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The Threshold of Visceral Adipose Tissue Areas Measured With QCT On Cardiometabolic Risk Factors In A Nationwide Study In China

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Research Article

Keywords: Visceral adipose tissue, Metabolic syndrome, Criteria, Computed tomography

Posted Date: December 8th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1130497/v1

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Abstract

Background: Abdominal adiposity is associated with increased cardiometabolic risk and visceral adipose tissue (VAT) area obtained from computed tomography (CT) is a key anthropometric index. The present study investigated the VAT criteria on cardiometabolic risk factors in a large-scale nationwide Chinese population.

Method: A total of 21,772 adults who underwent a low dose chest CT (LDCT) for lung cancer screening at one of 13 health checkup centers throughout China and had complete ancillary health records were evaluated. Abdominal VAT area at the center of L2 vertebra was measured with Mindways quantitative CT software using the existing LDCT dataset. Relevant anthropometric, serum and blood pressure measurements were obtained from the participants' records. The VAT distribution of the LDCT cohort was age-adjusted using the Chinese national census.

Results: The prevalence of metabolic syndrome based on the Chinese national guidelines was 29.5% and 10.5% in men and women respectively. Using ROC curves, the optimum threshold values for VAT area to identify metabolic syndrome were 213 cm^2 in men, and 136 cm^2 in women. For participants with VAT area above threshold, the odds ratio (95% confidence interval) for metabolic syndrome was 6.15 (5.65, 6.69) and 9.25 (7.58, 11.4) for men and women respectively. A further analysis of population attributable risk showed that VAT above threshold was significantly associated with an increased risk for metabolic syndrome.

Conclusion: In this large-scale nationwide population of China, sex-specific threshold values for VAT area measured by CT were established to identify the risk of metabolic syndrome. VAT area is a key anthropometric index of interventions to control cardiometabolic risk.

Introduction

As a worldwide target for the prevention of cardiometabolic risk, more and more attention is being paid to the prevention of obesity caused by sedentary lifestyles and changes in diet. In general, obesity is accompanied by a variety of adverse health effects such as insulin resistance, diabetes mellitus, hypertension, dyslipidemia and chronic inflammation, all of which may lead to atherosclerosis. In particular, body fat distribution is the most important determinant for the occurrence of metabolic and vascular diseases. As body weight increases, adipocytes not only increase in number (hyperplasia) but also in size (hypertrophy) and there is a greater increase in visceral adipose tissue (VAT) than in subcutaneous fat. These visceral fats are capable of secreting large amounts of pro-inflammatory cytokines and free fatty acids. Epidemiological studies suggest that VAT accumulation is a better predictor of metabolic abnormalities and atherosclerosis than total body fat [1,2], and visceral adiposity, as evaluated by computed tomography (CT) scanning [3], is more closely linked to cardiovascular events than is body mass index (BMI).

Several studies have demonstrated positive correlations of abdominal VAT accumulation with mortality, cardiovascular disease (CVD), and the risk of metabolic syndrome [4–8]. It is essential to establish appropriate ethnic-specific criteria of VAT area for the diagnosis of obesity, which can better identify the risk of cardiometabolic disease. A study including 1,193 Japanese adults scanned by CT at the umbilical level established a VFA threshold of 100 cm^2 as indicative of an increased risk of obesity-related disorders [9]. A cross-sectional study in the United Arab Emirates reported that the optimal VAT threshold to predict metabolic syndrome was 132 cm^2 for individuals under 50 years old [10]. A Chinese study which included 1744 individuals from Nanjing BENQ Medical Center showed that the optimal cut-points for VAT area at the umbilicus level and L2/3 level to identify participants with one or more cardiometabolic risk factors were 111 cm^2 and 142 cm^2 for men and 96 cm^2 and 115 cm^2 for women [11].

The aim of this study was to establish sex-specific VAT criteria capable of predicting cardiometabolic complications among adults in a nationwide population from the China Health Big Data (China Biobank) project. The Chinese guidelines for the definition of metabolic syndrome were used, which are ethnic-specific and more suitable for Chinese people than the International Diabetes Federation (IDF) criteria.

Methods

Study design and population

The China Biobank project is a prospective nationwide multicenter cohort study, which has been previously described in detail [12]. The study was approved by the ethics committees of all participating institutions and written informed consent was provided by the study participants.

This program has been registered with the US clinical trials database (clinicaltrials.gov) (trial identifier: NCT03699228). The participants were recruited from 13 health checkup centers throughout China. All were over 30 years old and had had a low-dose chest CT (LDCT) scanning for lung cancer screening as part of his/her health checkup procedure between January 2018 and June 2019. The study involved the post-processing of existing LDCT raw data for fat measurement.

As parts of the health checkup procedure, the blood sampling and laboratory analysis were conducted in a certified clinical examination center at each of the collaborating medical centers. Anthropometric indices and blood pressure were also measured.

Abdominal adipose tissue assessment

Abdominal fat measurements were made from existing chest CT scan image data. Abdominal total adipose tissue (TAT) and VAT were determined at the level of the 2nd lumbar vertebra (L2) and calibrated by qualified radiology technicians using the same standard protocol with Mindways quantitative CT phantoms (Mindways, Austin, TX, USA). Subcutaneous adipose tissue (SAT) area at the same level was obtained by subtracting VAT area from TAT area.

Definition of metabolic syndrome

Following the Chinese guidelines on the prevention and treatment of type 2 diabetes [13], metabolic syndrome was defined as having three or more of the following abnormalities: (1) high blood pressure, defined as blood pressure ≥130/85 mmHg and/or having been previously diagnosed with hypertension and taking blood pressure-lowering medications; (2) high plasma glucose, defined as fasting plasma glucose ≥6.10 mmol/L and/or having been previously diagnosed with diabetes and taking glucose-lowering medications; (3) high triglyceride, defined as a fasting triglyceride ≥1.70 mmol/L; (4) low high-density lipoprotein cholesterol, defined as a fasting high-density lipoprotein cholesterol <1.04 mmol/L; and/or (5) abdominal obesity, defined as waist circumference ≥90 cm for men or ≥85 cm for women.

The baseline characteristics of the cohort consisting of 59,429 adults were reported elsewhere [14]. 21,772 subjects with waist circumference measurement were included in this study for further analysis.

Statistics

Descriptive statistics were performed using one-way analysis of variance or chi-square tests. Nonnormally distributed variables were log transformed before the analyses. The prevalence of metabolic abnormalities in the Chinese population at different thresholds of VAT area was estimated by adjusting the China Biobank cohort for age using a direct method of standardization, based on the year 2010 national census data for the Chinese population.

The sensitivity and specificity of VAT area for diagnosing metabolic syndrome were evaluated using the receiver operating characteristic (ROC) curve. The point with the maximum Youden index (Youden index = sensitivity + specificity - 1) was defined as the optimal VAT area thresholds. Calibration plots was drawn to evaluate goodness of fit for VAT area. Age-adjusted odds ratio (OR) and 95% confidence interval (CI) of each metabolic abnormality and metabolic syndrome at the values above the optimal threshold was calculated using logistic regression models. Population attributable risks percent (PAR, %) for metabolic abnormalities was calculated according to OR and the percentage (P) of the study population with VAT area above the optimal threshold points (PAR, % = 100 * P * (OR - 1) / (P * (OR - 1) + 1)) %. A two-sided P value <0.05 was considered statistically significant. All analyses were conducted using R 3.4.4 software.

Results

A total of 21,772 subjects with complete data sets were included in the final analysis. Most participants were from central China (56.9%), and some were from the southwest, east and north. The mean age was 49.9 ± 12.3 years and 64.2% of the subjects were male (Table 1). The prevalence of metabolic syndrome was 29.5% and 10.5% in men and women respectively.

Table 1. General characteristics of the participants

	Total (n=21772)	Men (n=13968)	Women (n=7804)	P value
Age, years	49.9 ± 12.3	50.1 ± 12.5	49.6 ± 11.8	0.0033
Region of China, n (%)				<0.0001
North	80 (0.4)	47 (0.3)	33 (0.4)	
East	3052 (14.0)	1917 (13.7)	1135 (14.5)	
Center	12390 (56.9)	7686 (55.0)	4704 (60.3)	
Southwest	6250 (28.7)	4318 (30.9)	1932 (24.8)	
BMI, kg/m^2	24.6 ± 3.2	25.2 ± 3.0	23.4 ± 3.1	<0.0001
Visceral adipose tissue area, cm^2	175 ± 82	207 ± 76	119 ± 56	<0.0001
Waist circumference, cm	86 ± 10	90 ± 8	79 ± 9	<0.0001
Systolic blood pressure, mmHg	126 ± 19	128 ± 18	123 ± 20	<0.0001
Diastolic blood pressure, mmHg	77 ± 12	79 ± 12	73 ± 11	<0.0001
Fasting plasma glucose, mmol/L	5.26 ± 1.39	5.38 ± 1.51	5.04 ± 1.11	<0.0001
Triglycerides, mmol/L	1.44 (1.02, 2.11)	1.59 (1.12, 2.31)	1.21 (0.89, 1.73)	<0.0001
HDL cholesterol, mmol/L	1.36 ± 0.36	1.27 ± 0.32	1.52 ± 0.36	<0.0001
Rate of metabolic abnormalities, n (%)				
High blood pressure	9094 (41.8)	6536 (46.8)	2558 (32.8)	<0.0001
High fasting plasma glucose	2598 (11.9)	2063 (14.8)	535 (6.86)	<0.0001
High triglycerides	8363 (38.4)	6320 (45.2)	2043 (26.2)	<0.0001
Low HDL cholesterol	3475 (16.0)	3021 (21.6)	454 (5.82)	<0.0001
High waist circumference	9050 (41.6)	7115 (50.9)	1935 (24.8)	<0.0001
Metabolic syndrome	4943 (22.7)	4123 (29.5)	820 (10.5)	<0.0001
Age-adjusted metabolic syndrome	19.6	25.9	8.3	

Values are shown as mean ± standard deviation, median (quartiles), or n (%). BMI, body mass index; HDL, high-density lipoprotein.

Age-adjusted prevalence of metabolic abnormalities among levels of VAT area

With increasing VAT area, the prevalence of hypertension, dyslipidemia, high waist circumference and metabolic syndrome increased significantly in both males and females ($P<0.05$, Figure 1). Compared with patients with low VAT ($<60cm^2$), men with high VAT ($>360cm^2$) were more likely to have metabolic syndrome (0.7% vs. 62.2%, $p<0.0001$). Similarly, women with high VAT ($>240cm^2$) had a higher prevalence of metabolic syndrome than those with low VAT ($<40cm^2$, 0% vs. 38.9%, $p<0.0001$).

Optimal VAT thresholds based on cardiometabolic risk factors

The optimal VAT measurements for identifying metabolic syndrome that were obtained from ROC curves (Figure 2A) were 213 cm^2 in men, and 136 cm^2 in women, respectively. These thresholds were found to be the optimum thresholds for discriminating metabolic syndrome. The corresponding sensitivity and specificity were 77.0% and 65.1% in men and 84.3% and 71.2% in women respectively (Table 2). The positive and negative predictive values are also presented in Table 2. The calibration plot performed well both in the male and female cohorts (Figure 2B). Similar optimal VAT thresholds for subjects from different regions of China are shown in Supplement Table 1.

Table 2. Thresholds of visceral adipose tissue area for the identification of metabolic syndrome in men and women

	Men	Women
Threshold points, cm^2	213	136
Sensitivity, %	77.0	84.3
Specificity, %	65.1	71.2
Positive predictive value, %	48.0	25.5
Negative predictive value, %	87.1	97.5
Diagnostic accuracy, %	68.6	72.5

Status of cardiometabolic risk factors stratified by VAT threshold values

Table 3 compares cardiometabolic risk factors for men and women with VAT area above and below their sex specific threshold points (213 cm^2 for men and 136 cm^2 for women). The subjects with VAT area over the threshold values had significantly higher BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, triglycerides and lower HDL cholesterol for both men and women ($P<0.0001$).

Table 3. Levels of risk factors for metabolic syndrome in male and female participants stratified by thresholds of visceral adipose tissue area

	Men (n=13968)			Women (n=7804)		
	<213 cm^2 (n=7361)	≥213 cm^2 (n=6607)	P value	<136 cm^2 (n=5099)	≥136 cm^2 (n=2705)	P value
Age, years	47.8 ± 12.9	52.6 ± 11.7	<0.0001	46.1 ± 11.1	56.1 ± 10.3	<0.0001
BMI, kg/m^2	23.7 ± 2.4	27.0 ± 2.6	<0.0001	22.1 ± 2.4	25.8 ± 2.8	<0.0001
Waist circumference, cm	85 ± 7	95 ± 7	<0.0001	75 ± 7	86 ± 7	<0.0001
Systolic blood pressure, mmHg	124 ± 16	133 ± 18	<0.0001	117 ± 17	133 ± 20	<0.0001
Diastolic blood pressure, mmHg	76 ± 11	83 ± 12	<0.0001	70 ± 11	77 ± 11	<0.0001
Fasting plasma glucose, mmol/L	5.16 ± 1.34	5.63 ± 1.64	<0.0001	4.84 ± 0.75	5.44 ± 1.51	<0.0001
Triglycerides, mmol/L	1.37 (0.99, 1.95)	1.87 (1.34, 2.70)	<0.0001	1.07 (0.81, 1.45)	1.60 (1.16, 2.20)	<0.0001
HDL cholesterol, mmol/L	1.33 ± 0.33	1.20 ± 0.29	<0.0001	1.58 ± 0.36	1.40 ± 0.33	<0.0001

Values are shown as mean ± standard deviation or median (quartiles). BMI, body mass index; HDL, high-density lipoprotein.

Prevalence ratio of cardiometabolic risk factors with the VAT threshold values

Age adjusted logistic regression analysis showed that the prevalence of hypertension, hyperglycemia, dyslipidemia, high waist circumference and metabolic syndrome significantly increased among subjects with VAT area ≥ 213 cm^2 for men or 136 cm^2 for women. Table 4 shows the odds ratios and results for population attributable risk.

Table 4. Population attributable risks for metabolic abnormalities by visceral adipose tissue area threshold points of 213 cm^2 for men and 136 cm^2 for women

	Men		Women	
	OR (95% CI) *	PAR (%)	OR (95% CI) *	PAR (%)
High BP	2.33 (2.17, 2.50)	38.6	2.23 (2.00, 2.50)	29.9
High FPG	2.22 (2.01, 2.46)	36.6	3.36 (2.73, 4.14)	45.0
High TG	3.08 (2.87, 3.31)	49.6	3.61 (3.22, 4.05)	47.5
Low HDL-C	2.09 (1.92, 2.28)	34.0	2.85 (2.30, 3.53)	39.0
High WC	14.5 (13.4, 15.8)	86.5	12.6 (11.0, 14.4)	80.0
Metabolic syndrome	6.15 (5.65, 6.69)	70.9	9.25 (7.58, 11.4)	74.1

*Age-adjusted OR and 95% CI values.

BP, blood pressure; CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; OR, odd ratio; PAR, population attributable risk; TG, triglyceride; VAT, visceral adipose tissue; WC, waist circumference.

Discussion

As the potential link between obesity and the development of atherosclerosis and its complicating events, VAT has a close link to cardiovascular events. In our nationwide population-based sample, volumetric CT measures of VAT area were correlated with multiple cardiometabolic risk factors. Compared with simple anthropometrics, including BMI and waist circumferences, VAT can provide more information related to risk factor stratification.

When central obesity was defined by increased waist circumference or waist to hip ratio, a cross-sectional study of participants with multiple comorbidities found that central obesity was found to be associated with adverse cardiac mechanics [15], and in a multiethnic cohort of adults without heart failure, increasing adiposity over time was observed to be associated with pathologic cardiac remodeling [16]. A lifestyle intervention study showed that excess android or visceral fat contributes to the development of cardiovascular disease through modulating oxidative stress [17].

A cross-sectional study in South Africa reported that one in every three adults considered to have normal weight based on their BMI is centrally obese, and normal-weight central obesity was significantly associated with hypertension [18]. People with normal BMI combined with central obesity might have increased risk of metabolic syndrome. Our previous study revealed that VAT area could not be predicted from BMI in a Chinese population [14].

However, the waist circumference and waist to hip ratio cannot identify VAT and SAT, and the relative contribution of VAT versus SAT to cardiovascular disease risk cannot be distinguished.

A cross-sectional study in a healthy population showed that lipid profiles, insulin and C-reactive protein had a more significant relationship with SAT than VAT, while VAT was associated with glucose control and the degree of fatty liver [19]. The Jackson Heart Study found that VAT is more metabolically deleterious than SAT [20].

Our results are consistent with these prior findings and extend these to a population-based sample from 13 health checkup centers throughout China. We found that with increasing VAT area, all the cardiometabolic risk factors examined were significantly increased. Using ROC curves, we determined that the optimal threshold of VAT area measured by CT at the L2 level for identifying metabolic syndrome was 213 cm^2 in men, and 136 cm^2 in women. Among subjects with VAT area above the threshold criteria, the prevalence of hypertension, hyperglycemia, dyslipidemia, high waist circumference and metabolic syndrome all significantly increased. Using the calibration plot, we found that the criteria performed well both in the male and female cohorts. For subjects with VAT area over the threshold, the odds ratios of metabolic syndrome were 6.15 (5.65, 6.69) and 9.25 (7.58, 11.4) for men and women respectively. Further population attributable risk analysis showed that VAT area over the threshold were significantly associated with an increased risk for metabolic syndrome.

A Korean study found that VAT cut-offs of 100 cm^2 in men and 70 cm^2 in women are useful for defining visceral obesity [21]. Another Korean study suggested that VFA values higher than the cut-off value of 134.6 cm^2 for men and 91.1 cm^2 for women are risk factors for predicting metabolic syndrome [22]. A previous study among 1744 individuals in a Chinese population analysed the optimal cut-points of VAT areas for metabolic syndrome using IDF 2005 criteria for metabolic syndrome and found that the optimal cut-points were 142cm^2 for men and 115 cm^2 for women [11]. In our nationwide study, we included subjects form 13 health checkup centers throughout China, and metabolic syndrome was diagnosed according to the Chinese ethnic-specific criteria, which included the data of waist circumferences, so we believe the criteria derived in this study are more suitable for the Chinese population.

One limitation of this large study was that it was a cross-sectional study, which cannot prove the predictability of CT measurements of VAT area for metabolic syndrome. A prospective study is essential to identify the reliability of the VAT criteria, and to examine whether intervention to decrease VAT area can reduce the risk of cardiovascular events.

In conclusion, using a large-scale nationwide population, we found that the prevalence of metabolic syndrome was 29.5% and 10.5% in men and women respectively. And we established the sex-specific VAT criteria to identify the risk of metabolic syndrome. As a key anthropometric index, VAT should be monitored and interventions made to control the cardiometabolic risk.

Declarations

Ethics approval and consent to participate: The study was approved by the ethics committees of all participating institutions and written informed consent was provided by the study participants. This program has been registered with the US clinical trials database (clinicaltrials.gov) (trial identifier: NCT03699228).

Consent for publication：Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests：The authors declare that they have no competing interests.

Funding：This work is supported by National Key Research and Development Program of China (No. 2020YFC2004902); Beijing Hospitals Authority Clinical Medicine Development of Special Funding Support, code: ZYLX202107.

Authors' contributions：Xiaojuan Zha wrote the main manuscript text. Yanhui Lu, Yongli Li, Dong Yan, Limei Ran, Yong Lu, Yingying Yang, Yandong Liu and Mingzhu Zou provided the resources and measurements. Kaiping Zhao taken charge of statistics analysis.Blake M. Glen checked language. Xiaoguang Cheng provided the conception and acquired Funding. **Min Chen** provided the conception and edited the main manuscript. All authors read and approved the final manuscript.

Acknowledgements: Not applicable.

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Figures

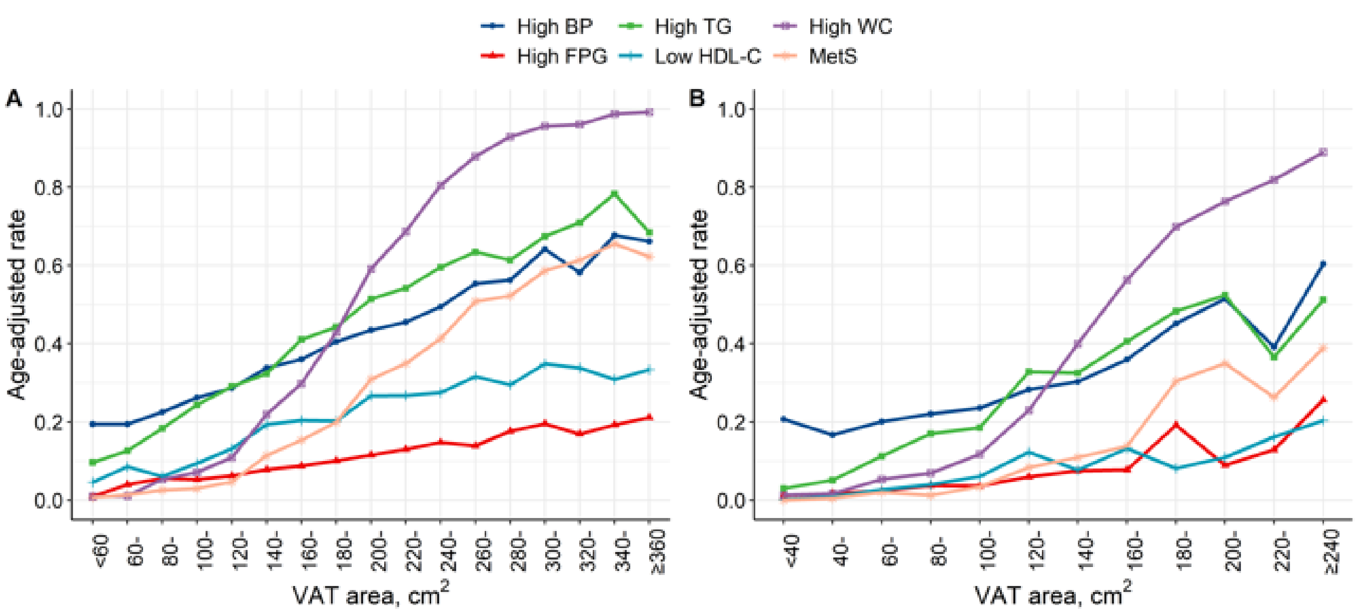

Figure 1

Age-adjusted prevalence of metabolic abnormalities for different levels of visceral adipose tissue area. The data has been binned in intervals of 20 cm2 in VAT area. (A) men; (B) women. Rates observed in the China Biobank cohort have been adjusted for age using national census data for the Chinese population. BP, blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; TG, triglyceride; VAT, visceral adipose tissue; WC, waist circumference.

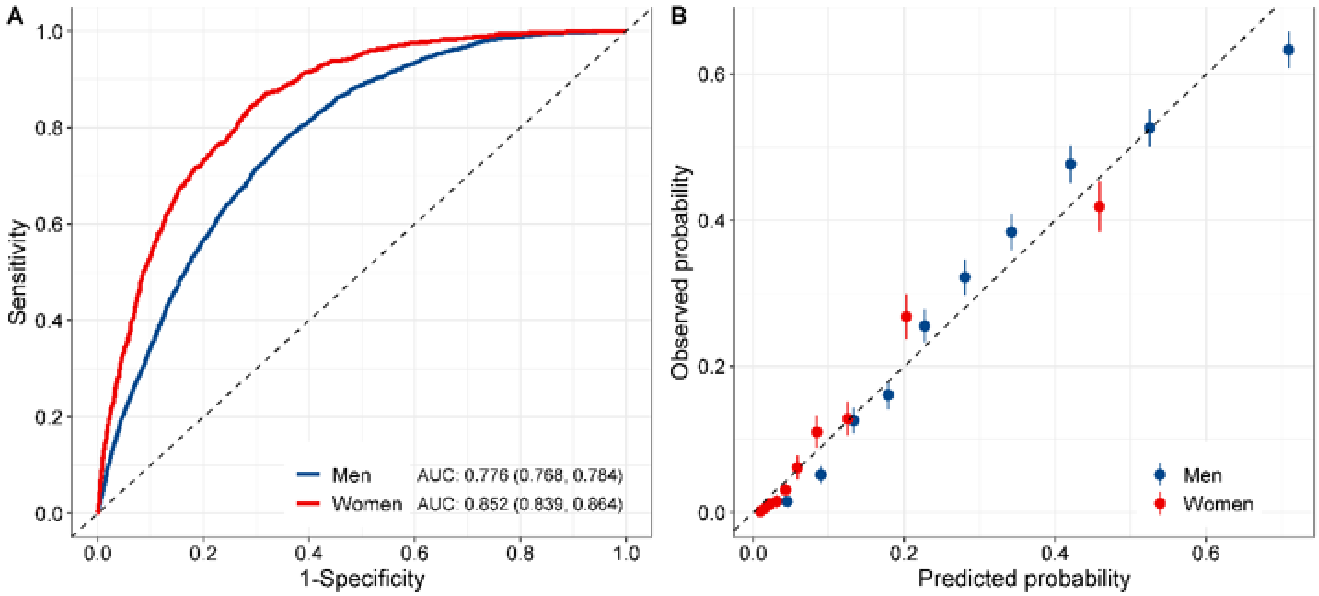

Figure 2

Discrimination and calibration of visceral adipose tissue area for the identification of metabolic syndrome. (A) ROC curves; (B) Calibration plot. AUC, area under the curve; ROC, receiver operating characteristic.

Supplementary Files

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- SupplementTable1.docx