

ORIGINAL RESEARCH

Early Identification of Metabolic Syndrome in Adults of Jiaxing, China: Utilizing a Multifactor Logistic Regression Model

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Purpose: The purpose of this study is to develop and validate a clinical prediction model for diagnosing Metabolic Syndrome (MetS) based on indicators associated with its occurrence.

Patients and Methods: This study included a total of 26,637 individuals who underwent health examinations at the Jiaxing First Hospital Health Examination Center from January 19, 2022, to December 31, 2022. They were randomly divided into training (n = 18645) and validation (n = 7992) sets in a 7:3 ratio. Firstly, the Least Absolute Shrinkage and Selection Operator (LASSO) regression algorithm was employed for variable selection. Subsequently, a multifactor Logistic regression analysis was conducted to establish the predictive model, accompanied by nomograms. Thirdly, model validation was performed using Receiver Operating Characteristic (ROC) curves, Harrell's concordance index (C-index), calibration plots, and Decision Curve Analysis (DCA), followed by internal

Results: In this study, six predictive indicators were selected, including Body Mass Index, Triglycerides, Blood Pressure, High-Density Lipoprotein Cholesterol, Low-Density Lipoprotein Cholesterol, and Fasting Blood Glucose. The model demonstrated excellent predictive performance, with an AUC of 0.978 (0.976–0.980) for the training set and 0.977 (0.974–0.980) for the validation set in the nomogram. Calibration curves indicated that the model possessed good calibration ability (Training set: Emax 0.081, Eavg 0.005, P = 0.580; Validation set: Emax 0.062, Eavy 0.007, P = 0.829). Furthermore, decision curve analysis suggested that applying the nomogram for diagnosis is more beneficial when the threshold probability of MetS is less than 89%, compared to either treating-all or treating-none at all.

Conclusion: We developed and validated a nomogram based on MetS risk factors, which can effectively predict the occurrence of MetS. The proposed nomogram demonstrates significant discriminative ability and clinical applicability. It can be utilized to identify variables and risk factors for diagnosing MetS at an early stage.

Keywords: metabolic syndrome, risk factors, nomogram, prediction

Introduction

In 1988, Reaven first described Metabolic Syndrome (MetS) as Syndrome X, representing a clinical metabolic disorder characterized by a collection of risk factors. These factors include hypertension, insulin resistance (IR), elevated blood glucose, high levels of low-density lipoprotein cholesterol (LDL-C), and increased triglycerides (TG). MetS is a multifaceted pathophysiological condition that may arise from an imbalance between energy intake and expenditure. It can also be influenced by individual genetics, unhealthy lifestyle, as well as other factors including food quality and composition.2 IR is one of the core characteristics of this disease. A series of metabolic disorders triggered by IR,

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including hyperglycemia, hyperinsulinemia, and lipid metabolism abnormalities, are significant contributors to MetS. The abnormal accumulation of adipose tissue, especially the increase in visceral fat, leads to obesity, which is not only a result of IR but also one of its causes. Additionally, chronic low-grade inflammation and oxidative stress play important roles in the occurrence and progression of MetS.^{3–5}

Regarding MetS, we do not have direct global prevalence data. Nevertheless, the occurrence of MetS is roughly threefold higher compared to diabetes (DM),⁶ with an estimated 529 million diabetes patients in 2021,⁷ it is estimated that globally about 1.6 billion people have MetS. MetS increases the risk of developing cardiovascular diseases (CVD), DM, and other conditions, as well as the risk of mortality.⁸ MetS and its components are associated with increased oxidative stress. Oxidative stress, through the production of a large amount of reactive oxygen species, leads to structural changes in organs and tissues. This plays a crucial role in the development and progression of MetS complications, such as atherosclerotic cardiovascular diseases and cancer.⁹⁻¹¹

Studies¹² have reported that MetS increases overall mortality by 1.27 times (95% CI 0.90–1.78), and the risks of CVD and DM by 1.65 times (95% CI 1.38–1.99) and 2.99 times (95% CI 1.96–4.57) respectively. Additionally, research by Wang et al¹³ analyzing a cohort of 1917 participants without alcoholic fatty liver disease (NAFLD) revealed a notable rise in the risk of NAFLD among those diagnosed with MetS (HR, 3.17; 95% CI, 2.42–4.14). Furthermore, the likelihood of NAFLD escalated in tandem with the number of MetS components (P < 0.001). Shen et al¹⁴ indicated in a meta-analysis that MetS is notably linked to an elevated risk of colorectal cancer (RR 1.36, 95% CI 1.26–1.47, P < 0.001). Furthermore, the risk of colorectal cancer rises in correlation with the number of MetS components. In summary, the presence of MetS significantly impacts people's health and quality of life. However, MetS often develops silently, and effective tools for identifying and diagnosing the risk of MetS are currently lacking. Many individuals may be unaware of their condition. Chen et al¹⁵ emphasized that the timely identification, preventive measures, and effective management of MetS are recognized as crucial avenues for mitigating the advancement of atherosclerosis and the onset of CVD. Therefore, it is crucial to find suitable tools for early identification and diagnosis of MetS and to stratify its risk.

Current research indicates that dietary habits, smoking, alcohol consumption, physical activity, blood pressure (BP), blood glucose, blood lipids, Body Mass Index (BMI), gender, and age are closely associated with the occurrence of MetS. Unhealthy dietary habits, lack of physical activity, smoking, and alcohol consumption are significant contributors to MetS. A diet high in sugar and fat can lead to obesity and dyslipidemia, while a sedentary lifestyle exacerbates IR. Smoking and alcohol consumption further increase the risk of CVD. Numerous studies have shown that improving lifestyle habits, such as adjusting diet, increasing physical activity, quitting smoking and limiting alcohol intake, can effectively reduce the incidence of MetS and enhance overall quality of life for patients. Therefore, this study is based on the aforementioned indicators to design and validate a clinical prediction model aimed at diagnosing MetS.

Materials and Methods

Ethics Statement

This study followed the principles outlined in the Helsinki Declaration and obtained approval from the Ethics Committee of the First Hospital of Jiaxing (Approval number 2022-KY-021). All participants have signed informed consent forms.

Study Population

The subjects of this study comprised individuals who participated in the annual health examination organized by the Health Management Center of the First Hospital of Jiaxing. These participants included staff from government institutions and enterprises, as well as self-paying individuals undergoing health check-ups, from January 19 to December 31, 2022. The study ultimately encompassed a total of 26,637 individuals. A self-designed questionnaire was employed to survey the participants, covering basic information, health details, laboratory indicators, as well as dietary structure and preferences.

All participants underwent measurements and data collection for basic human parameters such as height, weight, and BP. A standardized questionnaire was administered through one-on-one, face-to-face interviews conducted by trained medical professionals from various disciplines. The collected data were entered into a database using Epi-Data 3.1 software.

Exclusion criteria were as follows: (1) individuals aged below 18; (2) patients with hearing or cognitive impairments that prevent effective verbal communication; (3) individuals unwilling to cooperate in completing the survey; and (4) participants with missing data. Figure 1 provides a comprehensive overview of the patient selection process.

The diagnostic criteria for MetS, as defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), are established when three or more of the following conditions are present: (a) obesity, with a waist circumference greater than 102 centimeters(cm) for men or 88 cm for women; (b) TG ≥150 mg/dL (1.7 mmol/L) or undergoing lipid-lowering therapy; (c) high-density lipoprotein cholesterol (HDL-C) below 40 mg/dL (1.0 mmol/L) for men or below 50 mg/dL (1.3 mmol/L) for women; (d) BP≥130/85 mmHg orreceiving antihypertensive medication; (e) Fasting blood glucose (FBG) ≥100 mg/dL (5.6 mmol/L) or receiving treatment for diabetes. ¹⁹

Data Collection

This study collected research data on various factors, including gender, age, education level (junior high school or below, high school or college, undergraduate or above), occupation (civil servant, public institution employee, corporate employee, other), civil status (married, unmarried), smoking status, alcohol consumption, exercise habits, meal frequency (regular, irregular), food types consumed (do not eat or occasionally eat, regularly eat: potatoes, white meat, red meat, eggs, dairy products, soy products, vegetables, fruits, snacks, desserts, fast food, nuts), dietary preferences (sweet, spicy, salty, light diet), BMI, BP (elevated or not elevated), and laboratory indicators [total cholesterol (TC), TG, HDL-C, LDL-C, FBG].

Measurement of relevant indicators:(1) BP Measurement Method: Participants rested for 30 minutes in a quiet environment before measurement. BP was recorded on at least two occasions with a 1–2 minute interval. In cases where the systolic or diastolic pressure exhibited a difference of more than 5 mmHg, additional measurements were

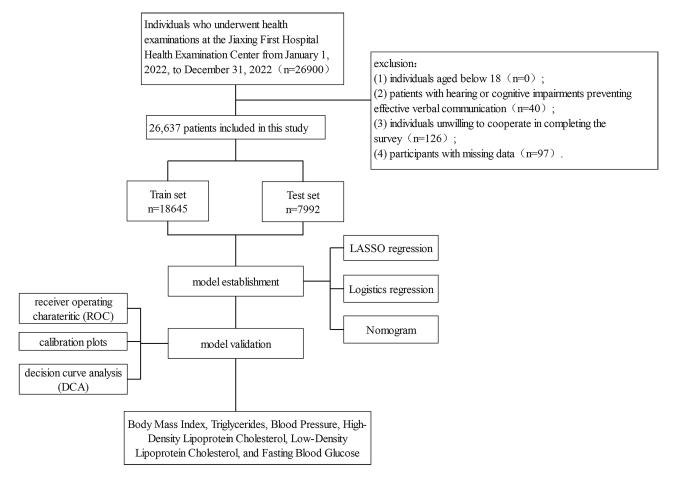


Figure I Inclusion and exclusion flowchart of the study.

conducted, and the average of three readings was taken as the final result. (2) Blood Collection and Measurement Method: Participants fasted for at least 8 hours. A 5 mL venous blood sample was collected using a vacuum blood collection tube without anticoagulants. After centrifugation at 3000 rpm, the separated serum was used to the detection of biochemical indicators such as TG, HDL-C, and FPG. Biochemical tests were conducted using the Roche COBAS 8000 fully automatic biochemical analyzer. Definitions of relevant indicators: (1) Smoking: Continuous or cumulative smoking for 6 months or more, or exposure to passive smoke for 3 or more days per week, was defined as smoking. (2) Exercise: Engaging in physical activity 3 times or more per week, with each session lasting 30 minutes or more, and sweating during exercise was defined as regular exercise. (3) Alcohol Consumption: Drinking alcohol once or more per week was defined as alcohol consumption. (4) Meal frequency: The number of meals consumed at fixed times throughout the day. (5) Dietary Preferences: Determined based on the participant's own judgment. (6) BMI: Defined as an individual's weight (in kilograms) divided by the square of their height (in meters). (7) Elevated BP: Specified as systolic pressure greater than or equal to 130 mmHg and/or diastolic pressure greater than or equal to 85 mmHg.

Statistical Analysis

Continuous variables that adhere to a normal distribution are presented using the mean and standard deviation (SD), while those with a non-normal distribution are represented by the median and interquartile range (IQR). Categorical variables are expressed in terms of counts and percentages (%). For continuous variables, the choice between the Students *t*-test or non-parametric tests for comparison depends on the distribution characteristics. Comparison of categorical variables is performed using either the Pearson chi-square test or Fisher's exact test.

We utilized the Least Absolute Shrinkage and Selection Operator (LASSO) regression analysis to identify optimal variables with non-zero coefficients for prediction.²⁰ The selected variables were then included in a multivariable logistic regression model to analyze their correlation with MetS. Following this, a nomogram was developed based on these variables to provide a visual representation of the predictive relationships.

The validation of the predictive model primarily encompasses three main procedures: discrimination evaluation, calibration evaluation, and clinical applicability evaluation. In our study, the Receiver Operating Characteristic (ROC) curve [Area Under the Curve (AUC)], Harrell's concordance index (C-index), and calibration curve were utilized to appraise the model's discriminatory capabilities. Additionally, Decision Curve Analysis (DCA) was employed to gauge the practical application value of the model in clinical practice.

We conducted all statistical analyses using R software (http://www.R-project.org; version 4.2.3). All tests were two-sided, and a *P*-value less than 0.05 was deemed statistically significant. The "caret" package was employed to randomly partition the data into training and validation sets. The "comparegroups" package was used to analyze and compare baseline characteristics between the training and validation sets. LASSO regression analysis was conducted using the "glmnet" package, and multiple Logistic regression analysis was performed using the "glm" package. The "pROC" package, "ggROC" package, and "fbroc" package were utilized for drawing ROC curves and calculating the AUC. Calibration curves and nomograms were plotted using the "val.prob" function and "calibrate" from the "rms" package. The DCA was conducted using the "rmda" package.

Results

Characteristics of Included Patients

In this study, a total of 26,637 participants with comprehensive data were incorporated. These participants were randomly allocated into a training set (n = 18,645) and a validation set (n = 7992) following a 7:3 ratio. The median age was 42.0 years [33.0; 53.0], with 14,450 (54.2%) males. The majority had an undergraduate education or higher (61.6%), the majority of participants were married (94.8%), most had a regular eating schedule (93.8%), and regularly consumed vegetables (75.5%). In the end, 2413 (9.06%) individuals were diagnosed with MetS, with 1700 cases (9.12%) in the training group and 713 cases (8.92%) in the validation set. Single-factor analysis indicated no statistically significant differences in the relevant indicators between the training and validation sets (P > 0.05), suggesting a high level of comparability between the two groups (Table 1) (Supplementary file 1).

Table I Baseline and Clinical Characteristics of the Study Population

	Total (n = 26,637)	Test Set (n = 7992)	Training Set (n = 18645)	P-value
MetS	2413 (9.06%)	713 (8.92%)	1700 (9.12%)	0.608
Gender				0.009
Male	14450 (54.2%)	4433 (55.5%)	10,017 (53.7%)	
Female	12187 (45.8%)	3559 (44.5%)	8628 (46.3%)	
Age	42.0 [33.0;53.0]	43.0 [33.0;54.0]	42.0 [33.0;53.0]	0.028
Education Level				0.471
Junior high school or below	2335 (8.77%)	694 (8.68%)	1641 (8.80%)	
High school or college	7893 (29.6%)	2410 (30.2%)	5483 (29.4%)	
Undergraduate or above	16409 (61.6%)	4888 (61.2%)	11,521 (61.8%)	
Civil Status				0.144
Unmarried	1372 (5.15%)	387 (4.84%)	985 (5.28%)	
Married	25265 (94.8%)	7605 (95.2%)	17,660 (94.7%)	
Exercise				0.310
Regular	15538 (58.3%)	4624 (57.9%)	10,914 (58.5%)	
Irregular	11099 (41.7%)	3368 (42.1%)	7731 (41.5%)	
Occupation				0.143
Civil servant	6485 (24.3%)	1912 (23.9%)	4573 (24.5%)	
Public Institution Employee	5323 (20.0%)	1662 (20.8%)	3661 (19.6%)	
Corporate employee	7750 (29.1%)	2289 (28.6%)	5461 (29.3%)	
Other	7079 (26.6%)	2129 (26.6%)	4950 (26.5%)	
Alcohol consumption				0.189
NO	21500 (80.7%)	6490 (81.2%)	15,010 (80.5%)	
YES	5137 (19.3%)	1502 (18.8%)	3635 (19.5%)	
Smoking status				0.842
NO	4446 (16.7%)	1340 (16.8%)	3106 (16.7%)	
YES	22191 (83.3%)	6652 (83.2%)	15,539 (83.3%)	
Meal frequency				0.389
Regular	24984 (93.8%)	7480 (93.6%)	17,504 (93.9%)	
Irregular	1653 (6.21%)	512 (6.41%)	1141 (6.12%)	
Potatoes				0.412
Do not eat or occasionally eat	17770 (66.7%)	5361 (67.1%)	12,409 (66.6%)	
Regularly eat	8867 (33.3%)	2631 (32.9%)	6236 (33.4%)	

(Continued)

Table I (Continued).

	Total (n = 26,637)	Test Set (n = 7992)	Training S et (n = 18645)	P-value
White meat				0.648
Do not eat or occasionally eat	13427 (50.4%)	4011 (50.2%)	9416 (50.5%)	
Regularly eat	13210 (49.6%)	3981 (49.8%)	9229 (49.5%)	
Red meat				0.670
Do not eat or occasionally eat	15046 (56.5%)	4498 (56.3%)	10,548 (56.6%)	
Regularly eat	11591 (43.5%)	3494 (43.7%)	8097 (43.4%)	
Eggs				0.279
Do not eat or occasionally eat	8797 (33.0%)	2678 (33.5%)	6119 (32.8%)	
Regularly eat	17840 (67.0%)	5314 (66.5%)	12,526 (67.2%)	
Dairy products				0.762
Do not eat or occasionally eat	17399 (65.3%)	5209 (65.2%)	12,190 (65.4%)	
Regularly eat	9238 (34.7%)	2783 (34.8%)	6455 (34.6%)	
Soy products				0.445
Do not eat or occasionally eat	14405 (54.1%)	4293 (53.7%)	10,112 (54.2%)	
Regularly eat	12232 (45.9%)	3699 (46.3%)	8533 (45.8%)	
Vegetables				0.930
Do not eat or occasionally eat	6537 (24.5%)	1958 (24.5%)	4579 (24.6%)	
Regularly eat	20100 (75.5%)	6034 (75.5%)	14,066 (75.4%)	
Fruits				0.099
Do not eat or occasionally eat	7466 (28.0%)	2296 (28.7%)	5170 (27.7%)	
Regularly eat	19171 (72.0%)	5696 (71.3%)	13,475 (72.3%)	
Desserts				0.934
Do not eat or occasionally eat	24807 (93.1%)	7445 (93.2%)	17,362 (93.1%)	
Regularly eat	1830 (6.87%)	547 (6.84%)	1283 (6.88%)	
Fast food				0.535
Do not eat or occasionally eat	25177 (94.5%)	7565 (94.7%)	17,612 (94.5%)	
Regularly eat	1460 (5.48%)	427 (5.34%)	1033 (5.54%)	
Snacks				0.945
Do not eat or occasionally eat	24730 (92.8%)	7418 (92.8%)	17,312 (92.9%)	
Regularly eat	1907 (7.16%)	574 (7.18%)	1333 (7.15%)	
Nuts				0.778
Do not eat or occasionally eat	21762 (81.7%)	6538 (81.8%)	15,224 (81.7%)	
Regularly eat	4875 (18.3%)	1454 (18.2%)	3421 (18.3%)	

(Continued)

Table I (Continued).

	Total (n = 26,637)	Test Set (n = 7992)	Training Set (n = 18645)	P-value	
Sweet diet				0.810	
NO	19213 (72.1%)	5756 (72.0%)	13,457 (72.2%)		
YES	7424 (27.9%)	2236 (28.0%)	5188 (27.8%)		
Spicy diet				0.297	
NO	21510 (80.8%)	6485 (81.1%)	15,025 (80.6%)		
YES	5127 (19.2%)	1507 (18.9%)	3620 (19.4%)		
Salty diet				0.789	
NO	20932 (78.6%)	6289 (78.7%)	14,643 (78.5%)		
YES	5705 (21.4%)	1703 (21.3%)	4002 (21.5%)		
Light diet				0.281	
NO	12541 (47.1%)	3722 (46.6%)	8819 (47.3%)		
YES	14096 (52.9%)	4270 (53.4%)	9826 (52.7%)		
BMI, kg/m ²	23.3 [21.1;25.5]	23.3 [21.2;25.5]	23.3 [21.1;25.5]	0.718	
BP, mmHg				0.713	
Not elevated	20764 (78.0%)	6218 (77.8%)	14,546 (78.0%)		
Elevated	5873 (22.0%)	1774 (22.2%)	4099 (22.0%)		
TG, mmol/L	1.21 [0.86;1.79]	1.23 [0.87;1.82]	1.20 [0.85;1.79]	0.034	
HDL-C, mmol/L	1.35 [1.13;1.60]	1.34 [1.13;1.59]	1.35 [1.13;1.60]	0.078	
LDL-C, mmol/L	2.92 [2.44;3.45]	2.93 [2.46;3.46]	2.92 [2.44;3.45]	0.230	
TC, mmol/L	4.68 [4.15;5.28]	4.69 [4.15;5.28]	4.68 [4.15;5.28]	0.486	
FBG, mmol/L	4.93 [4.63;5.33]	4.94 [4.64;5.33]	4.93 [4.62;5.32]	0.060	

Abbreviations: TG, Triglycerides; BP, Blood Pressure; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; TC, total cholesterol; FBG, Fasting Blood Glucose; kg/m², kilograms per square meter; mmHg, millimeters of mercury; mmol/L, millimoles per liter.

Feature Selection

Among the numerous potential influencing factors, the LASSO regression model identified six potential predictor variables with non-zero coefficients based on the training set data. The selection of fitted features for constructing the predictive model was determined by choosing the maximum λ within one standard error range of the minimum Mean Squared Error (MSE). The selected variables include BMI, TG, BP, HDL-C, LDL-C, and FBG (Figure 2A and B).

Developing Nomogram

The six selected predictor variables identified above were included in a multiple logistic regression analysis to establish the predictive model (Table 2). To facilitate visualization and clinical application, we developed a nomogram. The score for each variable corresponds to the score (points) on the upper scoring axis. The total score corresponds to the probability of developing MetS on the lower axis. (Figure 3).

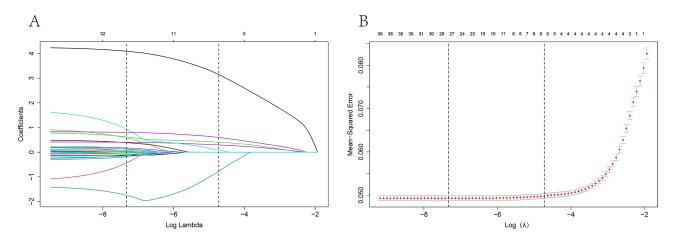


Figure 2 Variable selection by LASSO binary Logistics regression model. (A) Each curve with different colors represents the change trajectory of each independent variable coefficient, the y-axis is the coefficient value; the upper x-axis is the number of non-zero coefficients in the LASSO model. (B) Represented the cross-validation result with different λ value, the left dot line represented lambda min which was the lowest λ of minimum mean cross-validated error, the right dot line represented the lambda. Ise which was the largest value of λ such that error is within I standard error of the cross-validated errors for lambda. Min.

Validation of Predictive Models

MetS prediction model ROC curve analysis (Figure 4A and B) revealed AUCs of 0.978 (0.976–0.980) for the training set and 0.977 (0.974–0.980) for the validation set. The C-index values were 0.978 for the training set and 0.977 for the validation set. indicating good discriminative performance of the model. Calibration curve results, as shown in Figure 5A and B, indicated non-significant P-values from the Unreliability test (P = 0.580 for the training set, P = 0.829 for the validation set), suggesting excellent calibration of the model. Emax and Eavg values were 0.047 and 0.005 for the training set and 0.062 and 0.007 for the validation set, respectively, indicating no deviation between prediction and observation, suggesting a perfect fit. DCA curves (Figure 6A and B) demonstrated that applying the nomogram to forecast MetS risk in the population would provide greater advantages compared to treating all or adopting a no-treatment strategy, particularly when the threshold probability for MetS is below 89.0% in the training set and 83.7% in the validation set, respectively.

Discussion

In this research, we created and validated an inclusive and user-friendly diagnostic nomogram for predicting the risk of MetS in the population. The nomogram incorporates six significant potential predictor variables (BMI, TG, HDL-C, LDL-C, BP, and FBG). Our nomogram demonstrates sufficient discriminative ability (training set AUC: 0.978, 95% CI: 0.976–0.980) and good calibration (training set: Emax 0.081, Eavg 0.005, P = 0.580). Additionally, DCA curve illustrates its strong clinical applicability. Particularly, when the threshold probability for an individual's risk of MetS is less than 89%, using this nomogram for prediction is more effective than the "treat-all" or "treat-none" strategies. Furthermore, during internal validation, the model continues to demonstrate good diagnostic value. Therefore, our proposed nomogram may effectively assist individuals in quantifying their risk of developing MetS.

In today's era, non-communicable diseases have spread widely in both developed and developing countries. MetS, as a major non-communicable disease, has become a serious clinical and public health issue. 21,22 The incidence of MetS is sharply rising globally, but the prevalence varies in different countries and regions. Researches^{6,23} indicate that the United States is one of the countries most severely affected by MetS, with approximately one-third of the population suffering from MetS.⁶ Studies conducted earlier have indicated that the prevalence of MetS in Chinese rural adults is higher than that among urban adults in the United States.²⁴ Additionally, He²⁵ mentioned in a review that two crosssectional surveys representing the entire nation revealed that the prevalence of MetS among Chinese adults rose from 9.5% (95% CI: 9.2–9.7%) in 2002 to 18.7% (95% CI: 18.3–19.1%) in 2010–2012. Samson et al⁸ stated in a review that MetS is not considered a disease but rather an aggregation of factors associated with increased risk for diseases. The presence of MetS is linked to an elevated risk of CVD, DM, NAFLD, and cancer. Therefore, timely identification and diagnosis of MetS may play a role in lowering the risk of associated diseases. Among the overall population, if

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Table 2 Univariate and Multivariate Analysis of the Model

Characteristics	Univariate Analysis						Multivariate Analysis					
	Uni-B	Uni-SE	Uni-OR	Uni-CI	Uni-Z	Uni-P	Multi-B	Multi-SE	Multi-OR	Multi-CI	Multi-Z	Multi-P
FBG, mmol/L	0.932	0.02661	2.54	2.54(2.412–2.678)	35.038	0	0.876	0.0362	2.402	2.401 (2.239–2.581)	24.199	0
LDL-C, mmol/L	0.565	0.03099	1.76	1.76(1.656–1.87)	18.236	0	0.511	0.05469	1.667	1.666 (1.497–1.856)	9.341	0
HDL-C, mmol/L	-2.413	0.09313	0.09	0.09(0.074–0.107)	-25.916	0	-2.19	0.16898	0.112	0.111 (0.080-0.155)	-12.963	0
TG, mmol/L	0.76	0.02179	2.139	2.139(2.05–2.233)	34.888	0	0.535	0.03143	1.707	1.707 (1.606–1.817)	17.025	0
TC, mmol/L	0.451	0.02663	1.571	1.571(1.491–1.655)	16.956	0						
BP, mmHg	3.669	0.07687	39.218	39.21(33.81–45.71)	47.733	0	4.313	0.1194	74.628	74.62 (59.34–94.78)	36.117	0
BMI, kg/m ²	0.423	0.00968	1.526	1.526(1.498–1.556)	43.659	0	0.404	0.01542	1.498	1.498 (1.454–1.544)	26.226	0
Light diet	0.076	0.05107	1.079	1.079(0.976–1.192)	1.482	0.138						
Salt diet	0.027	0.06158	1.027	1.027(0.91–1.158)	0.44	0.66						
Spicy diet	0.077	0.06312	1.08	1.08(0.953–1.221)	1.218	0.223						
Sweet diet	-0.153	0.05848	0.858	0.858(0.765–0.962)	-2.611	0.009						
Nuts	0.043	0.06501	1.044	1.044(0.918–1.184)	0.663	0.508						
Fast food	-0.053	0.11338	0.949	0.949(0.755–1.178)	-0.465	0.642						
Desserts	0.098	0.09715	1.103	1.103(0.908–1.329)	1.007	0.314						
Snacks	0.024	0.09793	1.024	1.024(0.841-1.236)	0.243	0.808						
Fruits	-0.044	0.05639	0.957	0.957(0.858–1.07)	-0.774	0.439						
Vegetables	0.005	0.05917	1.005	1.005(0.896–1.13)	0.089	0.929						
Soy products	-0.06	0.05119	0.942	0.942(0.852-1.041)	-1.175	0.24						
Dairy products	0.145	0.05261	1.156	1.156(1.042–1.281)	2.749	0.006						
Eggs	0.02	0.05434	1.021	1.021(0.918–1.136)	0.375	0.708						
Red meat	0.002	0.05132	1.002	1.002(0.906–1.108)	0.038	0.97						
White meat	-0.012	0.05089	0.988	0.988(0.895-1.092)	-0.228	0.82						
Potatoes	0.076	0.0534	1.079	1.079(0.971–1.198)	1.424	0.154						

Table 2 (Continued).

Characteristics	Univariate Analysis							Multivariate Analysis					
	Uni-B	Uni-SE	Uni-OR	Uni-CI	Uni-Z	Uni-P	Multi-B	Multi-SE	Multi-OR	Multi-CI	Multi-Z	Multi-P	
Meal frequency	0.238	0.09777	1.268	1.268(1.043-1.53)	2.432	0.015							
Exercise	-0.04	0.05179	0.961	0.961(0.868-1.063)	-0.769	0.442							
Alcohol consumption	-0.03 I	0.06472	0.97	0.97(0.853-1.099)	-0.477	0.633							
Smoking status	-0.027	0.06778	0.973	0.973(0.854–1.114)	-0.396	0.692							
Civil Status	1.677	0.23306	5.349	5.349(3.491–8.75)	7.195	0							
Occupation													
Civil servant	-0.212	0.07736	0.809	0.809(0.694–0.941)	-2.745	0.006							
Public institution employee	-0.41	0.07241	0.664	0.664(0.576–0.765)	-5.663	0							
Corporate employee	0.115	0.06664	1.121	1.121(0.984–1.278)	1.719	0.086							
Education Level													
Junior high school or below	-0.301	0.08278	0.74	0.74(0.63–0.872)	-3.634	0							
High school or college	-0.717	0.07896	0.488	0.488(0.419–0.571)	-9.084	0							
Age	0.045	0.00184	1.046	1.046(1.042–1.05)	24.462	0							
Gender	-1.398	0.06349	0.247	0.247(0.218–0.279)	-22.023	0							

Abbreviations: TG, Triglycerides; BP, Blood Pressure; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; TC, total cholesterol; FBG, Fasting Blood Glucose; kg/m², kilograms per square meter; mmHg, millimeters of mercury; mmol/L, millimoles per liter.

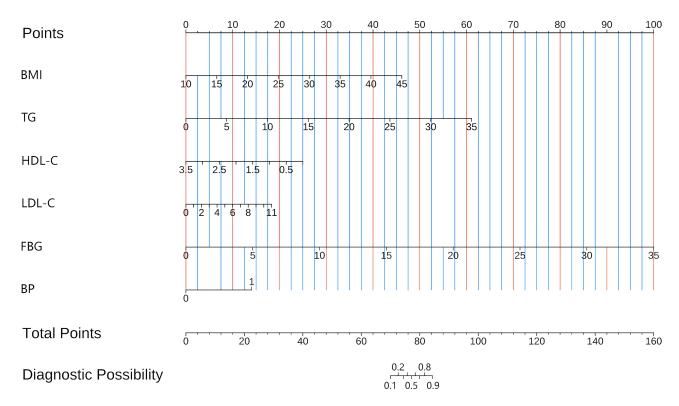


Figure 3 The proposed nomogram for predicting metabolic syndrome (MetS).

Notes: First, find point for each predictor of an individual on the uppermost rule; then add all points together and find the total points on the penultimate rule below. The corresponding predicted probability of developing MetS could be found on the lowest rule.

Abbreviations: BMI, Body Mass Index; TG, Triglycerides; BP, Blood Pressure; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; FBG, Fasting Blood Glucose.

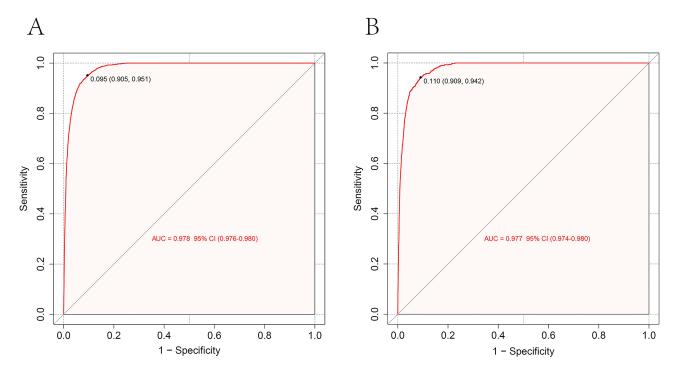


Figure 4 The receiver operating characteristic (ROC) curve of the training and validation cohort. (A) The ROC curve for the training cohort. (B) The ROC curve for the validation cohort.

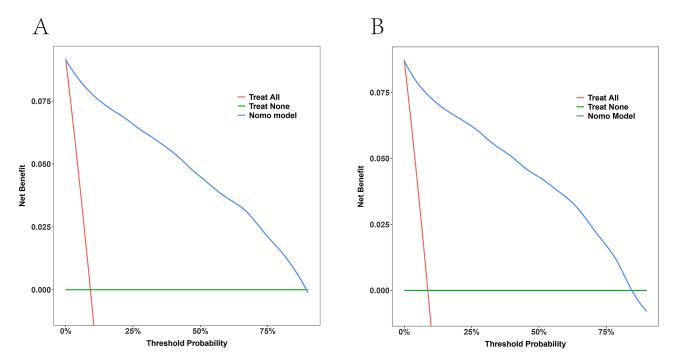


Figure 5 The calibration curve for training and validation set. (A) The calibration curve for training set. (B) The calibration curve for validation set.

Notes: It shows a good fit between the predicted risks of developing metabolic syndrome (MetS) and the observed outcomes. The Unreliability test yielded a P value of 0.580 (P > 0.05) in the training set, indicating that there was no statistical departure of the calibration from a perfect fit between the ideal model and the proposed model, and an Emax of 0.047 and an Eavg of 0.005 indicates that the deviation between the predicted outcomes and the observed outcomes is very little. The grey solid line represents a perfect prediction by an ideal model, and the dotted line shows the performance of the nomogram.

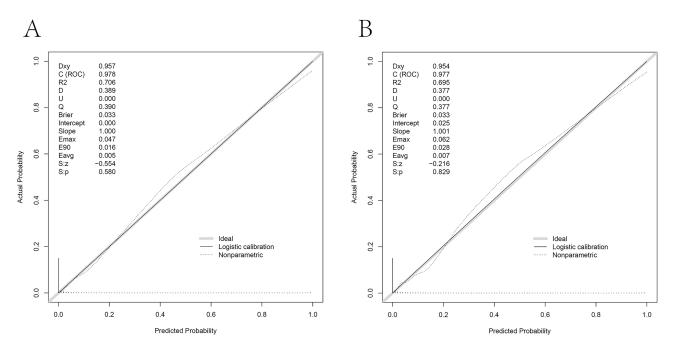


Figure 6 The DCA for the training and validation set. (A) The Decision curve analysis (DCA) for training set. (B) The DCA for validation set.

Notes: The green (horizontal) line means that all samples are negative (treat-none), and the red (oblique) line means that all samples are positive (treat-all). The blue line represents the risk nomograms.

individuals do not fulfill the diagnostic criteria of MetS, they may overlook preventive measures for their condition. However, in reality, they might be considered as having "preclinical MetS". Therefore, the development of a quantitative tool for predicting MetS is considered crucial.

In the past, decision trees were commonly used to predict the occurrence of MetS.^{27–29} The model for classifying decision trees³⁰ is illustrated through a structure reminiscent of a tree, where each internal node signifies a test for a feature, each branch represents a possible test outcome, and each leaf node denotes a classification. While this method can predict MetS, the algorithm in this model cannot quantitatively measure and predict the risk factors leading to MetS.

Considering the shortcomings of decision trees, nomograms have been widely adopted in recent years. Nomograms integrate valuable variables and present complex mathematical formulas in a graphical form, offering excellent visibility. As a practical tool, the nomogram model can stratify populations based on risk characteristics, facilitating early detection and diagnosis of MetS. This, in turn, enables effective personalized treatment and management. In the context of MetS, Wang et al attempted to use a nomogram model for identification and diagnosis, achieving favorable results. The study incorporated non-invasive anthropometric measurements such as gender, age, smoking status, systolic and diastolic BP, waist circumference, BMI, waist-to-height ratio, body fat percentage, among others. Ultimately, six variables—age, smoking, body fat percentage, waist circumference, systolic blood pressure, and diastolic blood pressure—were selected for multifactorial analysis to construct the nomogram. ROC curves and DCA curves demonstrated the model's excellent discriminative ability [The AUC for the training set and validation set were 0.901 (95% CI 0.895–0.906) and 0.899 (95% CI 0.894–0.905), respectively] and clinical applicability.

In addition to the aforementioned non-invasive indicators, our study incorporated certain factors closely associated with the occurrence of MetS and its core manifestations. These factors include lipid abnormalities (elevated LDL, TG, TC levels, and decreased HDL levels), elevated arterial blood pressure, increased blood glucose, obesity, dietary habits, and other relevant factors. Additionally, our research considers the usage of antidiabetic drugs, antihyperlipidemic drugs, and antihypertensive drugs. Through LASSO regression, we selected 6 predictive factors: BMI, TG, BP, HDL-C, LDL-C, and FBG.

Although these indicators have been confirmed to be related to MetS, there has been no research analyzing the extent to which these factors are correlated with MetS. Our study utilized these 6 indicators to develop and validate a nomogram aimed at predicting MetS. The model quantifies these factors, providing a more intuitive representation of their diagnostic value in MetS. The results showed that the model also demonstrated good if not better, discriminatory ability, with a training set AUC of 0.978 (95% CI 0.976–0.980). A previous study³⁴ mentioned that the consumption of alcohol was associated with trait anger, trait anxiety, and stress (r > 0.09, P < 0.05); and smoking status was associated with depression (r = 0.15, P = 0.001). Additionally, each one standard deviation increase in depressive symptoms was found to increase the risk of MetS by 1.21 to 1.43 times. The study also found that experiencing a highly stressful life event within the past six months increased the risk of developing MetS by 1.49 to 2.12 times. In a prospective study,³⁵ Chandola et al. highlighted that social status and socioeconomic status are inversely related to the prevalence of MetS. The study also indicated that experiencing three or more instances of chronic work-related stress increased the likelihood of developing MetS by twofold for men and fivefold for women. BMI is a key indicator for assessing obesity. Obesity, elevated LDL-C levels, increased TG levels, and decreased HDL-C levels all contribute to visceral fat accumulation, which increases the release of fatty acids.³⁶ Fatty acids induce oxidative stress through various pathways, including activation of the PKC pathway, accumulation of ceramides, JNK-mediated phosphorylation, and activation of protein tyrosine kinase-1B. This oxidative stress generates inflammatory factors. Additionally, fatty acids can lead to the occurrence of MetS through lipotoxic responses such as endoplasmic reticulum stress, apoptosis, and inflammation.³⁷ As one of the five main components of MetS, hypertension not only influences the metabolism of fat and glucose by activating the sympathetic nervous system and the renin-angiotensin-aldosterone system, thereby increasing the risk of MetS, but also induces systemic low-grade inflammation and oxidative stress. These factors impair endothelial cell function and promote the development of atherosclerosis. Simultaneously, inflammation and oxidative stress exacerbate insulin resistance and dysfunction of adipocytes, contributing to the onset of MetS. On the other hand, the loss of insulin-mediated vasodilation, vascular constriction induced by free fatty acids, and excessive sympathetic nervous system activity in MetS patients further lead to elevated BP. Additionally, high blood glucose levels can lead to IR, fat storage and metabolic disorders, inflammatory responses, and impaired endothelial function, all of which contribute to the development of MetS.²

Strengths and Limitations of This Study

The strengths of this study are as follows: First, the study included 26,637 participants, which provides a large sample size that enhances the generalizability of the results and accurately reflects the real situation of the target population. Second, the six predictor factors selected through Lasso regression are all easily obtainable indicators. This not only enhances the practicality and operability of the model but also facilitates its application in clinical settings, contributing to the wider adoption and dissemination of the predictive model. Lastly, the predictive model developed in this study demonstrated excellent predictive capability, offering a reliable decision support tool for clinical practice. However, this study has certain limitations. Firstly, the data is derived from a single center, and the prevalence of MetS may vary in different regions. Therefore, the application of the model to other regions may introduce bias. Further external validation is needed, involving multiple centers and diverse ethnic groups, to determine whether the model is applicable to populations in other countries. Secondly, the diagnosis of MetS in this study was based on the NCEP-ATP III definition, and other diagnostic criteria were not examined, which may introduce bias. In conclusion, while this study suggests that the nomogram may be an effective tool for predicting and diagnosing MetS, further confirmation is warranted through additional prospective, multicenter research.

Conclusions

A nomogram has been created and validated utilizing factors related to MetS, which can effectively facilitate the risk assessment of MetS. Furthermore, the proposed nomogram demonstrates good ability to distinguish and significant usefulness in clinical settings, making it suitable for early recognition of elements and risk factors in diagnosing MetS.

Data Sharing Statement

The datasets supporting the conclusions of this article are included within the article and the supplementary materials.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Shiyu Hu, Wenyu Chen and Xiaoli Tan are co-first authors for this study. Lifang Huang and Jianwen Duan are co-correspondence authors for this study. The authors report no conflicts of interest in this work.

References

- 1. Rochlani Y, Pothineni NV, Kovelamudi S, Mehta JL. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. Ther Adv Cardiovasc Dis. 2017;11(8):215–225. doi:10.1177/1753944717711379
- Fahed G, Aoun L, Bou Zerdan M, et al. Metabolic Syndrome: updates on Pathophysiology and Management in 2021. Int J Mol Sci. 2022;23(2):786. doi:10.3390/ijms23020786
- 3. Jakubiak GK, Osadnik K, Lejawa M, et al. "Obesity and insulin resistance" is the component of the metabolic syndrome most strongly associated with oxidative stress. *Antioxidants*. 2021;11(1):79. doi:10.3390/antiox11010079
- Jakubiak GK, Osadnik K, Lejawa M, Kasperczyk S, Osadnik T, Pawlas N. Oxidative stress in association with metabolic health and obesity in young adults. Oxid Med Cell Longev. 2021;2021:9987352.
- Schmidt AM. Insulin resistance and metabolic syndrome: mechanisms and consequences. Arterioscler Thromb Vasc Biol. 2012;32(8):1753. doi:10.1161/ATVBAHA.112.255588
- 6. Saklayen MG. The global epidemic of the metabolic syndrome. Curr Hypertens Rep. 2018;20(2):12. doi:10.1007/s11906-018-0812-z
- 7. Lancet T. Diabetes: a defining disease of the 21st century. Lancet. 2023;401(10394):2087. doi:10.1016/S0140-6736(23)01296-5

- 8. Samson SL, Garber AJ. Metabolic syndrome. Endocrinol Metab Clin North Am. 2014;43(1):1-23. doi:10.1016/j.ecl.2013.09.009
- Rotariu D, Babes EE, Tit DM, et al. Oxidative stress Complex pathological issues concerning the hallmark of cardiovascular and metabolic disorders. Biomed Pharmacother. 2022;152:113238.
- 10. Ebrahimi SO, Reiisi S, Shareef S. miRNAs, oxidative stress, and cancer: a comprehensive and updated review. *J Cell Physiol.* 2020;235 (11):8812–8825. doi:10.1002/jcp.29724
- 11. Belladelli F, Montorsi F, Martini A. Metabolic syndrome, obesity and cancer risk. Curr Opin Urol. 2022;32(6):594–597. doi:10.1097/MOU.000000000001041
- 12. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care*. 2005;28(7):1769–1778. doi:10.2337/diacare.28.7.1769
- 13. Wang Y, Li YY, Nie YQ, Zhou YJ, Cao CY, Xu L. Association between metabolic syndrome and the development of non-alcoholic fatty liver disease. *Exp Ther Med*. 2013;6(1):77–84. doi:10.3892/etm.2013.1090
- 14. Shen X, Wang Y, Zhao R, et al. Metabolic syndrome and the risk of colorectal cancer: a systematic review and meta-analysis. *Int J Colorectal Dis.* 2021;36(10):2215–2225. doi:10.1007/s00384-021-03974-y
- 15. Chen Q, Liu Y, Yin Y, Huang W, Li G, Ke D. Relationship between metabolic syndrome (MS) and coronary heart disease (CHD) in an aged group. *Arch Gerontol Geriatr.* 2008;46(1):107–115. doi:10.1016/j.archger.2007.03.002
- Fallah Z, Darand M, Salehi-Abargouei A, Mirzaei M, Ferns GA, Khayyatzadeh SS. The association between dietary habits and metabolic syndrome: findings from the Shahedieh-cohort study. BMC Nutr. 2022;8(1):117. doi:10.1186/s40795-022-00609-5
- 17. Lee J, Lee H. Effects of risk factor numbers on the development of the metabolic syndrome. *J Exerc Rehabil*. 2020;16(2):183–188. doi:10.12965/jer.2040202.101
- 18. Fan J, Liu Y, Yin S, et al. Small dense LDL cholesterol is associated with metabolic syndrome traits independently of obesity and inflammation. *Nutr Metab.* 2019;16:7.
- Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults E. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486–2497. doi:10.1001/jama.285.19.2486
- 20. Hu JY, Wang Y, Tong XM, Yang T. When to consider logistic LASSO regression in multivariate analysis? Eur J Surg Oncol. 2021;47(8):2206. doi:10.1016/j.ejso.2021.04.011
- 21. Reisinger C, Nkeh-Chungag BN, Fredriksen PM, Goswami N. The prevalence of pediatric metabolic syndrome-A critical look on the discrepancies between definitions and its clinical importance. *Int J Obes*. 2021;45(1):12–24. doi:10.1038/s41366-020-00713-1
- 22. Belete R, Ataro Z, Abdu A, Sheleme M. Global prevalence of metabolic syndrome among patients with type I diabetes mellitus: a systematic review and meta-analysis. *Diabetol Metab Syndr*. 2021;13(1):25. doi:10.1186/s13098-021-00641-8
- 23. Madan K, Paliwal S, Sharma S, Kesar S, Chauhan N, Madan M. Metabolic Syndrome: the Constellation of Co-morbidities, A Global Threat. Endocr Metab Immune Disord Drug Targets. 2023;23(12):1491–1504. doi:10.2174/1871530323666230309144825
- 24. Trivedi T, Liu J, Probst JC, Martin AB. The metabolic syndrome: are rural residents at increased risk? *J Rural Health*. 2013;29(2):188–197. doi:10.1111/j.1748-0361.2012.00422.x
- 25. He Y, Li Y, Bai G, et al. Prevalence of metabolic syndrome and individual metabolic abnormalities in China, 2002-2012. *Asia Pac J Clin Nutr.* 2019;28(3):621–633. doi:10.6133/apjcn.201909_28(3).0023
- 26. Wang S, Wang S, Jiang S, Ye Q. An anthropometry-based nomogram for predicting metabolic syndrome in the working population. *Eur J Cardiovasc Nurs*. 2020;19(3):223–229. doi:10.1177/1474515119879801
- 27. Romero-Saldaña M, Fuentes-Jiménez FJ, Vaquero-Abellán M, Álvarez-Fernández C, Molina-Recio G, López-Miranda J. New non-invasive method for early detection of metabolic syndrome in the working population. Eur J Cardiovasc Nurs. 2016;15(7):549–558. doi:10.1177/1474515115626622
- 28. de Kroon ML, Renders CM, Kuipers EC, et al. Identifying metabolic syndrome without blood tests in young adults--The Terneuzen Birth Cohort. Eur J Public Health. 2008;18(6):656–660. doi:10.1093/eurpub/ckn056
- 29. Miller B, Fridline M, Liu PY, Marino D. Use of CHAID decision trees to formulate pathways for the early detection of metabolic syndrome in young adults. *Comput Math Methods Med.* 2014;2014:242717. doi:10.1155/2014/242717
- 30. Che D, Liu Q, Rasheed K, Tao X. Decision tree and ensemble learning algorithms with their applications in bioinformatics. *Adv Exp Med Biol.* 2011;696:191–199.
- 31. Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: more than meets the eye. *Lancet Oncol.* 2015;16(4):e173–180. doi:10.1016/S1470-2045(14)71116-7
- 32. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. BMC Med. 2011;9:48.
- 33. Marzoog BA. The Metabolic Syndrome Puzzles; Possible Pathogenesis and Management. *Curr Diabetes Rev.* 2023;19(4):e290422204258. doi:10.2174/1573399818666220429100411
- 34. Räikkönen K, Matthews KA, Kuller LH. Depressive symptoms and stressful life events predict metabolic syndrome among middle-aged women: a comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions. *Diabetes Care*. 2007;30 (4):872–877. doi:10.2337/dc06-1857
- 35. Chandola T, Brunner E, Marmot M. Chronic stress at work and the metabolic syndrome: prospective study. BMJ. 2006;332(7540):521–525. doi:10.1136/bmj.38693.435301.80
- 36. Legrand-Poels S, Esser N, L'Homme L, Scheen A, Paquot N, Piette J. Free fatty acids as modulators of the NLRP3 inflammasome in obesity/type 2 diabetes. *Biochem Pharmacol*. 2014;92(1):131–141. doi:10.1016/j.bcp.2014.08.013
- 37. Denisenko YK, Kytikova OY, Novgorodtseva TP, Antonyuk MV, Gvozdenko TA, Kantur TA. Lipid-Induced Mechanisms of Metabolic Syndrome. J Obes. 2020;2020:5762395. doi:10.1155/2020/5762395
- 38. Stanciu S, Rusu E, Miricescu D, et al. Links between Metabolic Syndrome and Hypertension: the Relationship with the Current Antidiabetic Drugs. Metabolites. 2023;13(1):87. doi:10.3390/metabo13010087

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