

# A Predictive Model of Metabolic Syndrome by Medical Examination: Evidence from an 8-Year Chinese Cohort

Huanyu Guo<sup>1,\*</sup>  
Wenwei Jiang<sup>2,\*</sup>  
Bo Zhao<sup>1</sup>  
Yanhua Xiong<sup>3</sup>  
Zhenya Lu<sup>1</sup>

<sup>1</sup>Department of FSTC Clinic of The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, 310009, People's Republic of China; <sup>2</sup>Department of Internal Medicine of Traditional Chinese Medicine, Huzhou Central Hospital, Huzhou, 310003, People's Republic of China; <sup>3</sup>Department of Internal Medicine of Traditional Chinese Medicine, Zhejiang Hospital, Hangzhou, 310007, People's Republic of China

\*These authors contributed equally to this work

**Purpose:** To develop a predictive model for the risk of metabolic syndrome (MetS).

**Patients and Methods:** Totally, 1556 residents without MetS were finally included in 2006 and they were observed for 8 years to check who developed MetS. Univariate and multivariate logistic regression analyses was adopted to explore the risk factors of MetS and develop the predictive model that used the medical examination information of MetS risk after 8 years. The receiver operating characteristic (ROC) curve was drawn to assess the predictive capacity of the model.

**Results:** The risk of MetS in overweight, prehypertension, hypertension subjects were 4.610 [95% confidence interval (CI): 2.415 to 8.800], 2.759 (95% CI: 1.519 to 5.011) and 3.589 (95% CI: 1.672 to 7.706) times higher than that in controls, respectively. The risk of MetS in people with high-density lipoprotein (HDL) <1.10 mmol/L was 3.716-fold in comparison with HDL  $\geq$ 1.55 mmol/L [odds risk (OR) = 3.716, 95% CI: 1.483 to 9.313]. Individuals with fatty liver had a higher risk of MetS (OR = 2.577, 95% CI: 1.472 to 4.512). The AUC of the predictive model was 0.831 (95% CI: 0.798 to 0.865), with the sensitivity of 0.898 (95% CI: 0.831 to 0.941) and the specificity of 0.676 (95% CI: 0.651 to 0.700).

**Conclusion:** The model performed well predictive power for the risk of MetS, which may provide a reference for clinicians to identify high-risk groups early.

**Keywords:** metabolic syndrome, predictive model, 8-year, Chinese cohort

## Introduction

Metabolic syndrome (MetS) is a series of metabolic disorders, mainly consisting of obesity [body mass index (BMI)  $\geq$ 25.0 kg/m<sup>2</sup>], dyslipidemia (TG  $\geq$ 1.7mmol/L), hypertension (BP  $\geq$ 140/90 mmHg), and dysglycemia [type 2 diabetes mellitus (T2DM)].<sup>1</sup> It manifests as insulin resistance (IR) and chronic low-grade inflammation.<sup>2,3</sup> IR has been identified as the central feature of the MetS, which is associated with increased risk of cardiovascular diseases (CVDs).<sup>4</sup> Over the past several decades, the prevalence of MetS is relatively high<sup>5,6</sup> ranged 30–50% in most Asian countries,<sup>7</sup> with major public consequences.

MetS is related to the risk of future cardiovascular diseases (CVDs) and T2DM both in children and adults.<sup>8,9</sup> As one of the leading global health burdens, the risk of CVD morbidity and mortality was reported to increase by 71% and 68% in males, 89%, and 73% in females with the presence of MetS in a meta-analysis study towards the general Japanese population.<sup>10</sup> Besides, patients with MetS were also reported with a higher risk of postoperative complications and 30-day

Correspondence: Zhenya Lu  
Department of FSTC Clinic of The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, 310009, People's Republic of China  
Tel +86 13575458480  
Email l199026@zju.edu.cn

Received: 6 April 2021  
Accepted: 8 July 2021  
Published: 8 November 2021



readmission.<sup>11</sup> Thus, it is worthy of using the annual medical examination indicators to predict MetS risk in the future so that early intervention could be implemented to control and avoid MetS and its secondary diseases.

Single anthropometric indices, such as waist circumference and conicity index, have been used in previous cross-sectional studies to predict the possibility of MetS incidence.<sup>12</sup> This retrospective cohort study was mainly designed to construct a predictive system for MetS risk, using basic medical examination data. This study may also provide a basic reference with spontaneous change for further relative intervention study.

## Materials and Methods

### Data Collection

Data of 2054 participants were collected in a hospital in Hangzhou, Zhejiang province, China. According to the medical examination in 2006, 498 patients were excluded at the baseline, including 115 patients with systolic blood pressure (SBP) below 90 mmHg or diastolic BP (DBP) below 60 mmHg, 180 patients with blood glucose below 2.8 mmol/L, 77 patients with a body mass index (BMI) of  $<18.5 \text{ kg/m}^2$  and 126 with diagnosed MetS. Ultimately, 1556 residents without MetS were finally included in 2006 and they were observed for 8 years to check who developed MetS. The research including any relevant details was approved by the Institutional Review Board (IRB) of the First Affiliated Hospital of Zhejiang University School of Medicine [Ref. No. 2020\_IIT (405)] and performed in accordance with the Declaration of Helsinki, and the informed consent was obtained from all participants.

### Medical Examination Information

Basic information in the medical examination report included gender, age, BMI, and BP. The blood examination indicators included fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), total cholesterol (TC), very LDL-C (VLDL-C), hemoglobin (Hb), platelets (PLT), white blood cell (WBC), albumin (ALB), globulin (GLB), neutrophil (NEUT), serum uric acid (UA), and fatty liver disease.

According to the standard developed by Chinese diabetes society in 2004,<sup>13</sup> MetS could be diagnosed if the patient have three or more following symptoms: 1) overweight or obese:  $\text{BMI} \geq 25.0 \text{ kg/m}^2$ ; 2)  $\text{FPG} \geq 6.1 \text{ mmol/L}$  and 2-hour postprandial blood glucose (2hPG)  $\geq 7.8 \text{ mmol/L}$ ,

or  $2\text{hPG} \geq 7.8 \text{ mmol/L}$ ; or drug treatment for diabetes mellitus (DM); 3) BP:  $\text{SBP} \geq 140 \text{ mmHg}$  and  $\text{DBP} \geq 90 \text{ mmHg}$ , or  $\text{DBP} \geq 90 \text{ mmHg}$ ; or drug treatment for hypertension; (d) fasting serum TG  $\geq 1.7 \text{ mmol/L}$  and fasting HDL-C  $<0.9 \text{ mmol/L}$ ; or fasting HDL-C  $<0.9 \text{ mmol/L}$  and  $<1.0 \text{ mmol/L}$  in male and female patients, respectively.

Abdominal ultrasonographic examinations were performed by experienced radiologists using a Toshiba Nemio 20 sonography machine (Toshiba, Tokyo, Japan) with a 3.5-MHz probe. Fatty liver was diagnosed according to the criteria described by the Chinese Liver Disease Association.<sup>14</sup>

The BP was categorized into 1) normal group:  $\text{SBP} \leq 120 \text{ mmHg}$  and  $\text{DBP} \leq 80 \text{ mmHg}$ ; 2) prehypertension group:  $120 \text{ mmHg} < \text{SBP} < 140 \text{ mmHg}$  or  $80 \text{ mmHg} < \text{DBP} < 90 \text{ mmHg}$ ; (c) hypertension:  $\text{SBP} \geq 140 \text{ mmHg}$  or  $\text{DBP} \geq 90 \text{ mmHg}$ .

The FPG was categorized into three levels: 1) normal FPG:  $\text{FPG} \leq 6.1 \text{ mmol/L}$ ; 2) impaired FPG:  $6.1 \text{ mmol/L} < \text{FPG} < 6.9 \text{ mmol/L}$ ; and 3) suspected T2DM:  $\text{FPG} \geq 6.9 \text{ mmol/L}$ .

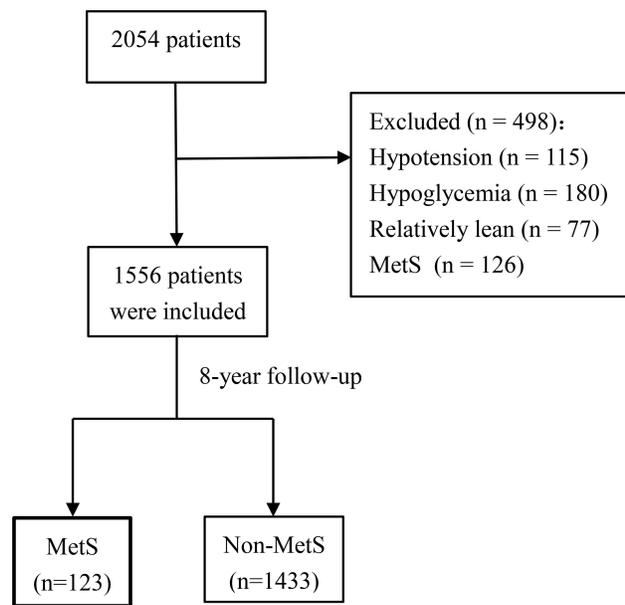
### Data Analysis

The statistical tests were performed using SAS v.9.4 (SAS Institute, Cary, NC, USA). According to the examination data of 2014, the participants were divided into MetS and non-MetS groups. Univariate and multivariate logistic regression analyses were used to explore the risk factors of MetS and develop the predictive model, which used the medical examination information for MetS risk after 8 years. The relative risk (RR) and odds risk (OR) were calculated, represented by 95% confidence interval (95% CI). The receiver operating characteristic (ROC) curves were adopted to estimate the predictive capacity of the model. Areas under the ROC curve (AUCs) were calculated. A significant  $P < 0.05$  was considered for all the analyses.

## Results

### Baseline Information

The flowchart of data filtering was shown in Figure 1. Ultimately, 1556 residents were finally included in the present research, including 1040 (66.84%) males and 516 (33.16%) females, with an average age of  $49.36 \pm 12.07$  years. Among these individuals, 980 (65.60%) suffered from fatty liver, 611 (39.27%) were overweight. There were 641



**Figure 1** Flowchart of data screening.

(41.20%) patients with prehypertension, 171 (10.99%) patients with hypertension. Sixteen (1.04%) people had pre-diabetes, and 19 (1.24%) had diabetes. The detailed information for all the included samples is presented in Table 1.

## Univariate Analysis Results

The results of the univariate analysis on general data are shown in Table 2. After an 8-year follow-up, 123 people developed MetS, and 1433 did not. The risk of MetS in people aged  $\geq 50$  years, overweight, and fatty liver patients were 1.511 (95% CI: 1.067 to 2.141,  $P < 0.05$ ), 9.644 (95% CI: 5.838 to 15.929,  $P < 0.05$ ), 5.59 (95% CI: 3.748 to 8.347,  $P < 0.05$ ) times higher than that in controls, respectively. Compared to participants with normal BP, the risk of MetS in those with prehypertension increased by 2.482 times (RR = 3.482, 95% CI: 2.242 to 5.407,  $P < 0.05$ ), and hypertension increased by 3.003 times (RR = 4.003, 95% CI: 2.330 to 6.878,  $P < 0.05$ ). Patients with FPG  $> 6.9$  mmol/L were more likely to suffer from MetS than those with FPG between 3.9 and 6.1 mmol/L (RR = 2.774, 95% CI: 1.141 to 6.744,  $P < 0.05$ ).

The results of the univariate analysis on laboratory examination indexes are shown in Table 3. The risk of MetS in people with TG levels between 0.89 and 1.32 mmol/L and between 1.32 and 2.03 mmol/L,  $\geq 2.03$  mmol/L were 6.546 (95% CI: 1.961 to 21.847,  $P < 0.05$ ), 11.574 (95% CI: 3.595 to 37.265,  $P < 0.05$ ) and 20.948 (95% CI: 6.639 to 66.098,  $P < 0.05$ ) times in comparison with TGs  $< 0.89$  mmol/L,

**Table 1** Baseline Information of the Participants [n (%) or  $\bar{x} \pm s$ ]

Characteristics	
Sex	
Male	1040 (66.84)
Female	516 (33.16)
Age (years)	49.36 $\pm$ 12.07
BMI (kg/m <sup>2</sup> )	
Normal (18.5–23.9)	945 (60.73)
Overweight ( $\geq 23.9$ )	611 (39.27)
FPG (mmol/L)	
Normal (3.9–6.1)	1502 (97.72)
Impaired FPG (6.1–6.9)	16 (1.04)
Suspected T2DM ( $\geq 6.9$ )	19 (1.24)
BP (mmHg)	
Normal (60–80/90–120)	744 (47.81)
Prehypertension (80–89/120–139)	641 (41.20)
Hypertension ( $> 89/139$ )	171 (10.99)
Fatty liver	
Without	980 (65.60)
With	514 (34.40)

**Abbreviations:** BMI, body mass index; FPG, fasting plasma glucose; T2DM, diabetes mellitus type 2; BP, blood pressure.

respectively. The risk of MetS in people with HDL-C levels  $< 1.10$  mmol/L, between 1.10 and 1.30 mmol/L, and between 1.30 and 1.53 mmol/L were 7.955 (95% CI: 3.856 to 16.413,  $P < 0.05$ ), 4.370 (95% CI: 2.049 to 9.320,  $P < 0.05$ ) and 2.807 (95% CI: 1.258 to 6.259,  $P < 0.05$ ) folds in comparison with  $\geq 1.53$  mmol/L, respectively. The MetS risk was relatively higher among those with VLDL-C levels between 0.91 and 1.49 mmol/L (RR = 4.021, 95% CI: 1.973 to 8.195,  $P < 0.05$ ) and  $\geq 1.49$  mmol/L (RR = 4.880, 95% CI: 2.424 to 9.823,  $P < 0.05$ ) in comparison to those with  $< 0.56$  mmol/L. Individuals with TC level  $\geq 4.66$  mmol/L exhibited higher MetS risks in comparison to those with  $< 4.66$  mmol/L (RR = 1.711, 95% CI: 1.202 to 2.436,  $P < 0.05$ ). Participants with Hb levels between 147 and 156 g/L (RR = 2.636, 95% CI: 1.431 to 4.858,  $P < 0.05$ ) and  $\geq 156$  g/L (RR = 3.235, 95% CI: 1.770 to 5.911,  $P < 0.05$ ) tended to have a higher risk of MetS than those with  $< 134$  g/L. Higher risk of MetS in those with WBC between  $5.90$  and  $6.80 \times 10^9/L$  (RR = 1.820, 95% CI: 1.041 to 3.184,  $P < 0.05$ ) and  $\geq 6.80 \times 10^9/L$  (RR = 2.203, 95% CI: 1.282 to 3.787,  $P < 0.05$ ) compared with those  $< 5.10 \times 10^9/L$  were observed. Individuals with NEUC  $\geq 4.00 \times 10^9/L$  were more likely to suffer from MetS than those  $< 2.70 \times 10^9/L$  (RR = 2.050, 95% CI: 1.228 to 3.425,  $P < 0.05$ ).

**Table 2** Comparison of General Data Between the Two Groups [n (%)]

Variables	Number of Samples	Group		RR (95% CI)	P
		Non-MetS (n = 1433)	MetS (n = 123)		
Age (years)					
<50	765	717 (50.03)	48 (39.02)	Ref	0.019
≥50	791	716 (49.97)	75 (60.98)	1.511 (1.067–2.141)	
BMI (kg/m <sup>2</sup> )					
Normal (18.5–23.9)	945	928 (64.76)	17 (13.82)	Ref	<0.001
Overweight (≥ 23.9)	611	505 (35.24)	106 (86.18)	9.644 (5.838–15.929)	
BP (mmHg)					
Normal (60–80/90 – 120)	744	719 (50.17)	25 (20.33)	Ref	<0.001
Prehypertension (80–89/120 – 139)	641	566 (39.50)	75 (60.98)	3.482 (2.242–5.407)	
Hypertension (>89/139)	171	148 (10.33)	23 (18.70)	4.003 (2.330–6.878)	
FPG (mmol/L)					
Normal (3.9–6.1)	1502	1388 (98.02)	114 (94.21)	Ref	0.007
Impaired FPG (6.1–6.9)	16	13 (0.92)	3 (2.48)	2.470 (0.877–6.956)	
Suspected T2DM (≥6.9 0)	19	15 (1.06)	4 (3.31)	2.774 (1.141–6.744)	
Fatty liver					
Yes	980	950 (69.04)	30 (25.42)	Ref	< 0.001
No	514	426 (30.96)	88 (74.58)	5.593 (3.748–8.347)	

**Abbreviations:** MetS, metabolic syndrome; RR, relative risk; CI, confidence interval; BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose; T2DM, diabetes mellitus type 2.

## Multivariate Analysis for the Risk of MetS

The results of the multivariate analysis are shown in [Table 4](#). Factors with differences in univariate analysis were further analyzed using stepwise multivariate logistic regression, including age, BMI, BP, FPG, TG, HDL-C, Hb, WBC, NEUT, UA, TC, VLDL-C, and fatty liver. The results showed that BMI, prehypertension, hypertension, HDL-C, and fatty liver were the independent predictors of the occurrence of MetS. The risk of MetS in overweight, prehypertension, hypertension subjects were 4.610 (95% CI: 2.415 to 8.800,  $P < 0.05$ ), 2.759 (95% CI: 1.519 to 5.011,  $P < 0.05$ ), and 3.589 (95% CI: 1.672 to 7.706,  $P < 0.05$ ) times higher than that in controls, respectively. The risk of MetS in people with HDL-C <1.10 mmol/L was 3.716-fold in comparison with HDL-C ≥1.55 mmol/L (OR = 3.716, 95% CI: 1.483 to 9.313,  $P < 0.05$ ). Individuals with fatty liver exert higher MetS risks (OR = 2.577, 95% CI: 1.472 to 4.512,  $P < 0.05$ ). A Logistic regression model was established:  $Y = 1.528 \times \text{BMI (overweight)} + 1.015 \times \text{BP (prehypertension)} + 1.278 \times \text{BP (hypertension)} + 1.313 \times \text{HDL-C (<1.10 mmol/L)} + 0.947 \times \text{fatty liver} - 5.570$ .

## The Predictive Performance of the Individualized Prediction Model

The ROC curves are shown in [Figure 2](#). The AUC of the predictive model was 0.831 (95% CI: 0.798 to 0.865), superior to either BMI (ROC = 0.818, 95% CI: 0.786 to 0.850) or HDL-C (ROC = 0.701, 95% CI: 0.654 to 0.748) alone in predicting MetS. As shown in [Table 5](#), the sensitivity of this model was 0.898 (95% CI: 0.831 to 0.941) with a specificity of 0.676 (95% CI: 0.651 to 0.700).

## Discussion

We developed a novel prediction tool for the risk of MetS using five readily available variables based on an 8-year Chinese cohort. The selected predictive factors included BMI, prehypertension, hypertension, HDL, and fatty liver. Based on this, a model for calculating the risk of MetS was established:  $Y = 1.528 \times \text{BMI (overweight)} + 1.015 \times \text{BP (prehypertension)} + 1.278 \times \text{BP (hypertension)} + 1.313 \times \text{HDL-C (<1.10 mmol/L)} + 0.947 \times \text{fatty liver} - 5.570$ . The AUC of this multi-factor model was 0.831, with a sensitivity of 0.898 and a specificity of

**Table 3** Comparison of Laboratory Examination Indicators Between the Two Groups [n (%)]

Variables	Numbrella of Samples	Group		RR (95% CI)	P
		Non-MetS (n = 1433)	MetS (n = 123)		
TG (mmol/L)					<0.001
Q <sub>1</sub> (<0.89)	380	377 (26.46)	3 (2.44)	Ref	
Q <sub>2</sub> (0.89–1.32)	387	367 (25.75)	20 (16.26)	6.546 (1.961–21.847)	
Q <sub>3</sub> (1.32–2.025)	394	358 (25.12)	36 (29.27)	11.574 (3.595–37.265)	
Q <sub>4</sub> (≥ 2.025)	387	323 (22.67)	64 (52.03)	20.948 (6.639–66.098)	
HDL-C (mmol/L)					<0.001
Q <sub>1</sub> (<1.10)	379	319 (22.39)	60 (48.78)	7.955 (3.856–16.413)	
Q <sub>2</sub> (1.10–1.30)	391	357 (25.05)	34 (27.64)	4.370 (2.049–9.320)	
Q <sub>3</sub> (1.30–1.53)	376	355 (24.91)	21 (17.07)	2.807 (1.258–6.259)	
Q <sub>4</sub> (≥1.53)	402	394 (27.65)	8 (6.50)	Ref	
ALB (g/L)					0.701
Q <sub>1</sub> (<46.50)	370	338 (24.76)	32 (26.67)	Ref	
Q <sub>2</sub> (46.50–48.40)	359	333 (24.40)	26 (21.67)	0.837 (0.510–1.376)	
Q <sub>3</sub> (48.40–50.60)	381	346 (25.35)	35 (29.17)	1.062 (0.672–1.678)	
Q <sub>4</sub> (≥50.60)	375	348 (25.49)	27 (22.50)	0.833 (0.509–1.361)	
GLB (g/L)					0.132
Q <sub>1</sub> (<25.20)	369	334 (24.50)	35 (29.17)	Ref	
Q <sub>2</sub> (25.20–27.60)	362	327 (23.99)	35 (29.17)	1.019 (0.653–1.592)	
Q <sub>3</sub> (27.60–30.00)	370	349 (25.61)	21 (17.50)	0.598 (0.355–1.008)	
Q <sub>4</sub> (≥30.00)	382	353 (25.90)	29 (24.17)	0.800 (0.500–1.282)	
Hb (g/L)					<0.001
Q <sub>1</sub> (<134)	355	342 (24.62)	13 (11.11)	Ref	
Q <sub>2</sub> (134–147)	384	362 (26.06)	22 (18.80)	1.565 (0.800–3.058)	
Q <sub>3</sub> (147–156)	404	365 (26.28)	39 (33.33)	2.636 (1.431–4.858)	
Q <sub>4</sub> (≥156)	363	320 (23.04)	43 (36.75)	3.235 (1.770–5.911)	
PLT (10 <sup>3</sup> /mL)					0.923
Q <sub>1</sub> (<173)	379	348 (24.39)	31 (25.41)	Ref	
Q <sub>2</sub> (173–207)	390	360 (25.23)	30 (24.59)	0.940 (0.581–1.522)	
Q <sub>3</sub> (207–240)	379	350 (24.53)	29 (23.77)	0.936 (0.575–1.521)	
Q <sub>4</sub> (≥240)	401	369 (25.86)	32 (26.23)	0.976 (0.608–1.567)	
WBC (10 <sup>9</sup> /L)					0.002
Q <sub>1</sub> (<5.10)	355	338 (23.74)	17 (13.93)	Ref	
Q <sub>2</sub> (5.10–5.90)	361	336 (23.60)	25 (20.49)	1.446 (0.795–2.631)	
Q <sub>3</sub> (5.90–6.80)	413	377 (26.47)	36 (29.51)	1.820 (1.041–3.184)	
Q <sub>4</sub> (≥6.80)	417	373 (26.19)	44 (36.07)	2.203 (1.282–3.787)	
NEUC (10 <sup>9</sup> /L)					0.008
Q <sub>1</sub> (<2.70)	339	320 (22.42)	19 (15.57)	Ref	
Q <sub>2</sub> (2.70–3.30)	387	357 (25.02)	30 (24.59)	1.383 (0.793–2.411)	
Q <sub>3</sub> (3.30–4.00)	414	388 (27.19)	26 (21.31)	1.121 (0.631–1.989)	
Q <sub>4</sub> (≥4.00)	409	362 (25.37)	47 (38.52)	2.050 (1.228–3.425)	
UA (mmol/L)					<0.001
Q <sub>1</sub> (<259)	332	324 (25.88)	8 (8.42)	Ref	
Q <sub>2</sub> (259–318)	338	325 (25.96)	13 (13.68)	1.596 (0.670–3.801)	
Q <sub>3</sub> (318–375)	340	316 (25.24)	24 (25.26)	2.929 (1.335–6.427)	
Q <sub>4</sub> (≥375)	337	287 (22.92)	50 (52.63)	6.157 (2.965–12.787)	

(Continued)

Table 3 (Continued).

Variables	Numbrella of Samples	Group		RR (95% CI)	P
		Non-MetS (n = 1433)	MetS (n = 123)		
TC (mmol/L)					
<4.66	769	724 (50.81)	45 (36.59)	Ref	0.003
≥4.66	779	701 (49.19)	78 (63.41)	1.711 (1.202–2.436)	
LDL-C (mmol/L)					
Q <sub>1</sub> (<1.79)	374	342 (24.71)	32 (28.32)	Ref	0.774
Q <sub>2</sub> (1.79–2.35)	364	346 (25.00)	18 (15.93)	0.578 (0.330–1.011)	
Q <sub>3</sub> (2.35–2.86)	379	346 (25.00)	33 (29.20)	1.018 (0.639–1.620)	
Q <sub>4</sub> (≥2.86)	380	350 (25.29)	30 (26.55)	0.923 (0.573–1.487)	
VLDL-C (mmol/L)					
Q <sub>1</sub> (< 0.56)	359	350 (25.29)	9 (7.96)	Ref	<0.001
Q <sub>2</sub> (0.56–0.91)	385	365 (26.37)	20 (17.70)	2.072 (0.956–4.491)	
Q <sub>3</sub> (0.91–1.49)	377	339 (24.49)	38 (33.63)	4.021 (1.973–8.195)	
Q <sub>4</sub> (≥1.49)	376	330 (23.84)	46 (40.71)	4.880 (2.424–9.823)	

**Abbreviations:** MetS, metabolic syndrome; RR, relative risk; CI, confidence interval; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; ALB, albumin; GLB, globulin; Hb, hemoglobin; PLT, platelet; WBC, white blood cell; NEUC, neutrophil; UA, uric acid; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.

0.676, which indicated that the risk of MetS would be well predicted.

This study indicated that overweight might be a predictor affecting the risk of MetS. The occurrence of MetS has been proved to be related to excessive visceral adiposity.<sup>15</sup> Moreover, visceral adiposity, associated with BMI, has been evaluated as a cardiometabolic risk factor and might be adopted as a treatment target for cardiometabolic disease.<sup>16</sup> Additionally, it has been reported that one-third of American adolescents were overweight or obese, which increased the MetS risk.<sup>17</sup> The relationship and overweight and MetS could be attributed to the following explanations: 1) obesity could cause insulin resistance by inducing inflammation in various tissues, resulting in a higher risk of MetS;<sup>18</sup> 2) the destruction caused by obesity will break the integrity of lymphoid tissues with interfering with the distribution of leukocyte subsets and phenotypes,<sup>19</sup> which may lead to an increased risk of MetS.<sup>20</sup>

The present study demonstrated that prehypertension and hypertension might indicate a high risk of MetS because elevated BP is a part of the definition of MetS. A study indicated that with increasing BP, the prevalence of MetS increased, which is consistent with our results.<sup>21</sup> It has been demonstrated that poor BP control in hypertension was an independent risk factor for MetS.<sup>22</sup> Compared with hypertension patients with better BP management,

those with poor control were more likely to develop MetS.<sup>23</sup> Although the exact mechanism of MetS caused by abnormal BP was unclear, increased sympathetic activity was believed to be related to the higher risk of MetS following prehypertension or hypertension.<sup>24</sup>

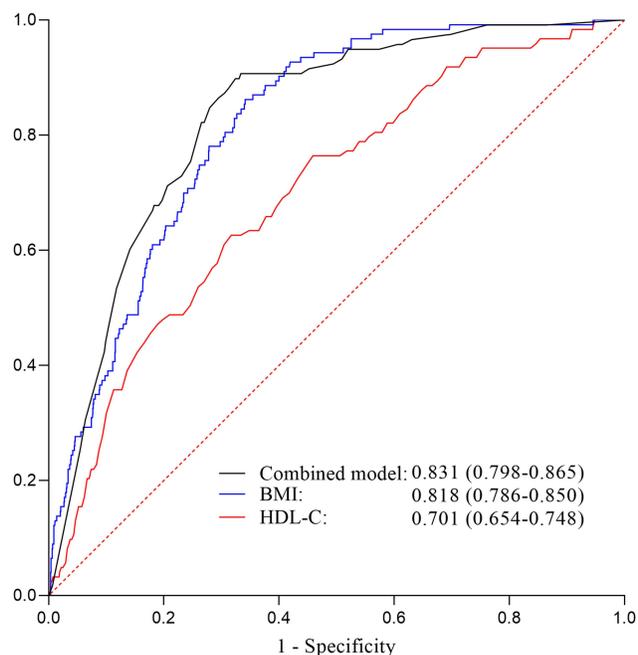
Low-HDL (<1.10 mmol/L) was observed to be related to the rising risk of MetS in the present research. Low HDL-C level, regarded as a part of atherogenic dyslipidemia, was associated with insulin resistance, visceral obesity, and worsened inflammation, and those findings were associated with MetS.<sup>25–27</sup> Currently, the causal relationship between fatty liver and MetS is in conclusion. Fatty liver has been reported as the hepatic manifestation of MetS.<sup>28</sup> However, other studies found that fatty liver might be a strong determinant for the high risk of MetS, which suggested that it might have potential clinical significance for diagnosing, preventing, and treating the MetS.<sup>29,30</sup> In another meta-analysis, fatty liver has been proved to be strongly associated with the MetS risk based on a 5-year cohort.<sup>31</sup> Our results are consistent with the latter that fatty liver could increase the risk of MetS. This is likely due to the following: 1) the existence of fatty liver could impair liver function that is responsible for regulating glucose metabolism<sup>32</sup> and 2) advanced glycation end products accumulating in the fatty liver are released into the circulation, activating their receptor in the liver, which results in low-grade inflammation.<sup>33</sup>

**Table 4** Multivariate Analysis for the Risk of MetS

Characteristics	$\beta$	SE	Wald	P	OR	95% CI	
						Lower	Upper
Constant	-5.570	0.520	114.927	<0.001			
BMI							
Normal	Ref						
Overweight	1.528	0.330	21.456	<0.001	4.610	2.415	8.800
BP							
Normal	Ref						
Prehypertension	1.015	0.304	11.115	<0.001	2.759	1.519	5.011
Hypertension	1.278	0.390	10.745	0.001	3.589	1.672	7.706
HDL-C (mmol/L)							
Q <sub>1</sub> (<1.10)	1.313	0.469	7.840	0.005	3.716	1.483	9.313
Q <sub>2</sub> (1.10–1.30)	0.752	0.481	2.442	0.118	2.121	0.826	5.447
Q <sub>3</sub> (1.30–1.55)	0.341	0.531	0.412	0.521	1.406	0.497	3.980
Q <sub>4</sub> ( $\geq$ 1.55)	Ref						
Fatty liver							
Yes	Ref						
No	0.947	0.286	10.975	<0.001	2.577	1.472	4.512

**Abbreviations:** SE, standard error; OR, odds risk, CI, confidence interval; BMI, body mass index; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol.

The MetS will increase the risk of suffering T2DM and cardiovascular diseases by 5 and 2 times, respectively, in the following 5 to 10 years,<sup>34</sup> demonstrating that accurate

**Figure 2** The ROC curve of the prediction model.

MetS prediction model might protect people from these diseases with individualized risk prediction and interventions. In this study, a convincing multi-factor prediction model was established, which may help clinicians identify people at high risk of MetS earlier. Several single indicators have been proposed to predict or diagnose diseases, such as HDL-C or BMI. However, in actual clinical work, the strength of clinical evidence may not be sufficient for clinicians to predict or diagnose diseases with only one predictive indicator. Moreover, early interventions such as lifestyle adjustment, weight loss, and fatty liver control could reduce the risk of MetS.<sup>35</sup> Of note, given the association between increased risk of MetS with elevated BP, medications to control BP should consider their antihypertensive effects and their effects on blood glucose and lipid metabolism. Herein, the accurate and personalized quantitative model proposed by this study will help physicians predict the risk of MetS and identify the population that needs close follow-up.

Several limitations cannot be ignored in this research. First, the data we collected was limited to participants only from Hangzhou, which did not represent all Chinese. People without medical examination were omitted. Secondly, factors such as eating habits and others that

**Table 5** The Performance of the Prediction Model

Variables	AUC (95% CI)	SE	Sensitivity (95% CI)	Specificity (95% CI)	Youden Index	Cut-off	Z	P
Combined model*	0.831 (0.798–0.865)	0.017	0.898 (0.831–0.941)	0.676 (0.651–0.700)	0.574	0.513		
BMI	0.818 (0.786–0.850)	0.016	0.862 (0.790–0.912)	0.659 (0.634–0.683)	0.521	23.96	0.557	0.578
HDL-C	0.701 (0.654–0.748)	0.024	0.626 (0.538–0.707)	0.683 (0.658–0.707)	0.309	1.175	4.420	<0.001

**Notes:** \*Combined model was built based on body mass index (BMI), prehypertension, prehypertension, high-density lipoprotein cholesterol (HDL-C), and fatty liver.

**Abbreviations:** SE, standard error; CI, confidence interval; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol.

may affect the development of MetS were not informed. Thirdly, as the 2004 Chinese Diabetes Society criteria were adopted to diagnose MetS, the arrival of further high-quality experimental studies with larger sample sizes has to be awaited to verify whether the results under different criteria are consistent with ours. Fourth, the specificity of the model presented is lower (0.676). However, the sensitivity of the model is relatively high (0.898), with the AUC of 0.831, which indicates that the model could effectively identify patients with higher risk of MetS for individualized intervention timely. Early intervention is essential for the management of chronic diseases. Furthermore, for patients with false positives, whether it is to control obesity, hypertension, or fatty liver, it is beneficial to the health of them. Further studies with rigorous design should be carried out to explore the results.

## Conclusion

The model performed well predictive power for the risk of MetS based on an 8-year Chinese cohort, which may provide a reference for clinicians to identify high-risk groups early. The selected predictors were used to construct the MetS prediction model, including BMI, prehypertension, prehypertension, HDL, and fatty liver. The AUC of the multi-factor model was 0.831, with a sensitivity of 0.898 and a specificity of 0.676, which indicated that the risk of MetS would be well predicted by this model. However, further researches are required to verify whether individual interventions based on this new model will prevent the risk of MetS.

## Acknowledgments

HuanYu Guo and Wenwei Jiang are co-first authors for this study.

## Disclosure

The authors report no conflicts of interest in this work.

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