], the prevalence of cardiometabolic risk factors in particular distribution of non-obese components of MetS across various obesity phenotypes has not been investigated yet. We therefore conducted the present study to determine the prevalence of obesity according to weight and obesity phenotypes, as well as to specify the number, type, and distribution of non-obese components of MetS across various obesity phenotypes.

2. Methods

2.1. Study design and subjects

The data of this study were extracted from a population-based cross-sectional study of lipids, glucose and MetS in Babol, a city located in the southern geographic region of the Caspian sea.The study population wascomprised of 1000adults who were recruited among the community dwelling adults' population aged 20–70 years. Nineteen participants were excluded because of underweight (BMI<18.5 kg/m^2) and missed data on anthropometric measures and the remaining 981 participants were analysed. The details of patients' selection have been described elsewhere [5]. In brief 25 clusters were selected randomly using the cumulative population size under the coverage of urban health centers. Within the center of each cluster about 40 adults were recruited in the study consecutively. All selected subjects had given an informed consent prior participation and the study protocol was authorized by the Ethical Committee of Babol University of Medical Sciences.

2.2. Measurements and dada collection

The data of demographic characteristics (e.g. age, sex, educational level and marital status) and individual lifestyle (e.g. smoking) were collected in–person interview in a household survey and the anthropometric indexes of weight, height and waist circumferences were measured using a standard method. Weight was measured with a portable scale to the nearest 0.1 kg with light clothes without shoes. Height was measured to the nearest 0.1 cm using a portable stadiometer without shoes as well. Then, we calculated BMI by dividing weight in kg to the square of height in meter. Waist circumference was measured at the end of usual experation, at the level of midpoint between the iliac crest and the lower border of tenth rib with a non-elastic tape to the nearest 0.1 cm. After 10 min resting, the systolic and diastolic blood pressure (SBP and DBP respectively) of the right arm were measured three times, with standard method by a trained nurse at sitting position, and the mean value of three times measurements were considered for analysis. Mean arterial pressure (MAP) was calculated with the equation of. $MAP = DBP + \frac{1}{3}(SBP - DBP)$.

All recruited subjects were invited for 10–12 h overnight fasting for blood venous sample in the central lab of Ayatollah Rohani hospital in the next morning. The total cholesterol (CHL), Triglyceride concentration (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), fasting blood sugar (FBS) were measured using enzymatic methods by an auto-analyzer. In addition, TG to HDL-C ratio and LDL to HDL-C ratio were calculated.

2.3. Definition of obesity phenotypes and non-obese components of MetS

The subjects were categorized into four groups based on the joint combination of general adiposity and central obesity. The general obesity defined based on the BMI scale: $18.5 \leq BM < 25$ as normal weight and BMI≥25 as overweight/obese. The ATP III criteria was used to define the central obesity (WC > 102 cm for men and WC > 88 cm for women). The different phenotypes of obesity were defined as.

1) normal weight (18.5 ≤ BMI<25 kg/m2) without central obesity (normal WC) (NWt & NWC)
2) overweight/obese without central obesity (Over/Obese & NWC);
3) normal weight with central obesity (abnormal WC) (NWt & AWC);
4) overweight/obese with central obesity (abnormal WC) (Over/obese & AWC).

Other components of the MetS including abnormal blood pressure (SBP>130 and DBP>85 mmHg systolic), TG ≥ 150 mg/dl, HDL<40 mg/dl in men and <50 mg/dl in women and also FBS≥110 mg/dl. The presence of at least 2 of 4 components other than abdominal obesity was categorized as non-obese components of MetS.

2.4. Statistical analysis

The data analysis was performed using SPSS software version 18. The descriptive statistics of continuous cardiometabolic risk factors were presented by mean ± SD and categorical data were presented as proportion according to obesity phenotypes and sex. The prevalence of cardiometabolic risk factors were alsoestimated based on the ATP- III cut-off values by obesity phenotype and sex. The analysis of variance was used to test the mean of normally distributed cardiometabolic risk factors between different phenotypes of obesity and the Kruscal-Walis test in bivariate analysis was used for data without normal distribution The logistic regression model was applied to estimate the unadjusted odds ratio (OR) and adjusted OR of different phenotypes of obesity and their 95% confidence interval (95%CI) as compared to the reference phenotype of normal weight and normal WC. We also adjusted the effect of age, sex and educational level in multiple logistic regression models. The p-value <0.05 was considered as significant level.

3. Results

The respective mean age of participants was 42.8 ± 13.4 years. The demographic characteristics of study population were presented in Table 1. Among individuals with phenotype of overweight/obese and central obese, a higher proportion were women, older age and lower level of education as compared with normal weight without abdominal obesity (p = 0.001). The obesity phenotypes of majority of subjects about 394 (398)(40.6%) were joint combination of overweight/obese and central obese and 295 (30.1%) individuals were both normal weight and non-central obese and the minority 28(2.9%) persons were normal weight but central obese and the remainder 260 (26.5%) subjects were overweight/obese and central obese. The joint combination phenotype of normal weight and not central obese were more common in men but the joint overweight/obese and central obese were the most prevalent in women (p = 0.001). Table 2 shows the mean of cardiometabolic characteristics of study samples according to obesity phenotype and sex. Except for HDL and FBS in men and HDL-C and LDL-C to HDL-C ratio, the higher level of other cardiometabolic risk factors were found in the phenotypes of overweight/obese and central obese (p = 0.001). Table 3 presented the prevalence of non-obese components of metabolic syndrome. Except for HDL-C, all other components were significantly more frequent in the joint combination of overweight/obese and central obese (p = 0.001) in both sexes. However, the frequency of data for phenotype of overweight/obese but normal waist was sparse. Table 4 indicated the results of logistic regression analysis of unadjusted and adjusted odds ratio of different phenotypes of combination of obesity and abdominal obesity as compared with normal weight and normal waist circumference. The adjusted odds ratio by age, sex and educational level shows that overweight/obese but normal WC increased the odds of presence of ≥ 2 non-obese components of MetS by 2.17 times (95%CI OR: 1.51, 3.13) but the odds ratio was elevated for the joint phenotype of overweight/obese and central obese (OR = 4.16 (95%CI 2.85, 6.06).

4. Discussion

The findings of this study indicate variations in distribution of non-obese components of MetS across various obesity phenotypes. Discrepancies are related to the pattern of obesity and BMI status. There is an association of overweight/obesity alone or in combination with abdominal obesity with non-obese components. In men these components are prevalent in subjects with both abdominal and general obesity whereas in women they are more frequent only in subjects with coexistence of both abdominal and general obesity. In multiple regression analysis after adjustment for other potential confounders such as age, sex, and the level of education, the presence of overweight/obesity was significantly associated with higher prevalence of non-obese components of MetS, and the presence of abdominal obesity combined with overweight/obesity increased the odds of association nearlyfour times.

Association of cardiometabolic risk factor with obesity and overweight as observed in this study has been also reported in other investigations that addressed the relationship of cardionmetabolic risk factors and mortality with obesity phenotypes [21,31–33]. The findings of current study are consistent with the results of a cross-sectional study of 1275 rural residents aged ≥35 years thatrevealed a higher prevalence of hypertension in subjects with coexistent general and abdominal obesity than in those with obesity alone [33]. A systematic review of 18 studies comprised 689 465 participants and 48421 deaths revealed significant association of both general and abdominal obesity with mortality during a follow-up period of 5–24 years. In this study, independent association of WC and WHR as measures of abdominal obesity were also observed with obesity-related mortality in adults [3]. A similar association between combined abdominal and general obesity with cardiometabolic risk factors has been reported in a large study of Iranian children and adults 10–18 years [34]. In one study of patients with coronary artery disease, central obesity was directly associated with mortality, but there was an inverse association of mortality with BMI, in particular subjects with normal BMI were at greater risk of mortality [35].

In a population-based cohort study of 3 632 674 people, there was a J-shaped association between BMI and overall mortality. In this study after a mean follow-up duration of 12.2 years lower BMI was associated with increased risk of mortality [36]. In the present study the prevalence of normal weight subjects with abdominal obesity was 2.8% which is lower than other studies which varied from 9.1% in Latin American people aged 23–25 years, to 36% of men and 29% of Korean women aged >20 years. Low prevalence of normal weight obesity in this study may be attributed to small sample size of this subgroup or difference in ethnicity [37]. Excess

Table 1
The distribution of characteristics of study samples according to combination of obesity and central obesity.

Characteristics	NWT& NWC n (%)	Over/Obese & NWC n (%)	NWT & AWC n (%)	Over/Obese & AWC n (%)	P-value
Gender					0.001
Male	177(60.0)	160(61.5)	8(28.6)	98(24.6)	
Female	118(40.0)	100(38.5)	20(71.4)	300(74.4)	
Age (year)					0.001
<40	160(54.2)	116(44.6)	15(53.6)	129(32.4)	
40–59	99(33.6)	118(45.4)	10(35.3)	199(50.0)	
≥60	36(12.2)	26(10.0)	3(10.7)	70(17.6)	
Educational level					0.001
<High School	104(35.3)	93(35.8)	8(28.6)	219(55.0)	
High School ≤	191(64.7)	167(64.2)	20(71.4)	179(45.0)	
Smoking status					0.11
Not at all	250(84.7)	222(85.4)	26(92.9)	364(91.5)	
Current smoker	33(11.2)	27(10.4)	2(7.1)	26(6.5)	
Ex-smoker	12(4.1)	11(4.2)	-(–)	8(2.0)	
Marital status					0.001
Single	59(20.0)	21(8.11)	3(10.7)	20(5.0)	
Married	228(77.3)	235(90.4)	25(89.3)	357(89.7)	
Divorced	1(0.3)	2(0.8)	(–)-	3(0.8)	
Widow	7(2.4)	2(0.8)	(–)-	18(4.5)	

NWt: Normal weight; Over/Obese: Overweight/Obese; NWC: Normal waist circumference; AWC: Abnormal waist circumference.

Table 2
The mean ± SD of cardiometabolic characteristics of participants according to obesity phenotypes and sex.

Cardiometabolic risk factors	NWt & NWC	Over/Obese & NWC	NWt & AWC	Over/Obese &AWC	P-value
Men					
DBP(mm Hg)	79.1 ± 12.6	84.5 ± 13.8	82.6 ± 7.0	82.5 ± 13.01	0.001
SBP(mm Hg)	123.6 ± 15.2	129.6 ± 15.4	128.0 ± 9.1	134.4 ± 15.1	0.001
CHL(mg/dl)	182.8 ± 67.2	198.9 ± 49.1	207.7 ± 72.1	194.8 ± 43.9	0.04
TG(mg/dl)	150.8 ± 110.1	214.1 ± 136.4	247.2 ± 176.0	220.6 ± 171.8	0.001
LDL(mg/dl)	113.5 ± 38.7	122.7 ± 48.4	126.6 ± 66.9	117.2 ± 40.3	0.25
HDL(mg/dl)	36.9 ± 10.6	34.8 ± 9.1	32.0 ± 5.7	36.4 ± 9.5	0.14
FBS(mg/dl)	104.1 ± 36.1	109.6 ± 34.5	115.7 ± 27.6	113.6 ± 32.8	0.12
MAP (mm Hg)	93.9 ± 12.3	99.5 ± 13.2	97.7 ± 6.8	101.8 ± 10.9	0.001
TG/HDL	4.4 ± 3.6	6.5 ± 4.5	8.4 ± 6.6	6.8 ± 6.7	0.001
LDL/HDL	3.2 ± 1.3	3.7 ± 1.7	3.9 ± 1.6	3.4 ± 1.3	0.03
Women					
DBP(mm Hg)	76.3 ± 13.2	77.8 ± 13.0	78.0 ± 10.6	84.8 ± 16.2	0.001
SBP(mm Hg)	118.8 ± 16.8	118.3 ± 14.6	118.4 ± 13.7	129.0 ± 20.4	0.001
CHL(mg/dl)	185.7 ± 41.2	187.3 ± 36.4	189.9 ± 47.1	209.1 ± 44.3	0.001
TG(mg/dl)	127.4 ± 103.5	122.1 ± 57.6	108.2 ± 44.2	184.7 ± 130.5	0.001
LDL(mg/dl)	122.3 ± 38.4	126.6 ± 31.1	127.4 ± 46.5	134.0 ± 41.2	0.001
HDL(mg/dl)	38.4 ± 13.8	37.5 ± 7.4	41.1 ± 11.7	38.8 ± 12.2	0.59
FBS(mg/dl)	102.1 ± 33.7	100.5 ± 22.4	95.0 ± 9.4	116.4 ± 51.7	0.001
MAP (mm Hg)	90.5 ± 13.0	91.3 ± 12.0	91.5 ± 11.1	99.6 ± 15.8	<0.001
TG/HDL	3.7 ± 4.2	3.4 ± 1.9	2.8 ± 1.4	5.1 ± 4.4	<0.001
LDL/HDL	3.3 ± 1.3	3.5 ± 1.1	3.3 ± 1.4	3.6 ± 1.2	0.1

NWt: Normal weight; Over/Obese: Overweight/Obese; NWC: Normal waist circumference; AWC: Abnormal waist circumference.

Table 3
The prevalence of non-obese components of MetS based on ATP III criteria according to obesity phenotypes and sex.

Cardiometabolic risk factors	ALL n(%)	NWt & NWC n(%)	Over/Obese & NWC n(%)	NWT & AWC n(%)	Over/Obese & AWC n(%)	P-value
Men	443(100)	177(40.0)	260(36.1)	8 (1.8)	98 (22.0)	–
BP > 130/85 mmHg	138(31.2)	38(21.5)	55(34.4)	2(25.0)	43(43.9)	0.001
TG ≥ 150 mg/dl	235(53.0)	62(35.0)	102(63.8)	5(62.5)	66(67.3)	0.001
FBS≥110 mg/dl	134(30.2)	36(20.3)	50(31.3)	4(50.0)	44(44.9)	0.001
FBS≥126 mg/dl	65 (14.7)	16(9.0)	24(15.0)	2(25.0)	23(23.5)	0.001
HDL<40 mg/dl	335(75.6)	129(72.9)	129(80.6)	6(75.0)	71(72.4)	0.33
Non-obese components of MetS≥2	315(71.1)	98(55.4)	129(80.6)	7(87.5)	81(82.7)	0.001
Women	538 (100)	118 (21.9)	100 (18.6)	20 (3.7)	300 (55.7)	–
BP > 130/85 mmHg	148(27.5)	20(16.9)	12(12.0)	3(15.0)	113(37.7)	0.001
TG ≥ 150 mg/dl	226(42.0)	31(26.3)	27(27.0)	3(15.0)	165(55.0)	0.001
FBS≥110 mg/dl	143(26.6)	21(17.8)	18(18.0)	1(5.0)	103(34.3)	0.001
HDL<50 mg/dl	469(87.2)	107(90.7)	90(90.0)	17(85.0)	255(85.0)	0.34
Non-obese components of MetS≥2	365(67.8)	57(48.3)	55(55.0)	8(40.0)	245(81.7)	0.001

NWt: Normal weight; Over/Obese: Overweight/Obese; NWC: Normal waist circumference; AWC: Abnormal waist circumference.

Table 4
The unadjusted and adjusted odds ratio of obesity phenotypes in association with presence of the number ofnon-obese components of MetS≥2.

Obesity phenotypes	Unadjusted OR (95% CI)	P-value	Adjusted OR⊨ (95% CI)	p-value
NWt & NWC (ref)	1 (–)	–	1 (–)	–
Over/Obese & NWC	2.18 (1.54,3.11)	0.001	2.17 (1.51,3.13)	0.001
NWt & AWC	1.04 (0.48,2.26)	0.92	1.23 (0.55,2.78)	0.61
Over/Obese & AWC	4.09 (2.90,5.76)	0.001	4.16 (2.85,6.06)	0.001

NWt: Normal weight; Over/Obese: Overweight/Obese; NWC: Normal waist circumference; AWC: Abnormal waist circumference; ⊨The odds ratio was adjusted by age, sex and education level.

body fat accumulation in subjects with normal BMI is associated with increased risk of cardiovascular morbidity and mortality. High mortality rate of normal weight obese patients with coronary artery disease has been reported also in a systematic review [38]. The lack of association of normal weight central obese in the present study may be attributed to the sample size of this subgroup in our study sample.

Accumulation of adipose tissue around the intra-abdominal organs is distinctly linked to several pathological conditions. Visceral fat as a hormonally active tissue, releases different bioactive molecules and hormones such as adiponectin, leptin, tumour necrosis factor, resistin and interleukin 6. Among these hormones, the adiponectin which has an antiatherogenic activity correlates negatively with visceral adiposity and its circulation level is lower in subjects with abdominal obesity [39]. A systematic review and meta-analysis of 89 relevant studies revealed association of both overweight and obesity phenotypes with the incidence of multiple co-morbidities including type II diabetes, cancer and cardiovascular diseases [40].

Amongst the measures of obesity such as BMI, WC, WHR, and WHtR which are used in epidemiological studies WC and WHR as measures of abdominal obesity is more useful than BMI and show closer association with metabolic risk factors than BMI, hence measurement of WC should become a standard component of cardiovascular risk evaluation in routine clinical practice [31,41–43].

Application of BMI at commonly used cut-off level exhibits high specificity but lower sensitivity in identification of adiposity, as half of the people with excess body fat cannot be diagnosed by using BMI. This issue was shown in a systematic review of 25 studies [44]. In another study of 1345 patients with coronary heart disease, WC was positively and BMI was negatively associated with mortality. After combining WC with BMI, subjects with WC ≥ 102 cm and BMI <25 kg/m2 had highest rates of both total and cardiovascular mortality of all coronary heart disease [45]. The impact of BMI and WC on the incidence of cardiovascular events and all-cause mortality was also determined during a 148-month follow-up period. In this study, after adjustment for confounders, only baseline BMI remained an independent predictor cardiovascular mortality [46].

This study has some limitations including study design which is cross-sectional and thus the association does not indicate causality. Furthermore, lack of association between normal weight but abnormal WC and metaboloic abnormalities in this study should be attributed to inadequate sample size in this subgroup. However, classification of study population according to pattern of obesity should be considered as a strength, because, these findings are helpful in recognizing high-risk individuals based on their pattern of obesity.

In conclusion, this study indicates an association between the prevalence of non-obese components of MetS and obesity phenotypes. Overweight/obese subjects in particular individuals with coexistent abdominal and general obesity are at greater risk of these cardiometabolic abnormalities. Further longitudinal studies are required to determine the outcomes of subjects with different obesity phenotypes.

Conflicts of interest

The authors declare that they have no conflict of interest to disclose.

Acknowledgment

The authors would like to acknowledge the deputy of research of Babol University of Medical Sciences for support.

References

[1] Sidney CS. Multiple risk factors for cardiovascular disease and diabetes mellitus. Am J Med 2007;120(3A). S3–S11.
[2] James PT, Leach R, Kalamara E, Shayeghi M. The worldwide obesity epidemic. Obes Res 2001;9(Supl 4). 228S–33S.
[3] Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the global burden of disease study 2010. Lancet 2012;380(9859):2197–223.
[4] Hajian-Tilaki K, Heidari B, Hajian-Tilaki A. Solitary and combined negative influences of diabetes, obesity and hypertension on health-related quality of life of elderly individuals: a population-based cross-sectional study. Diabetes Metab: Clin Res Rev 2016;1092(Suppl):S37–42.
[5] Hajian-Tilaki K. Metabolic syndrome and the associated risk factors in Iranian adults: a systematic review. Caspian J Intern Med 2015;6(2):51–61.
[6] Jaacks LM, Vandevijvere S, Pan A, McGowan CJ, Wallace C, Imamura F, et al. The obesity transition: stages of the global epidemic. Lancet Diabetes Endocrinol 2019;7(3):231–40.
[7] Sung H, Siegel RL, Torre LA, Pearson-Stuttard J, Islami F, Fedewa SA, et al. Global patterns in excess body weight and the associated cancer burden. Ca - Cancer J Clin 2019;69(2):88–112.
[8] Jensen MD. Role of body fat distribution and the metabolic complications of obesity. J Clin Endocrinol Metab 2008;93(11 Suppl 1):S57–63.
[9] Kissebah AH, Peiris AN. Biology of regional body fat distribution: relationship to non-insulin-dependent diabetes mellitus. Diabetes Metab Rev 1989;5(2): 83–109.
[10] Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK, Erwin PJ, et al. Jimenez%20F%5BAuthor%5D&cauthor=true&cauthor_uid=20125098Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obes 2010;34(5):791–9. https://www.ncbi.nlm.nih.gov/pubmed/?term=Lopez-.
[11] Romero-Corral A, Somers VK, Sierra-Johnson J, Thomas RJ, Collazo-Clavell ML, KorinekJ, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. Int J Obes 2008;32(6):959–66.
[12] Carmienke S, Freitag MH, Pischon T, Schlattmann P, Fankhaenel T, Goebel H, et al. General and abdominal obesity parameters and other combination in relation to mortality: a systematic review and meta-regression analysis. Eur J Clin Nutr 2013;67(6):573–85.
[13] Executive summary of the third report of the national cholesterol education program expert panel on detection, evaluation, and treatment of High blood cholesterol (NCEP) in adults (adult treatment panel III). J Am Med Assoc 2001; 285:2486–2497.
[14] Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C. Definition of metabolic syndrome: report of the national heart, lung and blood Institute/ American Heart Association Conference on scientific issues related to definition. Circulation 2004;109:433–8.
[15] Azizi F, Hadaegh F, Khalili D, Esteghamati A, Hosseinpanah F, Delavari A, et al. Appropriate definition of metabolicsyndrome among Iranian adults: report of the Iranian National Committee of Obesity. Arch Iran Med 2010;13(5):426.
[16] Hajian-Tilaki K, Heidari B. Is waist circumference a better predictor of diabetes than body mass index or waist-to-height ratio in Iranian adults? Int J Prev Med 2015;6:5.
[17] Hajian-Tilaki K, Heidari B, Hajian-Tilaki A, Firouzjahi AR, Bagherzadeh M. The

discriminatory performance of body mass index, waist circumference, waist-to-hip ratio and waist-to-height ratio for detection of metabolic syndrome and their optimal cutoffs among Iranian adults. JRHS 2014;14(4):276–81.

[18] Grundy SM. Metabolic syndrome: connecting and reconciling cardiovascular and diabetes worlds. J Am Coll Cardiol 2006;47(6):1093–100.

[19] Liaw FY, Kao TW, Wu LW, Wang CC, Yang HF, Peng TC, et al. Components of metabolic syndrome and the risk of disability among the elderly population. Sci Rep 2016;6:22750.

[20] Gordon-Larsen P1, Adair LS, Meigs JB, Mayer-Davis E, Herring A, Yan SK, Zhang B, Du S, Popkin BM. Discordant risk: overweight and cardiometabolic risk in Chinese adults. Obesity 2013;21(1):E166–74.

[21] Villanueva B, Arteaga A, Maiz A, Cortés VA. Abdominal obesity is a common finding in normal and overweight subjects of Chilean is associated with increased frequency of cardiometabolic risk factors. PLoS One 2018;26(3): e0194644. 13.

[22] Nichols GA, Horberg M, Koebnick C, Young DR, Waitzfelder B, Sherwood NE, Daley MF, Ferrara A. Cardiometabolic risk factors among 1.3 million adults with overweight or obesity, but not diabetes, in 10 geographically diverse regions of the United States, 2012-2013. Prev Chronic Dis 2017;9(14):E22.

[23] Lee CM, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. J Clin Epidemiol 2008;61:646–53.

[24] Czernichow S, Kengne AP, Stamatakis E, Hamer M, Batty GD. Body mass index, waist circumference and waist-hip ratio: which is the better discriminator of cardiovascular disease mortality risk? Evidence from an individual-participant meta-analysis of 82 864 participants from nine cohort studies. Obes Rev 2011;12(9):680–7.

[25] Taylor AE, Ebrahim S, Ben-Shlomo Y, Martin RM, Whincup PH, Yarnell JW, et al. Comparison of the associations of body mass index and measures of central adiposity and fat mass with coronary heart disease, diabetes, and all-cause mortality: a study using data from 4 UK cohorts. Am J Clin Nutr 2010;91:547–56.

[26] Bakhtiari A, Hajian-Tilaki K, Ghanbarpour A. Metabolic syndrome and different obesity phenotypes in the elderly women population: Iran's Health System on aging. Caspian J Intern Med 2018;9(3):252–9.

[27] Song P, Li X, Bu Y, Ding S, Zhai D, Wang E, et al. Temporal trends in normal weight central obesity and its associations with cardiometabolic risk among Chinese adults. Sci Rep 2019;9:5411.

[28] Iacobini C, Pugliese G, BlasettiFantauzzi C, Federici M, Menini S. Metabolically healthy versus metabolically unhealthy obesity. Metabolism 2019;92:51–60.

[29] Goossens GH. The metabolic phenotype in obesity: fat mass, body fat distribution, and adipose tissue function. Obes Facts 2017;10(3):207–15.

[30] Heianza Y, Kato K, Kodama S, Ohara N, Suzuki A, Tanaka S, et al. Risk of the development of Type 2 diabetes in relation to overall obesity, abdominal obesity and the clustering of metabolic abnormalities in Japanese individuals: does metabolically healthy overweight really exist? The Niigata Wellness Study. Diabet Med 2015;2(5):665–72.

[31] Nicklas BJ, Cesari M, Penninx BW, Kritchevsky SB, Ding J, Newman A, et al. Abdominal obesity is an independent risk factor for chronic heart failure in older people. J Am Geriatr Soc 2006;54(3):413–20.

[32] Carmienke S, Freitag MH, Pischon T, Schlattmann P, Fankhaenel T, Goebel H, et al. General and abdominal obesity parameters and their combination in relation to mortality: a systematic review and meta-regression analysis. Eur J Clin Nutr 2013;67(6):573–85.

[33] Gao W, Qiao X, Wang Y, Wan L, Wang Z, Wang X, et al. The interactive association of general obesity and central obesity with prevalent hypertension in rural lanzhou, China. PLoS One 2016;11(10):e0164409.

[34] Ataie-Jafari A, Heshmat R, Kelishadi R, Ardalan G, Mahmoudarabi M, Rezapoor A, et al. Generalized or abdominal obesity: which one better identifies cardiometabolic risk factors among children and adolescents? The CASPIAN III study. J Trop Pediatr 2014;60(5):377–85.

[35] Coutinho T, Goel K, Corrêa de Sá D, Carter RE, Hodge DO, Kragelund C, et al. Combining body mass index with measures of central obesity in the assessment of mortality in subjects with coronary disease: role of "normal weight central obesity. J Am Coll Cardiol 2013;61(5):553–60.

[36] Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L. Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3·6 million adults in the UKES. Lancet Diadetes Endorinol 2018;6(12):944–53.

[37] Franco LP, Morais CC, Cominetti C. Normal-weight obesity syndrome: diagnosis, prevalence, and clinical implications. Nutr Rev 2016;74(9):558–70.

[38] Coutinho T, Goel K, Corrêa de Sá D, Kragelund C, Kanaya AM, Zeller M, et al. Central obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. J Am Coll Cardiol 2011;10(19):1877–86. 57.

[39] Shuster A, Patlas M, Pinthus JH, Mourtzakis M. The clinical importance of visceral adiposity: a critical review of methods for visceral adipose tissue analysis. Br J Radiol 2012;85(1009):1–10.

[40] Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009;9:88.

[41] Després JP. Abdominal obesity: the most prevalent cause of the metabolic syndrome and related cardiometabolic risk. Eur Heart J Suppl 2006;8(suppl B):B4–12.

[42] Bosy-Westphal A, Geisler C, Onur S, Korth O, Selberg O, Schrezenmeir J, et al. Value of body fat mass vs anthropometric obesity indices in the assessment of metabolic risk factors. Int J Obes 2006;30(3):475–83.

[43] Abdelaal M, le Roux CW, Docherty NG. Morbidity and mortality associated with obesityAnn. Transl Med 2017;5(7):161.

[44] Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK, Erwin PJ, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obes 2010;34(5):791–9.

[45] Sobiczewski W1, Wirtwein M, Jarosz D, Gruchala M. Superiority of waist circumference and body mass index in cardiovascular risk assessment in hypertensive patients with coronary heart disease. Blood Press 2015;24(2): 90–5.

[46] Bombelli M, Facchetti R, Fodri D, Brambilla G, Sega R, Grassi G, et al. Impact of body mass index and waist circumference on the cardiovascular risk and all-cause death in a general population: data from the PAMELA study. Nutr Metabol Cardiovasc Dis 2013;23(7):650–6.