


## RESEARCH ARTICLE

# Association between obesity categories with cardiovascular disease and its related risk factors in the MASHAD cohort study population

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## Abstract

**Background:** Cardiovascular disease (CVD) is a significant cause of morbidity and mortality globally. Obesity is an important CVD risk factor and is increasing in prevalence.

**Methods:** In this study, 3829 men and 5720 women (35-65 years) were enrolled as part of the MASHAD cohort study. Four categories were identified according to body mass index and waist circumference that was defined by the World Health Organization. Logistic regression analysis was used to determine the adjusted odds ratio (OR) for the occurrence of CVD, and Cox regression model was used to evaluate the association of obesity with CVD incidence.

**Results:** We found that the higher risk groups defined by categories of adiposity were significantly related to a higher prevalence of a high serum total cholesterol (TC), and triglycerides (TG), and lower high-density lipoprotein cholesterol (HDL), and higher fasting blood glucose (FBG) in both genders and a higher low-density lipoprotein cholesterol (LDL) in women ( $P < .001$ ). Additionally, a high percentage of participants with dyslipidemia, high LDL, high TC, and low HDL and a high percentage of participants with metabolic syndrome, diabetes, hypertension, and a high serum TG were observed across obesity categories ( $P < .001$ ). Moreover, women with the very high degrees of obesity had a greater risk of CVD (HR: 1.91, 95% CI: 1.06-3.43,  $P = .03$ ).

**Conclusion:** Obesity strongly predicts several CVD risk factors. Following 6 years of follow-up, in individuals within increasing degrees of obesity, there was a corresponding significant increase in CVD events, rising to approximately a twofold higher risk of cardiovascular events in women compared with men.

Hamideh Ghazizadeh, Seyed Mohammad Reza Mirinezhad and Zahra Asadi Equal first authors.

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**KEYWORDS**

cardiovascular risk factors, obesity

## 1 | INTRODUCTION

In the last two decades, the progressive increase in the prevalence of obesity has occurred in many areas of the world, both in developing and developed countries such as Iran and the United States.<sup>1-4</sup> According to the cardiovascular diseases project (MONICA), Iran has the highest prevalence of childhood obesity among countries presented in the report of the World Health Organization (WHO). Over one billion adults worldwide are suffering from excess weight. Obesity is a multifactorial disorder, and environmental causes such as lifestyle, unhealthy diets, and physical inactivity, as well as genetic causes, are risk factors for excess weight and obesity which is associated with several non-communicable diseases including diabetes, arthritis, hypertension, hyperlipidemia, and cardiovascular diseases (CVD).<sup>1-7</sup> CVD is a primary chronic non-communicable disease that can be the cause of disability, which is more critical in active ages.<sup>8</sup> Studies show that chronic diseases are responsible for 50% of the burden of total disease in middle-income countries, and 12% of this percentage was related to CVD.<sup>8-10</sup> CVD mortality is related to the degree of obesity, and a threefold increased risk in men and women with excess weight and obesity has been reported in the USA.<sup>11</sup> Applying body mass index (BMI, kg/m<sup>2</sup>) as a marker of excess body fat accumulation, studies have shown either null, linear, J- or U-shaped associations with mortality risk.<sup>4,5</sup> It has been reported that overweight and obesity increase the risk of death specifically mortality related to CVD. All-cause mortality decreased in subjects aged 60 years with BMI of 20-25 kg/m<sup>2</sup>, meanwhile weight loss cannot prevent CVD events.<sup>12</sup>

It has been shown that there are gender-dependent cardiometabolic differences, while the role of gender in the severity of obesity is not apparent.<sup>13</sup> Therefore, we conducted this study to investigate the predictive values of anthropometric indices for CVD risk factors in Iranian men and women with different degrees of obesity.

## 2 | MATERIALS AND METHODS

### 2.1 | Study population

The population in this study comprised 3829 men with aged  $49.12 \pm 8.37$  years and 5720 women with an mean age of  $46.99 \pm 8.02$  years that were enrolled from the Mashhad stroke and heart atherosclerotic disorder (MASHAD) cohort study. MASHAD study aimed to identify the risk and incidence of cardiovascular events as described elsewhere.<sup>14</sup> Those participants with missing data regarding anthropometric measurements and biochemical factors ( $n = 155$ ) were excluded, and finally, 9549 individuals were included in the current analysis. Four groups were defined according to body mass index (BMI) and waist circumference in accordance with the World Health Organization (WHO) classification for obesity: no risk, increased risk, high risk, and very high risk.

### 2.2 | Baseline assessments

In the MASHAD study, biochemical parameters (including fasting blood glucose [FBG] and lipid profiles), demographic data (including educational level, gender, and age) and medical history as well as lifestyle information (including smoking habit), anthropometric data (including waist circumference [WC], body mass index [BMI], weight, and height) and physical activity (by Self-declaration form) were gathered by a nurse interview.<sup>15</sup> The methods of biochemical measurements using an automated analyzer and blood pressure assessments using a standard mercury sphygmomanometer are described elsewhere.<sup>16</sup> Participants with dyslipidemia were defined by lipid profiles, as described previously.<sup>17</sup>

We used the BMI categories as defined by the World Health Organization (WHO) recommendations for obesity Table 1. Also, the following four categories were used: underweight, normal,

BMI classification	BMI (kg/m <sup>2</sup> )	Waist circumference	
		Men < 102 cm Women < 88 cm	Men > 102 cm Women > 88 cm
Underweight	<18.5	No increased risk	No increased risk
Normal	18.5-24.9	No increased risk	No increased risk
Overweight	25-29.9	Increased risk	High risk
Obesity	30-34.9 35-39.9	High risk	Very high risk
		Very high risk	Very high risk
Extreme obesity	≥40	Very high risk	Very high risk

**TABLE 1** Categories of obesity based on combined BMI and WC, in accordance with the NIH Practical guide to obesity<sup>18</sup>

Note: Obesity categories as defined by World Health Organization recommendations.

Abbreviations: BMI, body mass index.

overweight, obesity, and extreme obesity for the current analysis. According to the WHO recommendations for obesity, BMI more than 25 kg/m<sup>2</sup> was defined as overweight, and BMI higher than 30 kg/m<sup>2</sup> was considered as obese. Based on the cutoff points of the NIH Practical guide to obesity, WC > 102 cm in men and >88 cm in women were considered high. The combination of BMI and WC was categorized too, no risk, increased risk, high risk, and very high risk according to WHO guideline. Having higher BMI and WC values are considered as a higher risk for developing CVD event and its risk factors.<sup>18</sup> Hypertension was diagnosed in individuals with systolic blood pressure at or above 140 mm Hg and, or diastolic blood pressure at or above 90 mm Hg, and in individuals who were on anti-hypertension medication.

### 2.3 | Follow-up

The participants with CVD were approved at follow-up to assess medical history and physical test by an expert Cardiologist. These data were collected during three follow-up periods; a total of 768 subjects claimed to have a CVD event. Further assessments of participants were performed, including a history of myocardial infarction or angina pectoris together with electrocardiographic evidence of a definite Q wave using the Minnesota Code;<sup>19,20</sup> physical examination, and a detailed medical history taken by a cardiologist and in suspicious cases, they were also investigated using echocardiography, stress echocardiography, radioisotope, angiography, computed tomography (CT) angiography, and Exercise Tolerance Test (ETT) at a complementary medical examination, if the cardiologist suspected to a test of participants at the third follow-up. Finally, the diagnosis was made according to the consensus decision of a panel of experts. Therefore, 235 patients were considered to have developed CVD including 120 subjects with unstable angina (UA), 75 subjects with stable angina (SA), and 40 subjects with myocardial infarction (MI).

### 2.4 | Ethical issues

Informed consent was obtained from all subjects (were written) using protocols approved by the Ethics Committee of the Mashhad University of Medical Sciences.

### 2.5 | Statistical analysis

Data were expressed as mean  $\pm$  SD (for normally distributed data) or median and inter-quartiles range (for non-normally distributed data). Data analyses were undertaken using SPSS version 18. It has been determined the normality of data using the Kolmogorov-Smirnov test. Based on data distribution pattern, Student's *t* test, analysis of variance (ANOVA), Mann-Whitney *U*, and Kruskal-Wallis tests were used to analyze data in the groups. We used a logistic regression analysis to determine the unadjusted and adjusted odds ratio (OR)

for the occurrence of CVD. Cox regression model was used to evaluate the association of obesity categories with CVD incidence. A *P*-value of <.05 was considered as statistically significant.

## 3 | RESULTS

### 3.1 | Characteristics of participants

Anthropometric and biochemical characteristics of participants by NIH Practical guide to obesity categories in men and women are described in Tables 2 and 3. Of the total 3834 participants, 1407, 506, and 491 individuals were classified for adiposity as at an increased risk, high risk, and very high-risk group in men, respectively. On the other hand, of the total 5722 participants, 577, 1842, and 2101 individuals were categorized as being at increased risk, high risk, and very high risk in the female group, respectively.

Tables 2 and 3 show a significant incremental rise in level of serum lipid profiles (TC, TG, LDL, and HDL), FBG, anthropometric factors (BMI, WC, HC, WHR, WHtR, and MAC) and SBP, DBP with an increasing degree of obesity in men and women participants (*P* < .001). We observed that very high-risk men and women were significantly older than the subjects in other groups (*P* < .001).

According to Tables 2 and 3, a high percentage of men with MetS, diabetes, HTN, and high TG were in groups of very high risk, high risk, and increased risk (% Mets: 65, 53.80, 33.20, % diabetes: 11.40, 10.30, 8.90; % HTN: 38.70, 31.80, 24.60; % high TG: 53, 46.40, 44.70, respectively) in comparison with women (% Mets: 58.80, 47.50, 25.10; % diabetes: 9.50, 9, 5.90; % HTN: 30.30, 24.20, 13.50; % high TG: 40.30, 32.80, 23.10, respectively). Moreover, the percentage of women with dyslipidemia, high LDL, high TC, and low HDL were higher for women across risk categories compared with men (% women with dyslipidemia 89.40, 85.40, 85.30; high LDL-C: 33.60, 30.60, 30.40; high TC: 39.90, 36.60, 37.10; and low HDL-C: 77.30, 73.30, 72.30 and % men with dyslipidemia: 89.40, 85.40, 85.30; high LDL-C: 33.60, 30.60, 30.40; high TC: 39.90, 36.60, 37.10; and low HDL-C: 60.30, 59.10, 60.80, respectively) in groups of very high risk, high risk, and increased risk, respectively). There was no statistically significant difference between LDL levels in the risk categories in men (*P* > .05).

### 3.2 | Association of CVD risk factors with obesity categories

Participants at raised CVD risk were examined using the multiple regression analysis to determine the predictive values of obesity categories for CVD risk factors Table 4. In model 1 (before adjusting for confounder factors) as we expected, increased risk, high risk, and very high-risk men compared with the reference group (no risk) had significantly higher risk of diabetes than women (OR:1.79, 2.10 and 2.36 in men group and OR: 0.97, 1.53 and 1.62 in women group, respectively) as well as hypertension (OR:1.65, 2.36 and 3.19 in men group and OR: 1.06, 2.16 and 2.94 in women group, respectively),

**TABLE 2** Characteristics of participants based on the NIH Practical guide to obesity categories in men

	Obesity categories				P
	No risk	Increased risk	High risk	Very high risk	
Number, n	1427	1405	506	491	
Age, y	48.26 ± 8.61	48.61 ± 8.30	50.48 ± 8.34	49.16 ± 8.24	<.001
BMI, kg/m <sup>2</sup>	22.21 ± 2.09	27.15 ± 1.33	29.19 ± 1.96	33.03 ± 2.51	<.001
WC, cm	84.76 ± 8.12	93.82 ± 5.69	102.30 ± 6.64	109.95 ± 6.33	<.001
HC, cm	95.17 ± 5.68	101.42 ± 5.24	105.50 ± 5.27	112.46 ± 6.15	<.001
WHR	0.89 ± 0.07	0.93 ± 0.06	0.97 ± 0.06	0.98 ± 0.05	<.001
WHtR	0.50 ± 4.75	0.56 ± 3.64	0.61 ± 4.03	0.65 ± 4.31	<.001
MAC, cm	27.99 ± 3.58	30.69 ± 3.53	31.77 ± 2.42	33.87 ± 3.40	<.001
SBP, mm Hg	117.95 ± 16.10	122.54 ± 16.36	127.03 ± 17.10	129.34 ± 18.51	<.001
DBP, mm Hg	80 ± 10.25	80.46 ± 10.14	83.15 ± 10.57	84.43 ± 10.56	<.001
TC, mg/dL	180.36 ± 37.68	190.19 ± 36.21	190.26 ± 40.11	192.10 ± 38.27	<.001
TG, mg/dL	98 (72, 137)	138.50 (97, 196)	144 (102, 197.25)	153 (114, 214)	<.001
LDL-C, mg/dL	112.42 ± 33.24	114.14 ± 34.15	113.95 ± 37.55	114.32 ± 35.72	.521
HDL-C, mg/dL	41.60 ± 9.52	38.92 ± 8.91	38.93 ± 8.41	38.54 ± 9.47	<.001
FBG, mg/dL	86.46 ± 34.21	91.54 ± 34.59	95.59 ± 38.40	96.57 ± 41.54	<.001
CVD risk factors					
Prevalence, %					
Diabetes	5.20	8.90	10.30	11.40	<.001
Hypertension	16.50	24.60	31.80	38.70	<.001
High TC	28.60	37.10	36.60	39.90	<.001
High TG	19.80	44.70	46.40	53	<.001
High LDL-C	27.50	30.40	30.60	33.60	.057
Low HDL-C	46.40	60.80	59.10	60.30	<.001
Dyslipidemia	70.20	85.30	85.40	89.40	<.001
MetS	5.20	33.20	53.80	65	<.001

Note: Hypertension was defined as systolic blood pressure  $\geq 140$  mm Hg, diastolic blood pressure  $\geq 90$  mm Hg. Diabetes was defined as fasting blood glucose  $\geq 126$  mg/dL. Dyslipidemia was defined as total cholesterol  $\geq 200$ , or triglycerides  $\geq 150$ , or low-density lipoprotein cholesterol (LDL-C)  $\geq 130$ , or high-density lipoprotein cholesterol (HDL-C)  $< 40$  (for men) and HDL-C  $< 50$  (for women).

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAC, mid-upper arm circumference; MetS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.

high TC (OR:1.47, 1.44 and 1.66 in men group and OR: 1.05, 1.60 and 1.58 in women group, respectively), high TG (OR: 3.27, 3.51 and 4.56 in men group and OR: 1.39, 2.26 and 3.13 in women group, respectively), dyslipidemia (OR: 2.46, 2.48 and 3.58 in men group and OR: 1.34, 2.23 and 2.66 in women group, respectively), high LDL-C (OR: 1.15, 1.16 and 1.34 in men group and OR: 0.88, 1.38 and 1.29 in women group, respectively), and MetS (OR: 8.98, 21 and 33.51 in men group and OR: 1.19, 3.20 and 5.04 in women group, respectively), while high-risk women had significantly higher risk of high LDL-C in comparison with men (OR: 1.38 and 1.16 in woman and men, respectively).

However, after the data in Table 4 were adjusted for confounding factors including age, smoking (ex-smoked and current smoking), and physical activity level, we found similar results with model 1 for risk factors of diabetes, hypertension, high TG, high TC, dyslipidemia,

and MetS. The results demonstrated that CVD risk factors have a graded linear relationship with risk categories, before and after adjusting for confounding factors.

In this regard, very high-risk participants had a significantly higher risk of MetS in comparison with reference group (No risk) (OR: 26.95; 95% CI: 19.83-36.61;  $P$ : <.001 and OR: 4.42; 95% CI: 3.69-5.28;  $P$ : <.001 in men and women, respectively), dyslipidemia (OR: 2.84; 95% CI: 2.06-3.92;  $P$ : <.001 and OR: 1.91; 95% CI: 1.50-2.43;  $P$ : <.001 in men and women, respectively), diabetes (OR: 1.90; 95% CI: 1.29-2.77;  $P$ : .001 and OR: 1.45; 95% CI: 1.07-1.98;  $P$ : .018 in men and women, respectively), hypertension (OR: 2.91; 95% CI: 2.28-3.71;  $P$ : <.001 and OR: 2.92; 95% CI: 2.36-3.61;  $P$ : <.001 in men and women, respectively), high TG (OR: 3.83; 95% CI: 3.04-4.83;  $P$ : <.001 and OR: 2.60; 95% CI: 2.15-3.15;  $P$ : <.001 in men and women, respectively), and high TC (OR: 1.53; 95% CI: 1.22-1.91;  $P$ :

**TABLE 3** Characteristics of participants by NIH Practical guide to obesity categories in women

	Obesity categories				P-value
	No risk	Increased risk	High risk	Very high risk	
Number, n	1202	577	1840	2101	
Age, y	46.76 ± 8.36	45.15 ± 7.87	47.77 ± 7.95	48.29 ± 7.90	<.001
BMI, kg/m <sup>2</sup>	22.64 ± 1.92	27.06 ± 1.38	28.01 ± 1.66	33.78 ± 3.29	<.001
WC, cm	84.72 ± 9.59	81.62 ± 4.49	96.71 ± 7.16	106.12 ± 9.85	<.001
HC, cm	95.43 ± 6.05	100.07 ± 5.67	104.19 ± 5.20	113.86 ± 8.27	<.001
WHR	0.89 ± 0.08	0.82 ± 0.06	0.93 ± 0.07	0.93 ± 0.07	<.001
WHtR	0.54 ± 6.23	0.53 ± 3.38	0.62 ± 4.69	0.69 ± 6.38	<.001
MAC, cm	27.37 ± 2.93	28.98 ± 3.49	30.54 ± 2.94	33.28 ± 3.61	<.001
SBP, mm Hg	114.79 ± 17.12	115.65 ± 26.34	122.35 ± 19.28	125.75 ± 19.55	<.001
DBP, mm Hg	74.57 ± 13.01	75.08 ± 10.32	79.16 ± 12.99	81.15 ± 11.39	<.001
TC, mg/dL	186.76 ± 39.24	189.11 ± 36.38	196.20 ± 39.15	198.19 ± 39.88	<.001
TG, mg/dL	92 (68, 132)	106 (74, 145)	118 (86, 168)	132 (97, 182)	<.001
LDL-C, mg/dL	114.90 ± 35.46	113.08 ± 32.95	121.23 ± 35.42	120.19 ± 35.95	<.001
HDL-C, mg/dL	47.25 ± 10.52	44.99 ± 10.12	44.76 ± 9.82	43.63 ± 9.22	<.001
FBG, mg/dL	87.68 ± 40.07	87.47 ± 34.57	93.52 ± 40.72	93.75 ± 35.29	<.001
CVD risk factors					
Prevalence, %					
Diabetes	6.10	5.90	9	9.50	.001
Hypertension	12.90	13.50	24.20	30.30	<.001
High TC	33.80	34.80	44.90	44.60	<.001
High TG	17.70	23.10	32.80	40.30	<.001
High LDL-C	30.70	28.10	37.90	36.40	<.001
Low HDL-C	64.90	72.30	73.30	77.30	<.001
Dyslipidemia	81.60	85.60	90.80	92.20	<.001
MetS	22	25.10	47.50	58.80	<.001

Note: Hypertension was defined as systolic blood pressure  $\geq$  140 mm Hg, diastolic blood pressure  $\geq$  90 mm Hg. Diabetes was defined as fasting blood glucose  $\geq$  126 mg/dL. Dyslipidemia was defined as total cholesterol  $\geq$  200, or triglycerides  $\geq$  150, or low-density lipoprotein cholesterol (LDL-C)  $\geq$  130, or high-density lipoprotein cholesterol (HDL-C)  $<$  40 (for men) and HDL-C  $<$  50 (for women).

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAC, mid-upper arm circumference; MetS, metabolic syndrome; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.

<.001 and OR: 1.58; 95% CI: 1.33-1.86;  $P <$  .001 in men and women, respectively).

After adjusting for confounding factors, we did not find a significant association between high LDL-C and degree of risk in men group ( $P$ : .09) while this association was significant for female group ( $P$ : .006). Moreover, on the basis of models 1 and 2, very high-risk participants in comparison with the reference group (no risk) had the highest risk significantly for low HDL-C in men (odds ratio: 1.43; 95% CI: 1.15-1.78;  $P$ : .001) and women (odds ratio: 1.36; 95% CI: 1.11-1.54;  $P$ : .001), respectively.

According to Table 5 and after adjusting for confounding factors, we demonstrated that women with a very high risk of obesity in comparison with the reference group (no risk) had significantly increased the risk of CVD (HR: 1.91, 95% CI: 1.06-3.43;  $P$ : .03) while these association were not significant among men.

## 4 | DISCUSSION

In the present study, after 6 years of follow-up, CVD was reported in 235 participants of the study population including 120 cases of unstable angina, 75 cases of stable angina, and 40 cases of myocardial infarction. Also, we found a significant direct association between extreme obesity, including both high BMI and WC, and CVD events only in women. However, our previous studies showed an association between genetic and environmental factors with cardiometabolic risk factors such as obesity and metabolic syndrome.<sup>21-24</sup> Sertic and colleagues reported an association between anthropometric factors including weight, BMI, and waist-hip ratio (WHR) with diet type. Additionally, these results showed that several genetic variants (ESR-1, LPL, and APO E) could be considered as predictive genetic risk factors for obesity-related metabolic disorders in healthy

**TABLE 4** Odds ratio of CVD risk factors based on obesity categories

	Men		Women	
	Model 1	Model 2	Model 1	Model 2
<b>Diabetes</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.79 (1.33-2.41)	1.58 (1.16-2.15)	0.97 (0.64-1.47)	0.97 (0.64-1.48)
High risk	2.10 (1.45-3.04)	1.70 (1.15-2.51)	1.53 (1.15-2.04)	1.44 (1.07-1.93)
Very high risk	2.36 (1.64-3.39)	1.90 (1.29-2.77)	1.62 (1.23-2.14)	1.45 (1.07-1.98)
P-value	<.001	.001	.001	.018
<b>Hypertension</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.65 (1.37-1.99)	1.56 (1.28-1.89)	1.06 (0.79-1.41)	1.08 (0.80-1.44)
High risk	2.36 (1.87-2.98)	2.14 (1.68-2.73)	2.16 (1.77-2.63)	2.11 (1.72-2.59)
Very high risk	3.19 (2.54-4.02)	2.91 (2.28-3.71)	2.94 (2.42-3.56)	2.92 (2.36-3.61)
P-value	<.001	<.001	<.001	<.001
<b>High TC</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.47 (1.26-1.72)	1.40 (1.19-1.65)	1.05 (0.85-1.29)	1.06 (0.86-1.30)
High risk	1.44 (1.16-1.78)	1.34 (1.07-1.67)	1.60 (1.37-1.86)	1.58 (1.35-1.85)
Very high risk	1.66 (1.34-2.05)	1.53 (1.22-1.91)	1.58 (1.36-1.83)	1.58 (1.33-1.86)
P-value	<.001	<.001	<.001	<.001
<b>High TG</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	3.27 (2.77-3.87)	2.99 (2.51-3.55)	1.39 (1.09-1.77)	1.34 (1.05-1.71)
High risk	3.51 (2.83-4.37)	3.03 (2.41-3.80)	2.26 (1.90-2.70)	2.07 (1.73-2.48)
Very high risk	4.56 (3.66-5.68)	3.83 (3.04-4.83)	3.13 (2.64-3.72)	2.60 (2.15-3.15)
P-value	<.001	<.001	<.001	<.001
<b>High LDL-C</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.15 (0.98-1.36)	1.10 (0.93-1.30)	0.88 (0.71-1.10)	0.88 (0.71-1.10)
High risk	1.16 (0.93-1.45)	1.07 (0.85-1.35)	1.38 (1.18-1.61)	1.35 (1.15-1.59)
Very high risk	1.34 (1.07-1.66)	1.22 (0.97-1.54)	1.29 (1.11-1.50)	1.27 (1.07-1.50)
P-value	.010	.091	.001	.006
<b>Low HDL-C</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.79 (1.55-2.08)	1.62 (1.38-1.89)	1.41 (1.13-1.75)	1.34 (1.08-1.67)
High risk	1.67 (1.36-2.05)	1.40 (1.13-1.74)	1.48 (1.27- 1.74)	1.31 (1.11-1.54)
Very high risk	1.76 (1.43-2.16)	1.43 (1.15-1.78)	1.84 (1.57-2.15)	1.36 (1.11-1.54)
P-value	<.001	.001	<.001	.001
<b>Dyslipidemia</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	2.46 (2.04-2.96)	2.19 (1.81-2.66)	1.34 (1.02-1.76)	1.28 (0.97-1.69)
High risk	2.48 (1.89-3.25)	2.02 (1.53-2.68)	2.23 (1.80-2.77)	1.91 (1.53-2.38)
Very high risk	3.58 (2.63-4.88)	2.84 (2.06-3.92)	2.66 (2.14 (3.30)	1.91 (1.50-2.43)
P-value	<.001	<.001	<.001	<.001
<b>MetS</b>				
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)

(Continues)

**TABLE 4** (Continued)

	Men		Women	
	Model 1	Model 2	Model 1	Model 2
Increased risk	8.98 (6.94-11.61)	8 (6.15-10.40)	1.19 (0.94-1.50)	1.17 (0.93-1.48)
High risk	21 (15.70-28.09)	17.42 (12.92-23.49)	3.20 (2.71-3.77)	2.99 (2.52-3.53)
Very high risk	33.51 (24.89-45.11)	26.95 (19.83-36.61)	5.04 (4.29-5.93)	4.42 (3.69-5.28)
P-value	<.001	<.001	<.001	<.001

Note: Model 1, unadjusted; Model 2, association adjusted for age category (35-44, 45-54, 55-65), smoking (ex-smoked and current smoking) and physical activity level.

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; TC, total cholesterol; TG, triglyceride.

**TABLE 5** Hazard ratio (HR) of cardiovascular disease events according to obesity categories

	Men		Women	
	Model 1	Model 2	Model 1	Model 2
No risk	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Increased risk	1.08 (0.66-1.74)	1.02 (0.62-1.67)	0.45 (0.15-1.34)	0.47 (0.16-1.39)
High risk	1.87 (1.08-3.23)	1.65 (0.92-2.94)	1.12 (0.63-2)	1.07 (0.59-1.94)
Very high risk	1.65 (0.92-2.93)	1.44 (0.78-2.65)	1.91 (1.13-3.24)	1.91 (1.06-3.43)
P-value	.090	.242	<b>.016</b>	<b>.030</b>

Note: Model 1, unadjusted; Model 2, association adjusted for age category (35-44, 45-54, 55-65), smoking (ex-smoked and current smoking) and physical activity level. A P-value of < .05 was considered as statistically significant and the bold format.

adults.<sup>25</sup> We also found that adherence to western pattern was associated with higher BMI.<sup>26,27</sup>

However, there are several conflicting results in previous investigations. Two prospective studies have shown that the association of BMI and coronary heart disease (CHD) is not different among males and females, though higher BMI significantly increased the risk of stroke among males.<sup>28,29</sup> Also, in another study a higher BMI was found among CVD patients compared to healthy individuals.<sup>30</sup> According to the EUROASPIRE III study, obesity is a more common risk factor, with 35% prevalence rate in CVD patients. The prevalence of central obesity as a common risk factor of metabolic disorders was present in 53%. This prevalence is higher in women with CHD than men with the prevalence of an obesity overall of 45%.<sup>31</sup> Several studies similar results have presented in CVD patients in Europe and throughout the world.<sup>32</sup> However, in a cohort design study among 13307 German participants aged 25-74 years, it was found that body adiposity index (BAI) and WHtR of males and WC and WHR of females were associated with increased risk of all-cause and CVD mortality.<sup>33</sup> Fat distribution differences could explain the difference of cardiovascular disease risk among men and women, so that waist-to-height ratio (WHtR) among males, and BMI among females are the best anthropometric indicators of arterial stiffness as an independent cardiovascular risk factor.<sup>34</sup>

We have found that obesity categories could predict the presence of many CVD risk factors in this study. We demonstrated that increased obesity categories were significantly correlated with the greater prevalence of higher serum levels of TC, higher TG, lower

HDL, and higher FBG in both gender and higher LDL in the only female. Furthermore, we showed that there was a significant positive association between risk elevation in obesity categories and a higher risk of diabetes, hypertension, dyslipidemia, and MetS in both male patient and female patient. Moreover, we found a higher risk of low HDL and increased TC, TG, and LDL level (only in female) across obesity categories. In a recent population-based study, these significant associations were not found for raised TC, TG and LDL, and low HDL.<sup>35</sup> In the HERMES study, the relationship between serum lipid profile and severity of obesity was investigated in obese patients. The results for TG and HDL were significant. However, the results for TC and LDL showed an insignificant relationship.<sup>36</sup> We found that the obesity categories in men were associated with a significantly higher risk of incidence of MetS compared with these categories in female patients. In contrast, in a study conducted by Yin et al although an increase in risk severity of obesity categories was associated with a higher risk of incidence of MetS, the odds ratio was somewhat similar in men and women.<sup>35</sup> On the other hand, the OR of MetS in our study was far higher in male-related obesity categories in comparison with the study of Yin et al (OR: 8, ~17, ~27 vs OR: ~2, ~3, ~8).<sup>35</sup>

#### 4.1 | Strength and limitations

To the best of our knowledge, the present study is the first study indicating that obesity categories can predict the risk of CVD outcomes in



an Iranian population. The data used in the present study as a cross-sectional has been extracted from a large cohort study which has been included individuals aged 35 to 65 years. Despite the mentioned strength, this study may also have some limitations. The present study has only evaluated a population in Mashhad city, and further studies can be conducted on a cohort population from more than one city in Iran.

## 4.2 | Conclusion

According to the results of the present study, obesity categories can strongly predict the presence of several CVD risk factors. Furthermore, our result suggested that increased obesity categories were significantly correlated with a greater prevalence of higher serum levels of TC, higher TG, lower HDL, and higher FBG. Our findings revealed that after 6 years follow-up, step-by-step increased obesity categories were significantly associated with up to approximately twofold higher risk of cardiovascular events in the female gender. In addition to the mentioned strength and limitations in the present study, these findings need more investigations for confirmation.

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## CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

## AUTHOR CONTRIBUTIONS

We declare that we contributed significantly toward the research study, that is, (a) Mohammad Reza Oladi, Ali Asghar Mahmoudi, Marziyeh Eidi, Zahra Asadi, Ehsan Mosa Farkhany, Payam Sharifan, Hamideh Ghazizadeh, Reza Zare-Feyzabadi, Fatemeh Saeidi, and Seyed Mohammad Reza Mirinezhad involved in conception, design, and/or analysis and interpretation of data; (b) Mohadese Rohban, Mohsen Moohebbati, Zahra Asadi, Seyed Mostafa Parizadeh, Mehran yadegari, Niloofar shabani, Habibollah Esmaily, and Hamideh Ghazizadeh contributed to drafting the article or revising it critically for important intellectual content; and (c) Gordon A. Ferns and Majid Ghayour-Mobarhan contributed to final approval of the version to be published.

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## REFERENCES

- Abdi E, Taiar R. Interventions for preventing childhood obesity in African-American children: a critical review. *Int J Series Multidiscip Res* (ISSN: 2455-2461). 2018;1(2):1-10.
- Czernichow S, Kengne A-P, 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):680-687.
- Larsson BY, Svärdsudd K, Welin L, Wilhelmsen L, Björntorp P, Tibblin GD. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *Br Med J*. 1984;288(6428):1401-1404.
- Wilcosky T, Hyde J, Anderson JJB, Bangdiwala S, Duncan B. Obesity and mortality in the lipid research clinics program follow-up study. *J Clin Epidemiol*. 1990;43(8):743-752.
- Collaboration, Prospective Studies. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*. 2009;373(9669):1083-1096.
- Gharakhanlou R, Farzad B, Agha-Alinejad H, Steffen LM, Bayati M. Anthropometric measures as predictors of cardiovascular disease risk factors in the urban population of Iran. *Arq Bras Cardiol*. 2012;98(2):126-135.
- Lee DH, Keum NaNa, Hu FB, et al. Comparison of the association of predicted fat mass, body mass index, and other obesity indicators with type 2 diabetes risk: two large prospective studies in US men and women. *Eur J Epidemiol*. 2018;33(11):1113-1123.
- Sadeghi M, Haghdoost AA, Bahrapour A, Dehghani M. Modeling the burden of cardiovascular diseases in Iran from 2005 to 2025: The impact of demographic changes. *Iran J Public Health*. 2017;46(4):506.
- Abegunde DO, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet*. 2007;370(9603):1929-1938.
- Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006;3(11):e442.
- Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983;67(5):968-977.
- Perk J, Backer DE, Guy G, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012) The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J*. 2012;33(13):1635-1701.
- Deng G, Yin LU, Liu W, et al. Associations of anthropometric adiposity indexes with hypertension risk: a systematic review and meta-analysis including PURE-China. *Medicine*. 2018;97(48):e13262.
- Ghayour-Mobarhan M, Moohebbati M, Esmaily H, et al. Mashhad stroke and heart atherosclerotic disorder (MASHAD) study: design, baseline characteristics and 10-year cardiovascular risk estimation. *Int J Public Health*. 2015;60(5):561-572.
- James WPT, Schofield EC. *Human Energy Requirements. A Manual for Planners and Nutritionists*. Oxford, UK: Oxford University Press; 1990.
- Emamian M, Hasanian SM, Tayefi M, et al. Association of hematocrit with blood pressure and hypertension. *J Clin Lab Anal*. 2017;31(6):e22124.
- Jellinger P, Smith D, Mehta A, et al. American Association of Clinical Endocrinologists' guidelines for management of dyslipidemia and prevention of atherosclerosis. *Endocr Pract*. 2012;18(Supplement 1):1-78.
- WHO. *Waist Circumference and Waist-Hip Ratio: Report of a WHO Expert Consultation*. Geneva, Switzerland: WHO; 2011:8-11. December 2008.



19. Luepker RV, Murray DM, Jacobs DR Jr, et al. Community education for cardiovascular disease prevention: risk factor changes in the Minnesota Heart Health Program. *American Journal of Public Health*. 1994;84(9):1383-1393.
20. Prineas RJ, Crow RS, Zhang ZM. *The Minnesota code manual of electrocardiographic findings*. London, UK: Springer Science & Business Media; 2009.
21. Barati E, Ghazizadeh H, Sadabadi F, et al. Association of the IL6 gene polymorphism with component features of metabolic syndrome in obese subjects. *Biochem Genet*. 2019;57(5):695-708.
22. Eshaghi FS, Ghazizadeh H, Kazami-Nooreini S, et al. Association of a genetic variant in AKT1 gene with features of the metabolic syndrome. *Genes Dis*. 2019;6(3):290-295.
23. Ghazizadeh H, Avan A, Fazilati M, et al. Association of rs6921438 A< G with serum vascular endothelial growth factor concentrations in patients with metabolic syndrome. *Gene*. 2018;667:70-75.
24. Kharazmi-Khorassani S, Kharazmi-Khorassani J, Rastegar-Moghadam A, et al. Association of a genetic variant in the angiotensin-like protein 4 gene with metabolic syndrome. *BMC Med Genet*. 2019;20(1):97.
25. Sertic J, Juricic L, Ljubic H, et al. Variants of ESR1, APOE, LPL and IL-6 loci in young healthy subjects: association with lipid status and obesity. *BMC Res Notes*. 2009;2(1):203.
26. Asadi Z, Shafiee M, Sadabadi F, et al. Association of dietary patterns and risk of cardiovascular disease events in the MASHAD cohort study. *J Hum Nutr Diet*. 2019;32:789-801.
27. Asadi Z, Shafiee M, Sadabadi F, et al. Association of dietary patterns and the risk of metabolic syndrome among Iranian population: a cross-sectional study. *Diabetes Metab Syndr*. 2019;13(1):858-865.
28. Collaboration, Asia Pacific Cohort Studies. Body mass index and cardiovascular disease in the Asia-Pacific Region: an overview of 33 cohorts involving 310 000 participants. *Int J Epidemiol*. 2004;33(4):751-758.
29. Whitlock G, Lewington S, Sherliker P, et al. Prospective studies collaboration: body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet*. 2009;373(9669):1083-1096.
30. Mandviwala T, Khalid U, Deswal A. Obesity and cardiovascular disease: a risk factor or a risk marker? *Current Atherosclerosis Reports*. 2016;18(5):21.
31. Dirk De B, Dallongeville J, Heidrich J, et al. Management of overweight and obese patients with coronary heart disease across Europe. *Eur J Cardiovasc Prev Rehabil*. 2010;17(4):447-454.
32. Bhatt DL, Steg PG, Ohman EM, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA*. 2006;295(2):180-189.
33. Rost S, Freuer D, Peters A, et al. New indexes of body fat distribution and sex-specific risk of total and cause-specific mortality: a prospective cohort study. *BMC Public Health*. 2018;18(1):427.
34. van den Munckhof ICL, Holewijn S, de Graaf J, Rutten JHW. Sex differences in fat distribution influence the association between BMI and arterial stiffness. *J Hypertens*. 2017;35(6):1219-1225.
35. Yin D, Yan Y, Xu N, et al. Predictive values of obesity categories for cardiovascular disease risk factors in Chinese adult population. *J Cell Biochem*. 2018;2(10):28002.
36. Soriano-Maldonado A, Aparicio VA, Felix-Redondo FJ, Fernandez-Berges D. Severity of obesity and cardiometabolic risk factors in adults: Sex differences and role of physical activity. The HERMEX study. *Int J Cardiol*. 2016;223:352-359.

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