



Comparing the power of obesity indices to predict cardiovascular diseases at different ages: An application of conditional time-dependent ROC curve in Healthy Heart Cohort of Yazd, Iran

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Abstract

BACKGROUND: This study was conducted to estimate the power of anthropometric markers to predict 10-year CVD across different age groups in the Yazd Healthy Heart cohort.

METHODS: A total of 1,623 individuals aged 20 to 74, who were free of CVD, participated in the study. A conditional time-dependent receiver operating characteristic (ROC) curve was used to estimate the predictive power of anthropometric indices, including the Abdominal Volume Index (AVI), Body Adiposity Index (BAI), and Waist-to-Height Ratio (WHtR), adjusted for age and sex.

RESULTS: Of the 1,623 participants, 818 were males (50.40%) and 805 were females (49.60%). The Area Under the Curve (AUC) for the BAI ranged from 0.50 to 0.70 for males aged 40 to 70 years. In females, the BAI biomarker demonstrated considerable to excellent predictive power (AUC > 0.8) for individuals aged 20 to approximately 33 years. For males, AVI and WHtR showed fair to considerable predictive power in participants aged 20 to 30 years. In the age group of 30 to approximately 68 years, the predictive power varied from poor to ineffective, except for individuals close to 50 years old. In females, the predictive power of the AVI and WHtR biomarkers ranged from fair to considerable for those aged 20 to around 33 years.

CONCLUSION: This study found that AVI and WHtR can fairly predict 10-year CVD risk in young individuals of both sexes, while the BAI was specifically applicable for predicting risk in young women. These markers are valuable and affordable tools for youth CVD screening.

Keywords: Cardiovascular Diseases; Anthropometry; ROC Curve; Time-Dependent ROC; Healthy Heart Cohort

Introduction

Globally, cardiovascular diseases (CVDs), such as ischemic heart disease, stroke, heart failure, peripheral arterial disease, and numerous other heart- and blood-vessel-related ailments, continue to be the primary cause of death and untimely demise, even with advancements in accessible prevention methods^{1,2}. An estimated 17.8 million deaths, 330 million years of life lost, and 35.6 million years lived with disability around the world in 2017 can be attributed to CVD. According to the literature, CVDs are the cause of nearly 80% of deaths in middle- and low-income countries, especially in the Eastern Mediterranean Region (EMR)^{2,3}. In these countries, the ongoing epidemiological transition has increased the CVD and risk factor burden². Even though CVD significantly contributes to the disease burden in high-income countries, the rates of age-adjusted mortality have significantly decreased in several developed countries in recent decades⁴. In 2019, out of the global 18.6 million CVD-related fatalities, a significant 58% occurred in Asia¹. CVD remains the most prevalent cause of death in Iran⁴. Based on the GBD 2015, Iran was among the countries with the highest worldwide CVD rates, with more than 9,000 cases of CVD per 100,000 persons³. Within the EMR, Iran holds a significant position regarding the elevated prevalence of CVD⁵. Considering that over 75% of early CVDs are preventable⁶, controlling potential risk factors such as blood pressure (BP), cholesterol, diabetes, smoking, and overweight can reduce the prevalence of CVD and its burden⁷. Although aging is the most significant factor contributing to the heightened risk of CVD, more than 60% of individuals who suffer from CVD are younger than 65 years old⁸. Furthermore, due to sex differences in lifestyle and environmental exposures, inequalities in healthcare, and/or biological differences, there are substantial differences between the two sex groups in terms of the prevalence, treatment, and control of CVD risk factors⁷.

The significance of obesity as a contributing factor to CVD has been thoroughly evaluated. Scientific evidence demonstrates that a sedentary lifestyle increases the risk of coronary heart disease, such that inactive people are twice as likely to contract this

disease compared to active individuals. Considering that obesity is known as the main cause of type 2 diabetes, CVDs, and many metabolic diseases, it is important to identify accurate indicators for diagnosing obesity. Body measurements are helpful tools for evaluating health and dietary status, diagnosing obesity, and assessing future disease risk in adults⁹. There is a wide range of methods for determining body fat. Although most are laboratory-based methods, some simpler measurement methods also exist. The disadvantages of methods such as skinfold thickness measurement include being time-consuming and requiring experienced professionals to perform them, making them unsuitable for clinical purposes and demographic studies¹⁰. As obesity rates continue to rise due to the industrialization of societies and the mechanization of people's lives, identifying reliable and efficient screening tools that are simple, inexpensive, and non-invasive is necessary for properly screening for chronic disease risk factors, such as CVDs, in each society¹¹.

To use a biomarker in clinical settings, it is necessary to assess its predictive power. The ROC curve (Receiver Operating Characteristic curve) is a tool that is useful for evaluating the diagnostic accuracy of a biomarker¹². The ROC curve describes the ability of the biomarker to distinguish between sick and healthy groups, which are specified by reference standards. On the one hand, in some medical studies, the condition of an individual may change over time. In such cases, it may not be appropriate to differentiate between individuals experiencing the event of interest before a specific time " t " and those encountering it after time " t ," regardless of time, because the disease status can only be determined in relation to a specific time point. Individuals who have not previously had the disease may develop it later as a result of long-term follow-up, and their marker values may also change during follow-up from baseline. Therefore, in such cases, it is more appropriate to consider the ROC curve as a function of time. On the other hand, the predictive power of biomarkers can sometimes be affected by variables such as the patient's age, necessitating the consideration of influential covariates in ROC analysis¹³.

Targeting individuals at great risk of developing CVD for lifestyle modification or pharmaceutical interventions is a fundamental step in primary prevention care programs¹⁴. To date, numerous studies have explored the relationship between CVD risk and anthropometric indicators¹⁵⁻¹⁷. Since the performance and diagnostic power of these indices may be influenced by factors such as age, and considering the effect of time until the occurrence of CVD leads to a more accurate prediction, conditional time-dependent ROC curve analysis was employed in the current study to evaluate the predictive power of anthropometric indicators (Abdominal Volume Index (AVI), Body Adiposity Index (BAI), and Waist-to-Height Ratio (WtHR)) in predicting the risk of CVD among 20–74-year-old Iranian adults.

Methods

Study design and population

The Yazd Healthy Heart Study (YHHS) was a community-based prospective cohort study initiated during 2005–2006, involving 2,000 urban residents of Yazd, aged between 20 and 74 years, selected using the cluster sampling method. From 2015 to 2016, participants were re-invited for follow-up evaluation by the Yazd Cardiovascular Research Center via telephone calls¹⁸.

Sample size and participants

Of the 2000 individuals who participated in this study, 116 participants with a prior history of CVD at baseline and 261 participants whose information was not completed were excluded from the study.

Ethics approval and consent to participate

Ethical clearance to carry out the project (ID:13212) was obtained from the Ethics Committee of Shahid Sadoughi Yazd University of Medical Sciences (IR.SSU.SPH.REC.1401.053). All the participants who met the inclusion criteria provided oral and written informed consent. All methods were carried out following relevant guidelines and regulations.

Anthropometric measurement

Adhering to a standardized protocol, trained observers meticulously assessed anthropometric

parameters, including height, weight, hip circumference (HC), and waist circumference (WC). Height was measured while the participant stood without shoes in a standardized position with shoulders in normal alignment. To accurately measure weight, a digital scale with a precision of 0.1 kg was used. WC was measured at a point midway between the lower rib margin and the iliac crest, ensuring no pressure on the body surface. HC was measured at the level of maximal gluteal protrusion over light clothing¹⁹. To predict CVD, AVI and BAI were calculated based on the following formula:

$$AVI = \left[2WC^2 (\text{cm}) + 0.7(WC - HC)^2 \right] / 1000$$

$$BAI = \left[\frac{HC(m)}{height(m)^{2/3}} \right] - 18$$

Outcome measurement

The information, including previous CVD history, medications being utilized, and details related to CVD diagnosis and treatment, was collected from participants by a trained interviewer. We considered each of the following items as an incidence of CVD: (1) individuals with coronary artery bypass graft (CABG), (2) individuals with percutaneous coronary intervention (PCI), (3) individuals with myocardial infarction (MI), (4) individuals with a Rose Angina Questionnaire (RAQ) (chest pain) score greater than 3, and (5) individuals with electrocardiographic (ECG) changes in favor of CAD. Censored subjects are those who did not experience CVD within the follow-up period. Since the time to CVD incidence is important, the time from inclusion in the study to CVD incidence was recorded for each individual during the 10-year follow-up period¹⁹.

Statistical analysis

To estimate the predictive power of biomarkers 120 months after the study started, over different ages, AUC (Area Under the ROC Curve) was calculated based on the conditional time-dependent ROC curve. The predictive power of a biomarker is classified as excellent for AUC values between 0.90 and 1, considerable for AUC values between 0.80

and 0.90, fair for AUC values between 0.70 and 0.80, poor for AUC values between 0.60 and 0.70, and failure for AUC values between 0.50 and 0.60²⁰. The analysis was conducted using the CondTimeROC package in RStudio software (version 1.4.1717).

Results

Of the 1,623 participants, 818 (50.40%) were males, and 805 (49.60%) were females. The mean (Standard Deviation (SD)) age was 48.13 (14.89). The baseline mean (SD) values of AVI, BAI, and WHtR for participants were 17.95 (4.51), 30.80

(60.37), and 0.56 (0.08), respectively. Among the 101 (6.2%) individuals who experienced CVD during the 10-year follow-up, 59 (58.42%) were males. Baseline characteristics of women and men, including demographic variables, anthropometric variables, and laboratory measures, are presented in Table 1 by CVD status.

The predictive power of the studied anthropometric markers to predict 10-year CVD risk was estimated after adjusting for age in both sex groups. Figure 1 illustrates the estimated AUC of BAI by gender at different ages.

Table 1. Baseline characteristics of women and men participated in Healthy Heart Cohort by CVD status

Characteristics	Male		Female	
	CVD cases (n=59)	Normal (n=759)	CVD cases (n=42)	Normal (n=763)
Demographic, N(%)				
Age groups				
20-44 years	3(0.90)	336(99.10)	2(0.60)	328(99.40)
45-64 years	29(8.80)	300(91.20)	19(5.60)	320(94.40)
65-74 years	27(18)	123(82)	21(15.40)	115(84.60)
Marital Status				
Married	57(7.70)	686(92.30)	34(4.90)	661(95.10)
Single	0(0)	65(100)	0(0)	14(100)
Divorced/widowed	1(14.30)	6(85.70)	8(8.30)	88(91.70)
Anthropometric, Mean (SD)				
Weight (kg)	74.73(13.15)	74.27(12.12)	66.48(11.10)	68.45(13.87)
Height (cm)	167.54(15.61)	171.86(10.08)	156.23(7.26)	157.89(7.38)
WHtR	0.57(0.06)	0.54(0.06)	0.61(0.07)	0.59(0.08)
BAI	28.51(4.45)	26.84(4.20)	34.81(5.22)	34.69(5.80)
AVI	19.42(4.54)	17.65(4.23)	18.86(4.06)	18.09(4.77)
Laboratory, Mean (SD)				
FBS	110.97(52.09)	99.59(38.64)	133.45(68.72)	101.69(46.59)
TG	175.32(83.66)	178.70(114.89)	208.31(83.05)	169.79(105.07)
CHOL	203.58(33.39)	190.27(41.69)	27.76(35.03)	205.12(78.11)
LDL	113.78(29.17)	102.93(35.50)	124.29(30.07)	112.08(37.05)
HDL	53.19(12.43)	51.82(13.17)	58.33(13.51)	56.05(13.78)

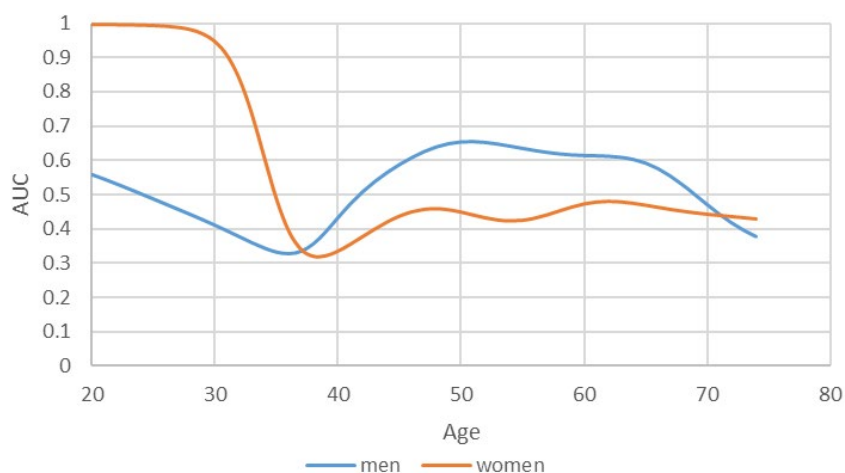


Figure 1. Estimated time-dependent AUC of the BAI biomarker adjusted by age for male and female

The predictive power of the BAI biomarker shows a downward trend and fails to predict CVD in males aged 20 to nearly 40 years. Based on this figure, the AUC of this biomarker ranges approximately between 0.50 and 0.70 for individuals aged 40 to nearly 70 years. Additionally, it is observed that, in females, the BAI biomarker demonstrates considerable to excellent predictive power (AUC > 0.8) for individuals aged 20 to approximately 33 years. After the age of 35, the AUC for this biomarker drops below 0.5. Overall, this biomarker performs best for males aged 40 to 70 years and females aged 20 to 33 years.

Figures 2 and 3 show the estimated AUC of AVI and WHtR for males and females at different ages. In males, these biomarkers demonstrate fair to considerable predictive power in participants aged 20 to 30 years. Between the ages of 30 and approximately 68 years, this predictive power varies from poor to failure, except for individuals around 50 years old. The AUC drops below 0.50 after the age of 68. It is also observed that, in females, the predictive power of the AVI and WHtR biomarkers is fair to considerable for individuals aged 20 to approximately 33 years. Overall, these biomarkers fail to predict CVD in females aged 35 to 74 years.

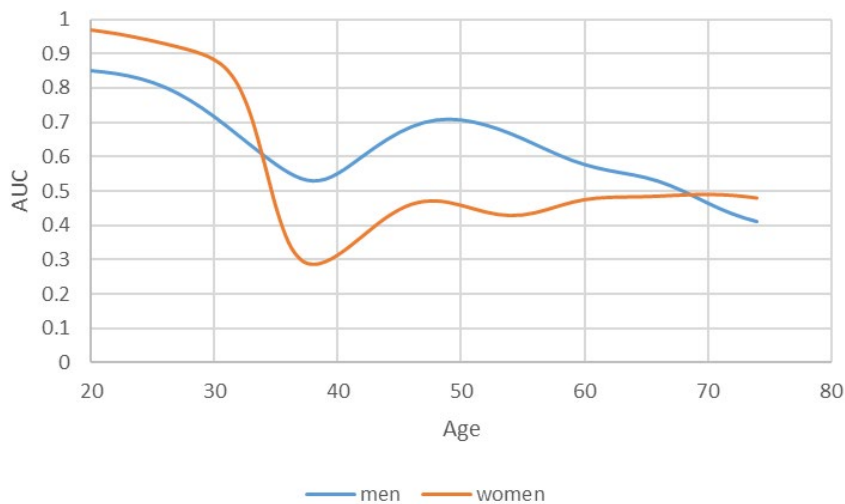


Figure 2. Estimated time-dependent AUC of the AVI biomarker adjusted by age for male and female

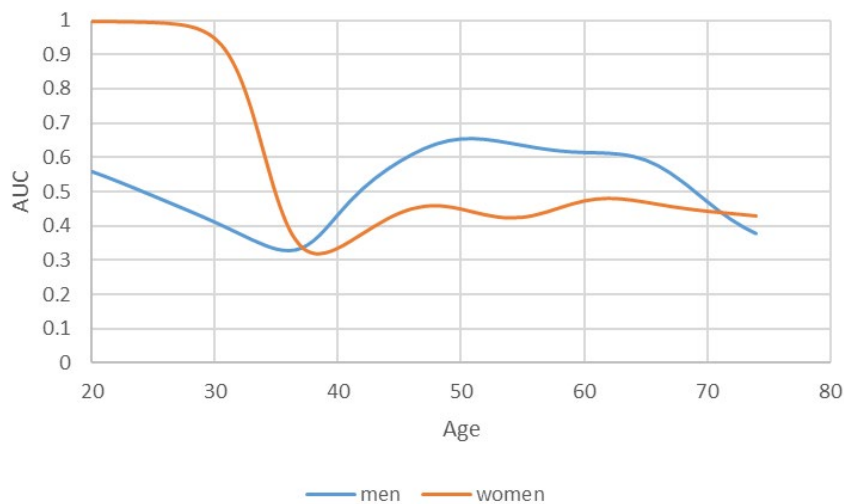


Figure 3. Estimated time-dependent AUC of the WHtR biomarker adjusted by age for male and female

Discussion

The prevalence of obesity in adults and children is a rapidly growing problem, associated with an increased risk of premature death and numerous adverse health outcomes, including CVD. Therefore, strategies aimed at obesity prevention and management must be given significant consideration. The primary step in controlling obesity is implementing screening methods that are both easy and accurate^{21,22}.

The aging process significantly contributes to the decline in cardiovascular function, which subsequently increases the risk of CVD among the elderly population. While age independently increases the risk of cardiovascular disease, it also indirectly influences it through changes in frailty, obesity, and diabetes. Additionally, in the elderly, sex may act as a potential risk factor. Older women have been reported to be at a higher risk of CVD compared to their male counterparts of the same age. As individuals age, the decline in sex hormones, such as estrogen and testosterone, further contributes to an increased risk of CVD in both men and women²³. For this reason, the current study investigated the predictive power of anthropometric indicators in assessing 10-year CVD risk at different ages in both sexes.

The findings of this study indicated that all three investigated indicators could effectively predict CVD in young women. However, after middle age, the predictive ability of these indices drastically decreased. BAI demonstrated only fair predictive power for approximately 50-year-old men. Additionally, the results showed that both AVI and WHtR predicted CVD well in men aged 20 to 30 years. For other age groups, AVI and WHtR were not effective tools for predicting CVD. A study conducted on a Chinese population also found that the association between CVD risk factors and anthropometric indices was strongest in the 20–44 age group, regardless of sex²⁴.

The preliminary investigation results showed that many epidemiological factors, including old age and obesity, are related to CVD incidence. In a 2020 study conducted by De Yang et al. on 25,231 individuals with a high risk of CVD and a 3-year follow-up, it was observed that older and

obese individuals were more at risk of CVD²⁵. In another study by Masaki Okamoto et al. in 2016, it was found that AVI was independently associated with age, suggesting that this index can predict CVD at different ages²⁶. Additionally, a 2016 study observed that obese individuals in younger age groups exhibited a higher CVD risk. Obesity in younger age groups also showed better predictive power for CVD risk factors compared to older groups, which is consistent with the current results. This finding implies that obesity may have a more significant impact on younger individuals²⁷. It is noteworthy that in the present study, the AUC values diminished as participants' age increased, suggesting that the ability to predict CVD became less effective over time. This correlation can be due to the presence of confounding variables, such as arterial stiffness and arterial hypertension, which have a direct relationship with age. Although these variables were not investigated in the present study, the literature shows that they increase with age^{28,29}. In other words, CVD in old age is influenced by factors such as arterial stiffness and arterial hypertension rather than anthropometric indicators. Arterial stiffness in old age can be caused by increasing obesity indices in young ages.

A strength of this research is the population-based sampling with a 10-year follow-up. The significance of this study lies in the relationship between age, CVD incidence, and anthropometric indicators. Since the associations between CVD risk and anthropometric indices varied based on sex and declined with age, further investigation into the age- and gender-specific predictive power of these indices is needed. The small number of CVD events was a limitation of this study, which caused some of the AUC versus age plots to be less smooth.

Conclusion

In conclusion, the detection and prevention of CVD through obesity control represents one of the most effective and cost-efficient intervention strategies. According to our findings, the obesity markers AVI and WHtR fairly predict the 10-year CVD risk in young individuals of both sexes. Additionally, the

BAI indicator is specifically applicable for predicting CVD risk in young women. Thus, these markers appear to be practical and affordable initial tools for youth CVD screening.

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Conflict of interests

The authors declare no conflict of interest.

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Author's Contributions

Study Conception or Design: MHK, RS, SJ

Data Acquisition: AH, MHK, RS, SJ

Data Analysis or Interpretation: MHK, RS, SJ, SMT, SMN

Manuscript Drafting: MHK, RS, SJ, SMT, SMN, AH

Critical Manuscript Revision: MHK, RS, SJ, SMT, SMN, AH

All authors have approved the final manuscript and are responsible for all aspects of the work.

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