Predictive ability of six obesity measures to identify 7-year fatal and non-fatal cardiovascular events: A population-based cohort study

Nima Motamed, Farzin Roozafzai, Mahmood Reza Khoonsari, Mojtaba Malek, Alborz Mahdavi, Mansooreh Maadi, Maral Ahmadi, Mohammad Hadi Karbalaei Niya, Mohammad Reza Babaei, Fahimeh Safarnezhad Tameshkel, Amir Hossein Faraji, Mehdi Nikkhah, Ramin Ebrahimi, Hossein Ajdarkosh, Farhad Zamani

**ABSTRACT**

**Background:** Globally, most people die from cardiovascular diseases. We aimed to compare predictive ability of six obesity indices, including body mass index, waist circumference, waist-to-hip ratio, waist-to-height ratio, conicity index, and abdominal volume index, to identify people at risk of fatal and non-fatal cardiovascular events in a cohort study.

**Methods:** We studied 5147 participants in a baseline population-based cohort study conducted in northern Iran. The obesity measures were calculated in enrollment phase (2009–2010), and the cardiovascular events were recorded during a 7-year follow-up phase (2010–2017). Receiver operating characteristic (ROC) analyses and Cox hazard regression models were applied, considering the obesity measures as predictors, and the 7-year cardiovascular events as outcomes. Multiple Cox models were adjusted by age, prior history of cardiovascular diseases, chronic kidney diseases, insulin resistance, diabetes mellitus, dyslipidemia, hypertension, and smoking status.

**Results:** Conicity index showed the highest performance in predicting 7-year fatal and non-fatal cardiovascular events with areas under the ROC curve of 0.77 [95% confidence interval: 0.71–0.82], and 0.63 [0.59–0.68] in men, and 0.80 [0.74–0.87], and 0.65 [0.60–0.71] in women, respectively. In multiple Cox models, the obesity measures had no significant associations with cardiovascular events in women. In men, only waist-to-height ratio was independently associated with 7-year non-fatal cardiovascular events (hazard ratio: 1.19 [95% confidence interval: 1.01–1.38]).

**Conclusions:** Although waist-to-height ratio had an independent association with 7-year non-fatal cardiovascular events in men, conicity index showed the best ability to predict 7-year fatal and non-fatal cardiovascular events in our study.

**ARTICLE INFO**

**Keywords:**
Cardiovascular disease
Obesity
Predictive ability

**Corresponding author.** Gastrointestinal and Liver diseases Research Center, Iran University of Medical Sciences, Firoozgar Hospital, Beh-Afarin St., Karim Khan Zand Ave., 1593748711, Tehran, Iran.

**E-mail addresses:** nima.motamed@gmail.com (N. Motamed), farzin.roozafzai@gmail.com (F. Roozafzai), khonsarimahmoodreza@gmail.com (M.R. Khoonsari), malekmoj@gmail.com (M. Malek), alborz_mahdavi@yahoo.com (A. Mahdavi), maadi_mansooreh@yahoo.com (M. Maadi), ahmadimaral42@gmail.com (M. Ahmadi), karbalaei.mh@iумs.ac.ir (M.H. Karbalaei Niya), doctorreza2012@yahoo.com (M.R. Babaei), fahimeh.1615@yahoo.com (F. Safarnezhad Tameshkel), amir.hfaraji6@gmail.com (A.H. Faraji), nikkhahmd@yahoo.com (M. Nikkhah), ebrahimih.r@iums.ac.ir (R. Ebrahimih), ajdarkosh.h@iums.ac.ir (H. Ajdarkosh), zamani.f@iums.ac.ir (F. Zamani).

**This author takes the responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.**

https://doi.org/10.1016/j.ijcrp.2022.200142

Received 28 February 2022; Received in revised form 17 June 2022; Accepted 22 June 2022

Available online 1 July 2022
1. Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide [1,2]. Although the incidence of CVDs has recently decreased in western countries due to effective preventive measures and appropriate therapeutic interventions, this decrease did not occur in low- and middle-income countries [3,4], such as Iran, which is facing a high prevalence of CVDs [5].

Owing to its health and socioeconomic burdens, obesity is an important public health problem regarded as the “21st century’s epidemic” by the World Health Organization. It is estimated that one billion adults are obese or overweight worldwide [6,7]. Obesity has strong associations with some important risk factors of CVDs, including hypertension, diabetes mellitus, and metabolic syndrome; and, it is considered a common risk factor for cardiovascular events [8–11]. Several indices have been used for measuring obesity, of which body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) are more popular. Conicity index and abdominal volume index (AVI) are also suggested in this context [12–14].

Using the data of a large population-based cohort study in northern Iran, we previously evaluated discriminative ability of those indices (except BMI) to detect individuals with higher 10-year CVD risks estimated by Framingham risk score (FRS), and pooled cohort equations of the American College of Cardiology and the American Heart Association (ACC/AHA) tool [15]. According to the results and compared with the other indices, conicity index, and WHR showed a better discriminatory ability to diagnose individuals with higher 10-year CVD risks [15]. Since then, we have followed up the cohort for seven years and recorded fatal and non-fatal cardiovascular events. The present study aimed to compare the ability of six obesity measures, including BMI, WC, WHR, WHtR, conicity index, and AVI, to predict fatal and non-fatal cardiovascular events in northern Iranian men and women.

2. Materials and methods

2.1. Design

In the present observation, we used the data of 5147 participants (2926 men, and 2221 women) in a baseline population-based cohort study conducted in Amol, a city in northern Iran, mainly to assess obesity and obesity-related diseases. This study is approved by research ethics committee of Iran University of Medical Sciences, Tehran, Iran (reference number: IR.IUMS.REC.1397.162). Abiding the Declaration of Helsinki, using stratified random sampling method, and after obtaining informed consents, we enrolled 5799 participants aged 18–89 years in the baseline cohort (2009–2010). Sampling frame was obtained from primary healthcare settings, where each registered resident had a health record. Target population was stratified into 16 subgroups based on sex and age groups with 10-year intervals (from 10 to 19 to 80–89 years). Participants were randomly and size-proportionally selected from each stratum.

We followed up the participants, both actively (annual) and passively (self-reports), for seven years (2010–2017), and recorded the incidence of cardiovascular events, including hospitalization due to myocardial infarction or other CVDs, angiographically proven coronary artery diseases, percutaneous coronary interventions, cerebrovascular accidents, and CVD-related death. We contacted with the deceased participants’ family members or caregivers to specify the cause of death. We confirmed the outcomes and verified self-reports by direct observation of medical documents, death certificates, and hospital records. After seven years (2016–2017), we conducted the repeated measurement phase. We also compared the annual follow-up data with the data of repeated measurements and verified the outcomes if there was any inconsistency. Supplementary Fig. 1 displays a schematic flowchart of the study.

2.2. Measurements

For all participants, demographic (age, sex, and smoking habit), anthropometric, and laboratory data have been collected in the enrollment and the repeated measurement phases. Trained staff measured weight, height, WC, hip circumference, and blood pressure of each participant according to the standard protocols. Before measuring, the participant was asked to remove the excess clothes and shoes.

Weight was measured using a digital scale (seca GmbH & Co.KG, Hamburg, Germany) placed on a horizontal hard surface. The scale was calibrated daily using standard weights. Height was measured in an upright position, where head, shoulders, buttocks, and heels of the participant were pressed up against a wall, using a wall-mounted manual stadiometer (seca GmbH & Co.KG, Hamburg, Germany). WC was measured at the midpoint between the lowest costal ridge and the upper border of the iliac crest. Hip circumference was the largest horizontal measurement between waist and knee. Obesity indices other than WC were calculated using the following formulae:

\[
BMI = \frac{\text{Weight (kg)}}{\text{Height}^2 (\text{m})}
\]

\[
WHR = \frac{\text{WC (cm)}}{\text{Hip circumference (cm)}}
\]

\[
\text{Conicity index} = \frac{\text{WC (cm)}}{0.109 \times \sqrt{\frac{\text{Weight (kg)}}{\text{Height (m)}}}}
\]

\[
\text{AVI} = \left(\frac{\text{Hip circumference (cm)}}{0.7 \times \text{WC (cm)}}\right)^2 / 1000
\]

Blood pressure was measured twice, using a calibrated mercury sphygmomanometer (Riester GmbH, Jungingen, Germany), following at least 5 min of rest in a sitting position. Systolic and diastolic blood pressures were determined based on the Korotkoff sounds. The average of two measurements was considered the participant’s blood pressure.

Following 12-h fasting, a 10 ml whole blood sample was obtained from each participant and kept in a serum separator tube. All laboratory tests, including fasting blood sugar (FBS), insulin, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and total cholesterol were assessed enzymatically using a BS200 Auto-Analyzer (Mindray, Shenzhen, China) and

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**Abbreviations**

- ACC: American college of cardiology
- AHA: American heart association
- AUC: area under the ROC curve
- AVI: abdominal volume index
- BMI: body mass index
- CI: confidence interval
- CVD: cardiovascular disease
- ECG: standard 12-lead electrocardiogram
- FBS: fasting blood sugar
- FRS: Framingham risk score
- HDL-C: high-density lipoprotein cholesterol
- HOMA-IR: homeostatic model assessment for insulin resistance
- LDL-C: low-density lipoprotein cholesterol
- n: count
- RM: repeated measurement
- ROC: receiver operating characteristic
- WC: waist circumference
- WHR: waist-to-hip ratio
- WHtR: waist-to-height ratio
diagnostic kits (Pars Azmoon Co., Tehran, Iran).

We also provided a standard 12-lead electrocardiogram (ECG) for each participant in the repeated measurement phase. An internist interviewed 21 participants showing ECG abnormalities whose data were not included as outcomes, and referred them to a cardiologist for evaluating the probable silent cardiovascular events.

2.3. Statistical methods

We reported the data through descriptive statistics (mean and standard deviation, and frequency distribution and confidence interval (CI)). We appropriately used independent samples t-test or non-parametric Mann-Whitney test to compare the study groups. Two-group proportion test was performed to compare the incidences of cardiovascular events between men and women.

To determine the predictive ability of the six obesity indices measured in 2010 (BMI, WC, WHR, WHR, conicity index, and AVI), we performed receiver operating characteristic (ROC) analyses for fatal and non-fatal cardiovascular events (evaluated from 2010 to 2017) as reference variables. Areas under the ROC curves (AUCs) were reported. Statistically significant AUCs greater than 0.5 implied the ability to discriminate the individuals with cardiovascular events from event-free individuals, ranging from poor (0.5 < AUC<0.7) to outstanding ability (0.9 = AUC<1) [16].

We also applied simple and multiple Cox hazard regression proportion models considering the six obesity indices (BMI, WC, WHR, WHR, conicity index, and AVI) as predictors, and fatal and non-fatal cardiovascular events as outcomes. In multiple Cox regression models, we entered age, HDL-C, LDL-C, homeostatic model assessment for insulin resistance (HOMA-IR), diabetes mellitus, hypertension, prior history of CVDs, history of chronic kidney diseases, and smoking status as potential mediators, in addition to entering the obesity measures. Hazard ratios were reported.

We used STATA v.12 (StataCorp LLC, College Station, TX, USA) to estimate AUCs and plot ROC curves, and SPSS v.21 (SPSS Inc., Chicago, IL, USA) to conduct survival analyses and apply regression models. The significance level in all analyses was 0.05.

3. Results

Based on our observation, while the incidence of fatal cardiovascular events was not statistically different (p-value = 0.142) between men (44 cases, 1.50% [95% CI: 1.06%–1.94%]) and women (23 cases, 1.04% [0.61%–1.46%]), the incidence of non-fatal cardiovascular events was significantly higher (p-value = 0.004) in men (150 cases, 5.13% [4.33%–5.93%]) than in women (77 cases, 3.46% [2.71%–4.22%]).

Table 1 represents the basic characteristics of men and women in this observation. While the mean age, weight, height, WHR, conicity index, and blood pressures were significantly higher in men (largest p-value = 0.022), hip circumference, BMI, WHR, AVI, FBS, total cholesterol, HDL-C, and LDL-C were significantly higher in women (largest p-value = 0.004). No significant differences of mean WC and triglycerides were observed between men and women.

Table 2 shows the mean and related standard deviation of obesity measures in men and women who experienced at least one incident cardiovascular event and those who were event-free. Obesity measures other than BMI were significantly higher in individuals with cardio vascular events in men and women. Conicity index showed the highest performance for fatal, and non-fatal cardiovascular events with AUCs of 0.77 [95% CI: 0.71–0.82], and 0.63 [0.59–0.68] in men, and 0.80 [0.74–0.87], and 0.65 [0.60–0.71] in women, respectively.

Table 3 shows the performance of six obesity measures in predicting 7-year fatal and non-fatal cardiovascular events in men and women. Conicity index showed the highest performance for fatal, and non-fatal cardiovascular events with AUCs of 0.77 [95% CI: 0.71–0.82], and 0.63 [0.59–0.68] in men, and 0.80 [0.74–0.87], and 0.65 [0.60–0.71] in women, respectively.

Table 4 reports the results of simple and multiple Cox hazard regression proportion models in which fatal and non-fatal cardiovascular events were considered as outcomes. Based on simple models, all obesity measures had a significant association with fatal and non-fatal cardiovascular events, except BMI that showed a significant relationship only with non-fatal cardiovascular events in men. In multiple regression models, no obesity measure showed any associations with fatal or non-fatal cardiovascular events, except WHR that was significantly associated with non-fatal cardiovascular events in men (hazard ratio: 1.19 [95% CI: 1.01–1.38]).

4. Discussion

We evaluated the ability of six obesity measures, including BMI, WC, WHR, WHR, conicity index, and AVI, to predict fatal and non-fatal cardiovascular events in northern Iranian men and women. The results showed that all the indices, except BMI, are able to predict fatal and non-fatal cardiovascular events. Among the evaluated indices, conicity index showed the strongest ability both in men and in women, where the AUC of conicity index in the diagnosis of fatal cardiovascular events was in lower threshold of excellent discrimination based on Hosmer-Lemeshow’s rule of thumb [16].

Overall, the predictive ability of the obesity measures was better for fatal cardiovascular events than for non-fatal cardiovascular events, and also better in women than in men. It is previously shown that conicity index and WHR had a better ability to discriminate individuals with a higher 10-year CVD risk estimated by FRS and ACC/AHA tools [15]. None of these two tools include obesity as a measure of 10-year CVD risk estimation.

Except for an independent relationship between non-fatal cardiovascular events and WHR in men, our multiple Cox regression models did not yield any independent association between cardiovascular events and obesity measures after removing the potential confounders, including age, history of CVDs and chronic kidney diseases, insulin resistance, diabetes mellitus, dyslipidemia, hypertension, and smoking status. Gelber and colleagues found that WHR, compared with BMI, WC, and WHR, represents the strongest association with CVDs [17]. Emerging Risk Factors Collaboration reported that obesity measures, such as BMI, WC, and WHR, do not significantly improve the prediction of CVDs when additional data pertaining diabetes mellitus, lipid
The predictive ability of six obesity measures, in terms of the area under the receiver operating characteristic curve, for 7-year fatal and non-fatal cardiovascular events was evaluated. Table 3 compiles the results for men and women.

### Table 3
The predictive ability of six obesity measures are not consistent. While some studies reported that WC had a better ability to predict CVDs, others showed no significant difference from WHR or WHtR. BMI showed a poor predictive ability for non-fatal cardiovascular events and WC had a better ability for fatal events.

### Table 2
Obesity measures in men and women who did or did not experience cardiovascular events during seven years.

| Obesity measure [unit] | Fatal event | Non-fatal event |
|------------------------|-------------|-----------------|
|                        | No | Yes | Mean ± Standard deviation | p-value | No | Yes | Mean ± Standard deviation | p-value |
| **Men (n = 2926)** | | | | | | | | |
| BMI [kg/m²]          | 26.53 ± 4.62 | 26.62 ± 3.22 | 0.901 | 26.48 ± 4.60 | 27.53 ± 4.52 | 0.006 |
| Waist circumference [cm] | 90.75 ± 12.46 | 95.45 ± 8.96 | 0.001 | 90.63 ± 12.44 | 94.37 ± 11.61 | <0.001 |
| WHR                   | 0.89 ± 0.08 | 0.95 ± 0.06 | <0.001 | 0.89 ± 0.08 | 0.93 ± 0.08 | <0.001 |
| WHR                   | 0.53 ± 0.07 | 0.57 ± 0.07 | <0.001 | 0.53 ± 0.07 | 0.56 ± 0.07 | <0.001 |
| Conicity index [m³/²·kg¹/²] | 1.24 ± 0.09 | 1.32 ± 0.07 | <0.001 | 1.24 ± 0.09 | 1.28 ± 0.08 | <0.001 |
| AVI [cm³]             | 16.90 ± 4.59 | 18.42 ± 3.49 | 0.006 | 16.86 ± 4.58 | 18.15 ± 4.31 | 0.001 |
| **Women (n = 2221)** | | | | | | | | |
| BMI [kg/m²]          | 29.64 ± 5.66 | 31.18 ± 6.29 | 0.190 | 29.63 ± 5.67 | 30.53 ± 5.71 | 0.175 |
| Waist circumference [cm] | 91.41 ± 13.40 | 98.69 ± 12.31 | 0.009 | 91.34 ± 13.41 | 95.65 ± 12.59 | 0.006 |
| WHR                   | 0.85 ± 0.08 | 0.92 ± 0.05 | <0.001 | 0.85 ± 0.08 | 0.89 ± 0.07 | <0.001 |
| WHR                   | 0.58 ± 0.09 | 0.66 ± 0.08 | <0.001 | 0.58 ± 0.09 | 0.62 ± 0.09 | <0.001 |
| Conicity index [m³/²·kg¹/²] | 1.23 ± 0.10 | 1.33 ± 0.05 | <0.001 | 1.23 ± 0.10 | 1.29 ± 0.09 | <0.001 |
| AVI [cm³]             | 17.29 ± 5.04 | 19.84 ± 5.14 | 0.027 | 17.26 ± 5.05 | 18.75 ± 4.66 | 0.011 |

AVI: abdominal volume index, BMI: body mass index, n: count, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio.

Independent samples t-test; significance level is 0.05.

Among various obesity indices, WHtR is a unique index which adjusts WC, a measure of central obesity, by height, an unchanging anthropometric measure in adults. In concinity index, WC is adjusted by the square root of weight-to-height ratio, and not directly or solely by height. However, this study was not conducted to evaluate the role of obesity in CVDs, but mainly aimed to find the obesity indices with the strongest ability to predict CVDs. This predictive ability could be mediated by many CVD risk factors affected by obesity. These mediators are not generally the case for evaluation of an index in clinical practice, when a simple, cost-effective, and affordable index can correctly represent them in predicting the clinical outcomes.

There are several mechanisms explaining the link between obesity and cardiovascular events. Insulin resistance in obesity might lead to development of CVDs through inflammation and oxidative stress [23–25]. Furthermore, obesity has relationships with some abnormalities in ECG, such as prolonged QT interval, and left ventricular hypertrophy through uncontrolled hypertension [26]. Increase in inflammatory cytokines, leptin levels, free fatty acids turnover, basal sympathetic tone, and prothrombotic state are the other possible mediators for obesity-related cardiovascular events [27–31].

Based on our observation, conicity index could predict cardiovascular events better than the other five indices, both in men and in women. Although no sex-discriminating body shape measure is included in its formula, three measures, including weight, and two measures of body frames (WC, and height), are used for calculating concinity index. This index was theoretically suggested as a volume model, in which, in addition to a specific emphasis on the expansion of abdominal region, weight is incorporated [13,14]. In fact, among various abdominal measures, only concinity index encompasses weight. Considering the strong ability of concinity index to predict fatal cardiovascular events, routine calculation of this index in cardiology settings might be valuable.

Based on our results, BMI did not have any predictive ability. While BMI showed a poor predictive ability for non-fatal cardiovascular events in men, it did not show any ability for other cases in this study. BMI is usually considered as an index for general obesity, and not for central obesity. Regarding BMI, some studies even reported an obesity paradox, i.e., an inverse relationship was suggested between BMI and mortality rate of CVDs. While almost consistent results are available for outcomes of heart failure and revascularization following ischemic heart diseases and obesity, the results are inconsistent in other cases [32–34].

Findings about the predictive ability of obesity indices are not consistent. While some studies reported that WC had a better ability than other indices to predict CVDs, other studies reported a higher ability of WHR or WHtR [17,21,35–39]. However, only few studies have evaluated the performance of concinity index.

We evaluated the ability of six obesity measures to predict the...
occurrence of cardiovascular events in a large population-based study on northern Iranians and found that conicity index had the highest performance in this context. Although calculating the conicity index seems relatively more complicated than the other indices, and three anthropometric measures are incorporated in its formula, an acceptable or even excellent performance of conicity index implies its value in clinical settings. In fact, this index just need one measure (WC) more than BMI, does, and can be calculated with a simple calculator. Although an obesity paradox of BMI in cardiovascular events could not be confirmed in our population, BMI was not found to be a reliable index for evaluation of individuals at risk of CVDs.

4.1. Study limitations

This study had some drawbacks. There was no baseline ECG data, and consequently, the pertinent data could not be compared between the enrollment and repeated measurement phases. Thus, participants with a history of silent myocardial infarction during 7-year follow-up could be missed; however, some of these cases might experience the related events prior to the repeated measurements. On the other hand, an internist interviewed and evaluated a few participants without any apparent history of cardiovascular events who showed ECG abnormalities in the repeated measurements. These participants were also referred to a cardiologist to exclude the probable silent cardiovascular events in the 7-year follow-up as a result of diabetes mellitus, aging, or other associated causes. It is worth noting that scenario analysis based on inclusion and exclusion of these few cases did not cause any significant and reportable change in our main findings.

4.2. Conclusions

While WHtR showed an independent association with non-fatal cardiovascular events in northern Iranian men, conicity index had the highest performance in predicting fatal and non-fatal cardiovascular events in our study. Calculating conicity index only requires three simple and available popular anthropometric measures. Conicity index might be a valuable obesity measure, particularly preferred in clinical cardiology settings.

CRediT author statement

Nima Motamed: Conceptualization, Methodology, Formal analysis, Writing-original draft, Writing-review & editing, Final approval.

Mahmood Reza Khoonsari: Investigation, Validation, Writing-review & editing, Final approval.

Fahimeh Safarinejad Tameshkel: Investigation, Writing-original draft, Writing-review & editing, Final approval.

Maral Ahmadi: Investigation, Writing-review

Mansooreh Maadi: Investigation, Data Curation, Writing-review & editing, Final approval.

Ramin Ebrahimi: Investigation, Validation, Writing-review & editing, Final approval.

Amir Hossein Faraji: Investigation, Validation, Writing-review & editing, Final approval.

Fahimeh Safarinejad Tameshkel: Investigation, Writing-review & editing, Final approval.

Ramin Ebrahimi: Investigation, Validation, Writing-review & editing, Final approval.

Mansooreh Maadi: Investigation, Data Curation, Writing-review & editing, Final approval.

Maral Ahmadi: Investigation, Validation, Writing-review & editing, Final approval.

Mehdi Nikkhah: Investigation, Validation, Writing-review & editing, Final approval.

Amir Hossein Faraji: Investigation, Validation, Writing-review & editing, Final approval.

Mansooreh Maadi: Investigation, Data Curation, Writing-review & editing, Final approval.

Fahimeh Safarinejad Tameshkel: Investigation, Writing-review & editing, Final approval.

Ramin Ebrahimi: Investigation, Validation, Writing-review & editing, Final approval.

Mansooreh Maadi: Investigation, Data Curation, Writing-review & editing, Final approval.

Nima Motamed: Conceptualization, Methodology, Formal analysis, Writing-original draft, Writing-review & editing, Final approval.

Farzin Roozafzai: Methodology, Formal analysis, Writing-original draft, Writing-review & editing, Final approval.

Funding

This work was supported by Iran University of Medical Sciences, Tehran, Iran [grant number 1397-2-30-12315].

Data availability

The data is available from the corresponding author on reasonable request.

Declaration of competing interest

None.
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcrp.2022.200142.

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