Diabetes, Metabolic Syndrome and Obesity

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Establishment of a Risk Prediction Model for Metabolic Syndrome in High Altitude Areas in Qinghai Province, China: A Cross-Sectional Study

Yanting Ma[1], Yongyuan Li[2], Zhanfeng Zhang[3], Guomei Du[4], Ting Huang[1], Zhi Zhong Zhao[5], Shou Liu[1], Zhancui Dang[1]

[1]Department of Public Health, Medical College, Qinghai University, Xining, Qinghai, People's Republic of China; [2]Disease Control department, Huangzhong District health Bureau, Xining, Qinghai, People's Republic of China; [3]Huangzhong District, Duoba County Health Services Center, Xining, Qinghai, People's Republic of China; [4]Clinical Laboratory, Qinghai Red Cross Hospital, Xining, Qinghai, People's Republic of China; [5]Disease Control Department, Qinghai Provincial Center for Endemic Disease Control and Prevention, Xining, Qinghai, People's Republic of China

Correspondence: Shou Liu; Zhancui Dang, Email liushou2004@aliyun.com; yxyyy2019@163.com

Purpose: The prevalence of metabolic syndrome (MetS) is increasing worldwide, and early prediction of MetS risk is highly beneficial for health outcomes. This study aimed to develop and validate a nomogram to predict MetS risk in Qinghai Province, China, and it provides a methodological reference for MetS prevention and control in Qinghai Province, China.

Patients and Methods: A total of 3073 participants living between 1900 and 3710 meters above sea level in Qinghai Province participated in this study between March 2014 and March 2016. We omitted 12 subjects who were missing diagnostic component data for MetS, ultimately resulting in 3061 research subjects, 70% of the subjects were assigned randomly to the training set, and the remaining subjects were assigned to the validation set. The least absolute shrinkage and selection operator (LASSO) regression analysis method was used for variable selection via running cyclic coordinate descent with 10-fold cross-validation. Multivariable logistic regression was then performed to develop a predictive model and nomogram. The receiver operating characteristic (ROC) curves was used for model evaluation, and calibration plot and decision curve analysis (DCA) were used for model validation.

Results: Of 24 variables studied, 6 risk predictors were identified by LASSO regression analysis: hyperlipidaemia, hyperglycemia, abdominal obesity, systolic blood pressure (SBP), diastolic blood pressure (DBP), and body mass index (BMI). A prediction model including these 6 risk factors was constructed and displayed good predictability with an area under the ROC curve of 0.914 for the training set and 0.930 for the validation set. DCA revealed that if the threshold probability of MetS is less than 82%, the application of this nomogram is more beneficial than both the treat-all or treat-none strategies.

Conclusion: The nomogram developed in our study demonstrated strong discriminative power and clinical applicability, making it a valuable reference for meets prevention and control in the plateau areas of Qinghai Province.

Keywords: metabolic syndrome, nomogram, prediction model, plateau section

Introduction

Metabolic syndrome (MetS) is a condition associated with the co-occurrence of multiple metabolic abnormalities, including insulin resistance or hyperglycemia, abdominal obesity, atherogenic dyslipidemia, and endothelial dysfunction.[1–3] Notably, the prevalence of MetS is increasing rapidly worldwide, due to the rapid economic growth, aging populations, lifestyle pattern, and the increasing prevalence of chronic non-communicable diseases(NCDs).[4] Research indicates a growing prevalence of MetS in the United States, with a notable trend towards affecting younger age groups.[5] Moreover, the prevalence of metabolic syndrome in China has already surpassed 30%.[6] According to the World Health Organization's World Health Statistics 2023, it is estimated that by 2048, NCDs will be the leading cause of global deaths.[7] In addition, MetS is a confirmed risk factor for colorectal cancer, endometrial cancer, hepatocellular cancer, and postmenopausal breast cancers and a variety of cardiovascular diseases.[8,9] Moreover, MetS has also been

Received: 20 October 2023
Accepted: 5 April 2024
Published: 17 May 2024

associated with an increased risk of cognitive impairment and dementia later in life.[10] MetS has become more prevalent worldwide and is increasingly recognized as a risk factor, for other diseases. Many studies are underway to confirm the relationship between a number of other diseases and MetS, to elucidate the underlying mechanisms, and even examine whether lifestyle interventions can prevent these diseases and improve MetS treatment.[11]

Currently, the diagnostic criteria for MetS have not been fully agreed upon. The WHO first proposed corresponding diagnostic criteria in 1998.[12] Over the past 2 decades, the diagnostic criteria for MetS have undergone many changes.[13–16] Although the diagnostic criteria are not uniform, the incidence of MetS is undeniably increasing. The early diagnosis and identification of patients with MetS and the management of high-risk groups through exercise therapy and other methods are very important.[17] In addition, by mining data collected from health check-ups and questionnaires, individuals at high risk for NCDs could be identified at an early stage, thus accelerating the timing of disease prevention and control forward.[18] Although scholars have focused on MetS in recent years, there remain relatively few related studies of the population of the Tibetan Plateau region of China. Researchers have defined high altitude as ranging from 1500–3500m, and areas inhabited at altitudes above 3500m are classified as extremely high-altitude regions.[19–21] In recent years, there has been increasing interest among researchers in studying the prevalence of chronic diseases in high altitude populations. One study indicated that BMI and altitude are important determining factors for MetS.[22] Another study found that nomads who relocated from high altitude pastoral areas to urban areas exhibited higher rates of MetS and obesity.[23] However, most of these studies have focused on investigating the influencing factors without constructing predictive models to identify high-risk individuals. Apart from the prediction model developed in Urumqi, Xinjiang Uygur Autonomous Region, incorporating variables such as SBP, history of diabetes and hypertension, DBP, fatty liver, smoking, physical activity, and BMI.[24] There remains a relative scarcity of research on predictive models for MetS, particularly in high altitude areas like Qinghai. Therefore, the objective of this study is to develop a prediction model for MetS in the high-altitude regions of Qinghai Province; this model could serve as a valuable reference for the prevention and management of MetS in this area.

Material and Methods

Simply Size

The sample size needed was calculated according to the prevalence of MetS specific to China.[6] Considering that the measurement results are binary variables for the diagnosis of MetS, it is necessary to ensure a sufficiently large sample size so that the obtained proportion can accurately approximate the overall proportion of the results. This is essential to ensure that the study has sufficient precision and confidence. We use the following formula to calculate the required sample size:

$$n = \left(\frac{1.96}{0.05}\right)^2 P(1-P)$$

The value of n was determined when P equated to 31.1% (0.311), resulting in a value of 330. It is worth noting that the sample size was calculated based on a disease prevalence of 31.1%, an absolute precision of 5%, and a confidence interval of 95%. Sample size criteria were considered met when our sample was greater than 330.

Study Population and Data Content

A total of 3073 participants living between 1900 and 3710 meters above sea level in Qinghai Province participated in this study between March 2014 and March 2016. We omitted 12 subjects who were missing diagnostic component data for MetS, ultimately resulting in 3061 research subjects. And our participants are mainly concentrated in county-level cities in Qinghai Province, mainly including in the autonomous prefectures region residents of Huangnan, Yushu, Hainan, Haibei, Haidong and a city of Xining. The study was approved by the Ethics Committee of Qinghai University (Xining, Qinghai, China, ratification No.2014–03) and was conducted following the Declaration of Helsinki. And all participants signed the informed consent. The data were collected by staff with uniform professional training and comprised three parts: baseline information, physical examination and laboratory testing. The baseline information included demographic characteristics (age, sex, ethnic groups, the nature of the job, marital status and educational level), and lifestyle (smoking,

drinking, (smoking, drinking, dietary habit, daily trip mode, exercise frequency and time) characteristics. The participants were divided into five group based on age: ≤ 30, 31~, 41~, 51~, and > 61 years. Ethnic groups was classified as Han or Minority. The nature of the job were classified according to mental or manual work. And the education level is divided into four levels: primary education, secondary education, vocational education and higher education. Smoking and drinking status were categorized as "yes" (current smokers or drinkers) or "no" (current nonsmokers or nondrinkers). Dietary habit included whether the participants like salty foods, fried foods, red meat, white meat, and the frequency of eating fish consumption(≤2 times/week, 3–4 times/week, ≥5 times/week). Daily trip mode were categorized walk and take bus. The exercise frequency was categorized into three groups(Less than 2 times per week, 2–4 times per week,and More than 5 times per week). The exercise duration was categorized as "Less than 30 minutes", "30 minutes~", "60minutes~" and"90 minutes or more". The Physical examination assessed height, weight, waistline, hipline, systolic blood pressure (SBP) and diastolic blood pressure((DBP), and standard measuring instruments were used.Height and waist circumference were accurate to 0.1 cm, and weight was accurate to 0.1 kg. BMI was calculated as weight in kilograms divided by height in meters squared. Waist-to-hip ratio (WHR) indicates the ratio of the waistline to hipline measurements. The blood pressure of the subjects was measured in a sitting position with a mercury sphygmomanometer according to a standardized protocol. Laboratory test measurements included serum fasting plasma glucose (FPG), total cholesterol (TC), fasting triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), and uric acid (UA) levels. All subjects fasted for 10–12 h before the laboratory testing, for FPG, TC, TG, LDL-c, and HDL-c levels according to a standard protocol. Sample collection was only received and managed by laboratories capable of performing all biochemical analyses of the study under strict quality assurance. Standardized blood collection protocols were used in all research centers. And all laboratories were given instructions on the protocols to follow.

Diagnostic Criteria

As all our subjects were residents of mainland China, we employed the diagnostic criteria outlined in the guidelines specific to our study. According to the diagnostic criteria recommended in the "Guidelines for the Prevention and Treatment of Type 2 Diabetes" issued by the Chinese Diabetes Association in 2020, subjects diagnosed people diagnosed with MetS had three or more of the following five conditions:[16] (1) Abdominal obesity: waist circumference ≥90 cm in men and ≥85 cm in women. (2) Hyperglycemia: fasting blood glucose ≥6.1 mmol/L or 2h blood glucose ≥7.8 mmol/L after glucose load and/or patients with diagnosed and treated diabetes. (3) High blood pressure: blood pressure ≥130/85 mmHg and/or confirmed and treated hypertension. (4) Fasting TG ≥1.70 mmol/L. (5) Fasting HDL-c <1.04 mmol/L.

For the diagnosis of dyslipidemia, refer to the definition in the "Dietary guidelines for adults with hyperlipemia (2023 edition)" published by the National Health and Health Commission of the People's Republic of China: TC ≥5.2 mmol/L, TG TC≥5.2mmol/L, TG≥1.7mmol/L, LDL-c≥3.4mmol/L, HDL-c<1.0mmol/L.[25]

Statistical Analysis

Statistical analyses were conducted with R software (version 4.3.0), and P <0.05 was considered statistically significant. Count data are described as frequencies and percentages, and the non-normally distributed measurement data are expressed as [M (P25; P750)]. Participants were placed randomly into the training or validation set at a ratio of 7:3. The training set was used to construct the risk prediction model, and the validation set was used for internal verification. We used '***CBCgrps***' package;[26] "**glmnet**" package: '***rms***'packages; "**pROC**" package and**nricens**' package was used in this study. The LASSO regression was used to analyze the data in the training sample set. The '**glmnet**' package was used for least absolute shrinkage and selection operator (LASSO) regression analysis, which is a shrinkage and variable selection method for linear regression models. Next, the R language '**rms**' package was used for multivariate logistic regression analysis, and a prediction model was built by introducing the feature selected in the LASSO regression model. The R software '**pROC**' package was used to plot Receiver Operating Characteristic (ROC) curves and calculate the Area Under the Curve (AUC) to evaluate the accuracy and discriminative ability of the risk prediction model. The calibration curve for the validation set was plotted using the calibrate function from the '**rms**' package, aiming to assess the model's calibration. Furthermore, the fit of the validation set was evaluated using the Hosmer-Lemeshow (H-L) test.

A decision curve analysis (DCA) was plotted with the "**nricens**" package in R software and used to evaluate the clinical usefulness of the predictive model.

Results

Of the 3061 participants, 2144(70%) were in the training set, and 917(30%) were in the validation set. Of the training and validation sets, 464 (21.6%) and 183 (20.0%) participants, respectively, were diagnosed with MetS, the detection rate of hypertension was 16.3% (499/3061), the prevalence of dyslipidemia was 73.0% (2233/3061), and the prevalence of hyperglycemia was 4.34% (133/3061). As expected, there were no statistical difference between the two groups. There were 1928 (63%) females and 1133 (37%) males. The number of people in the "41~" age group was the greatest (974), accounting for 31.8% of the total. A detailed comparison of the summary characteristics, of the validation and training sets are shown in Table 1.

Variables were selected using the LASSO regression analysis with 10-fold cross-validation, and the result are shown in Figure 1. We ultimately selected six variables that were filtered by *Lambda.1se*, including BMI, DBP, SBP, hyper

Table 1 Differences Between Baseline Information, Physical Examination and Laboratory Testing of MetS and Non-MetS Groups

Variables	Total (n = 3061) n (%)	Validation Set (n = 917) n (%)	Training Set (n = 2144) n (%)	P
MetS				0.318
No	2414 (78.9)	734 (80.0)	1680 (78.4)	
Yes	647 (21.1)	183 (20.0)	464 (21.6)	
1.Sex				1.000
Male	1928(63.0)	578(63.0)	1350(63.0)	
Female	1133(37.0)	339(37.0)	794 (37.0)	
2.Ethnic groups				0.932
Han	2576(84.2)	773(84.3)	1803(84.1)	
Minority	485(15.8)	144(15.7)	341(15.9)	
3.Age				0.524
≤30	557 (18.2)	154 (16.8)	403 (18.8)	
31~	852 (27.8)	248 (27.0)	604 (28.2)	
41~	974 (31.8)	300 (32.7)	674 (31.4)	
51~	434 (14.2)	140 (15.3)	294 (13.7)	
>60	244 (7.97)	75 (8.18)	169 (7.88)	
4.Nature of the job				0.559
More mental work	1636 (53.4)	498 (54.3)	1138 (53.1)	
Mainly physical work	1425 (46.6)	419 (45.7)	1006 (46.9)	
5.Marital status				0.327
Married	2716 (88.7)	822 (89.6)	1894 (88.3)	
Unmarried	345 (11.3)	95 (10.4)	250 (11.7)	
6.Education level				0.560
Primary Education	361 (11.8)	103 (11.2)	258 (12.0)	
Secondary Education	486 (15.9)	148 (16.1)	338 (15.8)	
Vocational Education	896 (29.3)	256 (27.9)	640 (29.9)	
Higher Education	1318 (43.1)	410 (44.7)	908 (42.4)	
7.Smoke				0.323
No	2067 (67.5)	607 (66.2)	1460 (68.1)	
Yes	994 (32.5)	310 (33.8)	684 (31.9)	
8.Drink				0.680
No	1787 (58.4)	541 (59.0)	1246 (58.1)	
Yes	1274 (41.6)	376 (41.0)	898 (41.9)	

(*Continued*)

Table 1 (Continued).

Variables	Total (n = 3061) n (%)	Validation Set (n = 917) n (%)	Training Set (n = 2144) n (%)	P
9.Salty food				0.182
Dislike	1688 (55.1)	523 (57.0)	1165 (54.3)	
Like	1373 (44.9)	394 (43.0)	979 (45.7)	
10.Fried food				0.942
Dislike	2650 (86.6)	795 (86.7)	1855 (86.5)	
Like	411 (13.4)	122 (13.3)	289 (13.5)	
11.Red meat				0.391
Dislike	693 (22.6)	198 (21.6)	495 (23.1)	
Like	2368 (77.4)	719 (78.4)	1649 (76.9)	
12.White meat				0.480
Dislike	1892 (61.8)	576 (62.8)	1316 (61.4)	
Like	1169 (38.2)	341 (37.2)	828 (38.6)	
13.Frequency of fish consumption				0.425
≤2 times/week	1467 (47.9)	435 (47.4)	1032 (48.1)	
3–4 times/week	868 (28.4)	251 (27.4)	617 (28.8)	
≥5 times/week	726 (23.7)	231 (25.2)	495 (23.1)	
14.Exercise frequency				0.022
Less than 2times/week	1630 (53.3)	522 (56.9)	1108 (51.7)	
2–4times/week	730 (23.8)	195 (21.3)	535 (25.0)	
More than 5times/week	701 (22.9)	200 (21.8)	501 (23.4)	
15.Exercise duration				0.647
Less than 30min	1524 (49.8)	462 (50.4)	1062 (49.5)	
30min~	814 (26.6)	238 (26.0)	576 (26.9)	
60min~	518 (16.9)	149 (16.2)	369 (17.2)	
90min~	205 (6.70)	68 (7.42)	137 (6.39)	
16.Daily trip mode				0.094
Walk	1443 (47.1)	454 (49.5)	989 (46.1)	
Take bus	1618 (52.9)	463 (50.5)	1155 (53.9)	
17.SBP	117 [108;128]	116 [107;128]	117 [108;128]	0.643
18.DBP	76.0 [69;83]	76.0 [69;83]	76.0 [69;83]	0.778
19.BMI				0.797
<18.5	160 (5.23)	48 (5.23)	112 (5.22)	
18.5~	1559 (50.9)	468 (51.0)	1091 (50.9)	
24~	1043 (34.1)	311 (33.9)	732 (34.1)	
28~	299 (9.77)	90 (9.81)	209 (9.75)	
20.High WHR				0.692
No	1644 (53.7)	498 (54.3)	1146 (53.5)	
Yes	1417 (46.3)	419 (45.7)	998 (46.5)	
21.Hyperuricemia:				0.581
No	2487 (81.2)	751 (81.9)	1736 (81.0)	
Yes	574 (18.8)	166 (18.1)	408 (19.0)	
22.Hyperglycemia:				0.401
No	2928 (95.7)	882 (96.2)	2046 (95.4)	
Yes	133 (4.34)	35 (3.82)	98 (4.57)	
23.Abdominal obesity:				0.643
No	2298 (75.1)	694 (75.7)	1604 (74.8)	
Yes	763 (24.9)	223 (24.3)	540 (25.2)	
24.Hyperlipidaemia				0.453
No	828 (27.0)	257 (28.0)	571 (26.6)	
Yes	2233 (73.0)	660 (72.0)	1573 (73.4)	

lipidaemia, hyperglycemia and abdominal obesity. These factors were entered into a multivariable logistic regression analysis to establish a predictive model.

A ROC curve was used to evaluate the discriminatory capacity of the predictive model. For the predictive model, the AUC of the nomogram was 0.918 (95% CI: 0.9064–0.9302) for the training set and 0.925 (95% CI:0.9085–0.9423) for the validation set; both results indicate good performance. The ROC curves, AUC, best segmentation threshold, specificity, and sensitivity are shown in Figure 2.

The nomogram for MetS risk prediction is shown in Figure 3. First, the score points corresponding to each predictor value for an individual were calculated; then, all the points were added together, and the total points were determined according to the antepenultimate rule. Finally, the corresponding predicted probability of developing MetS was found at the lowest rule.

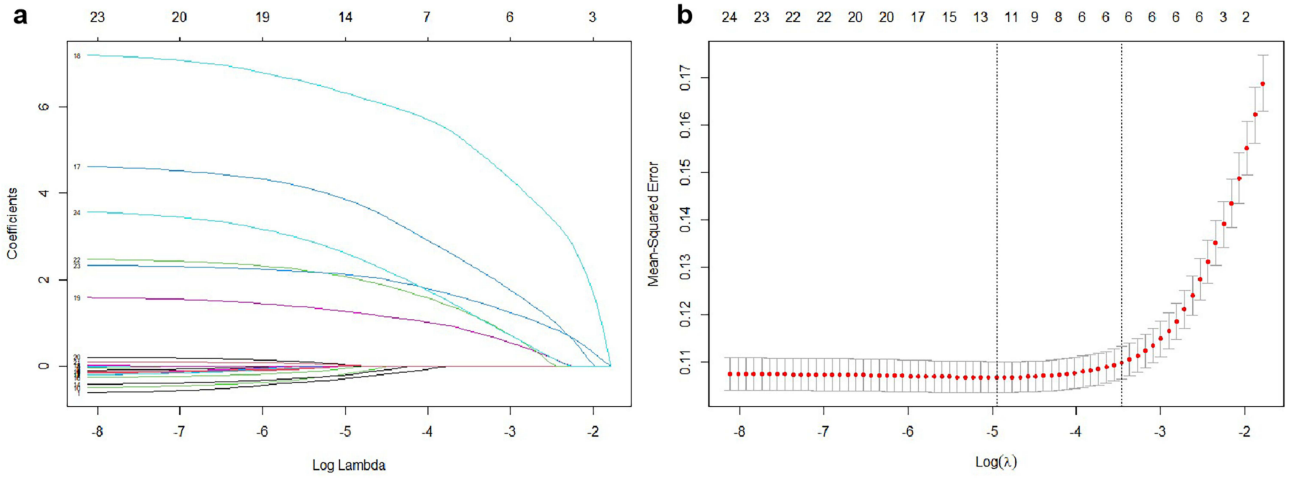

Figure 1 The least absolute shrinkage and selection operator (LASSO) regression analysis with 10-fold cross-validation.
Notes: (**a**): The least absolute shrinkage and selection operator (LASSO) regression analysis, 24 variables with nonzero coefficients were selected by deriving the optimal lambda. (**b**): The 10-fold cross-validation curve and drew dotted vertical lines based on one standard error criteria (the dotted line on the left) and minimum value (the dotted line on the right).

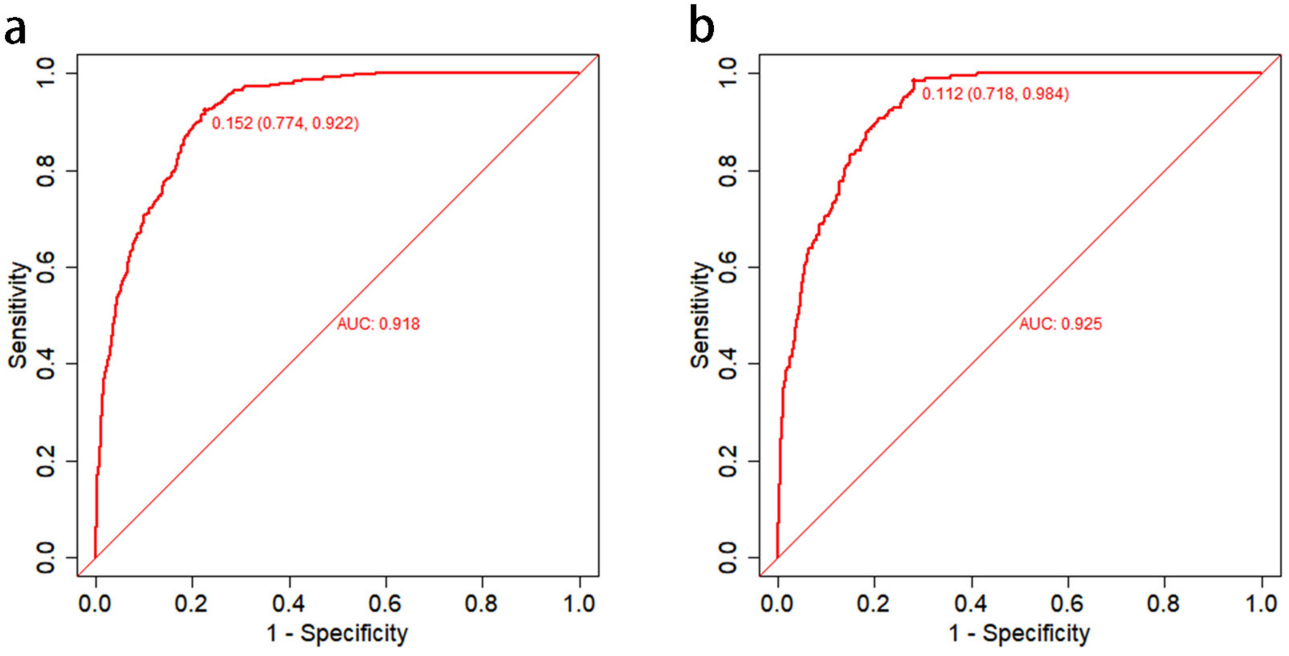

Figure 2 Receiver operating characteristic (ROC) curve of the MetS risk nomogram prediction.
Notes: The y-axis represents the true positive rate of the risk prediction; the x-axis represents the false positive rate of the risk prediction. The thick red line represents the performance of the nomogram in the training set (**a**) and validation set (**b**).

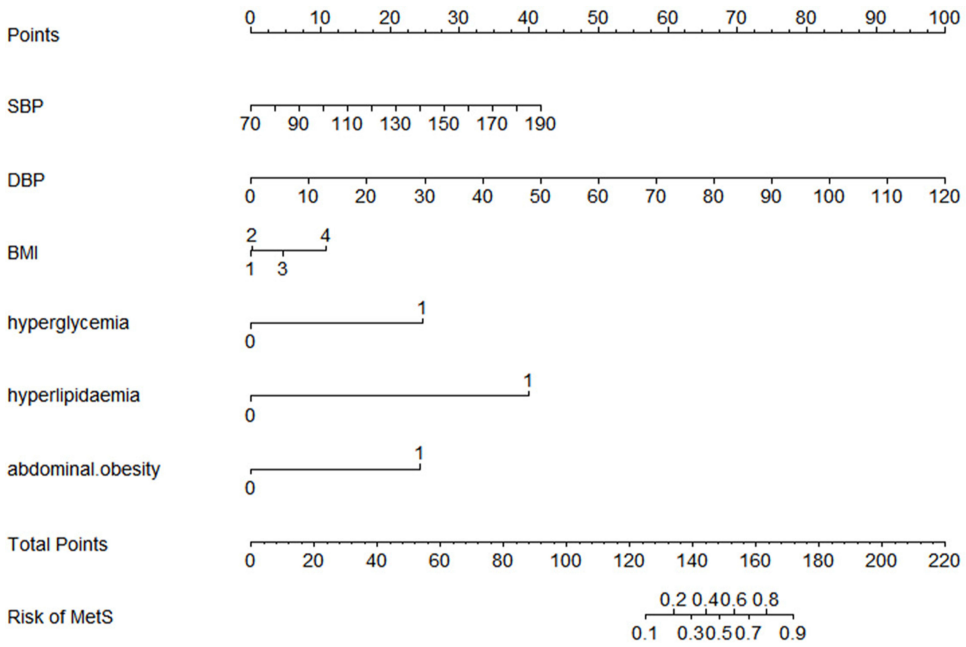

Figure 3 The nomogram for prediction metabolic syndrome (MetS) in population in high altitude areas in Qinghai Province.
Notes: BMI: 1, the BMI is less than<18.5; 2, the BMI is between 18.5 and 24(excluding 24); 3, the BMI is between 24 and 28(excluding 28); 4, the BMI is greater than 28. The diagnostic criteria for hyperlipemia were total cholesterol ≥5.2mmol/L, triglyceride ≥1.7mmol/L, low-density lipoprotein cholesterol ≥3.4mmol/L, and high-density lipoprotein cholesterol < 1mmol/L, if one of the above is met, it is judged as "hyperlipidemia". "0" represents no disease, and "1" represents have the disease.

To calibrate the predictive model, a calibration plot and Hosmer-Lemeshow test were conducted (Figure 4). The H-L test, revealed that the predicted probabilities were well calibrated against the actual probabilities (p=0.641). The calibration curves showed a high degree of fit between the predictive model and the validation set. The E_{max} and E_{avg} values for the model were 0.054 and 0.017, respectively, indicating that the deviation between the predicted outcomes and the observed outcomes was very small.

DCA is an innovative approach for evaluating diagnostic tests and prediction models, effectively incorporating accurate measurements, like sensitivity and specificity, with decision analysis techniques. This method aims to assess the net benefit of prediction models without altering the intended meaning. As is shown in Figure 5, DCA revealed that if the threshold probability of MetS was less than 82%, the application of this nomogram to predict MetS risk within the population would be more beneficial than either the treat-all or the treat-none strategies. The DCA abscissa is the threshold probability, and the ordinate is the net benefit after benefit minus disadvantages.

Discussion

MetS is estimated to affect almost 25% of the global adult population.[1] As revealed by National Health and Nutrition Examination Surveys (NHANES), the age-adjusted overall prevalence of MetS in adults 20 years and older in the US was 23% from 2013 to 2014.[27] Other research has reported a continuous increase in the prevalence of MetS in the Asia-Pacific region.[28] A survey of adults aged 20 years and older in China revealed that the standardized prevalence of MetS was 31.1% from 2015 to 2017.[6] It is important to note that the lower prevalence of MetS (21.1%) observed in our study, compared to the reported prevalence, could potentially be attributed to differences in the samples studied or diagnostic criteria; Additionally, research has confirmed that altitude affects the incidence of MetS.[29,30] And the previous report used the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria to define MetS, but we used the diagnostic criteria recommended in the "Guidelines for the Prevention and Treatment of Type 2 Diabetes" published by the Chinese Diabetes Association in 2020.

It is widely acknowledged in academia that LASSO regression analysis is considered superior to techniques based on the strength of univariate correlations with the outcome variable for selecting predictors.[31,32] The LASSO regression analysis in

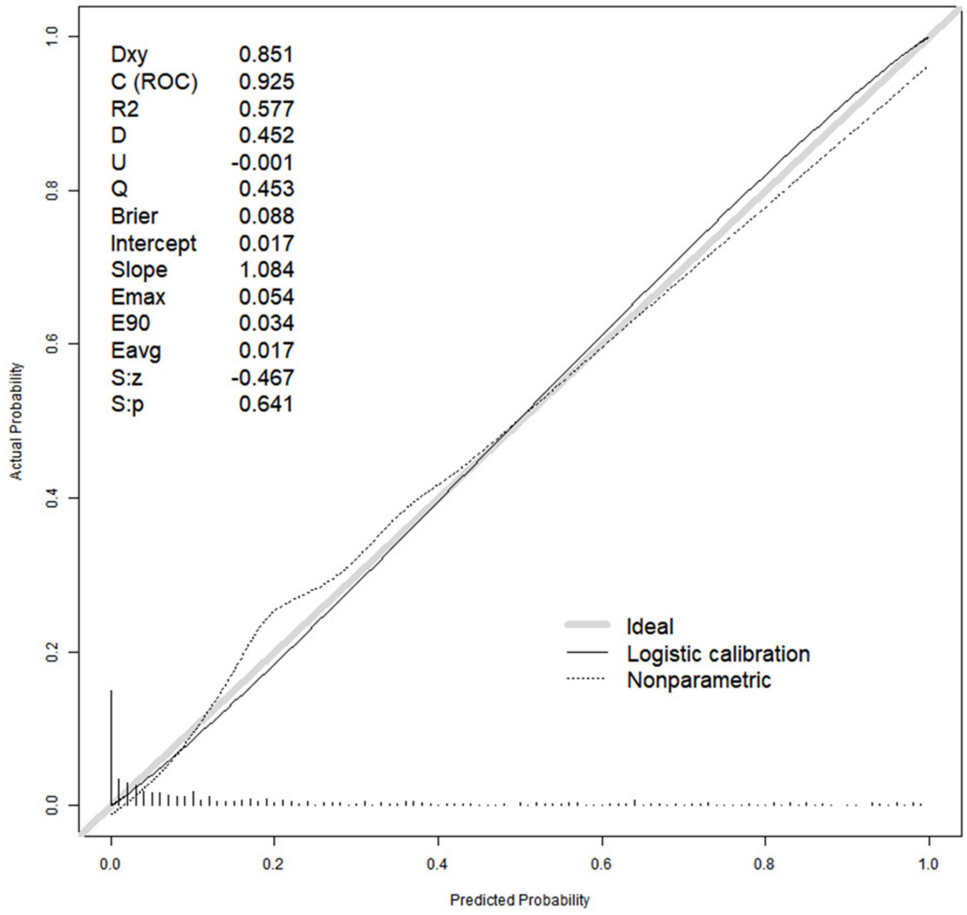

Figure 4 Calibration curves of the MetS risk nomogram.
Notes: The y-axis represents actual diagnosed cases of MetS, the x-axis represents the predicted risk of MetS. The diagonal line shows a perfect prediction by an ideal model, the solid line represents the performance of the validation set. The Hosmer-Lemeshow test resulted in a p-value is 0.641(P>0.05), indicating no statistically significant difference was observed between the calibration from a perfect fit of the proposed model and the ideal model.

R software runs a 10-fold cross-validation for the centralization and normalization of the included variables and then picks the **Lambda.1se** value. The ***Lambda.1se*** results provided a model with good performance but the least number of independent variables. Hence, the results of ***Lambda.1se*** were used to select the optimal predictors of the current risk factors. We developed and validated a simple Nomogram to determine the possible risk factors for MetS occurrence, based on the data we collected in in high altitude areas in Qinghai Province, China. Nomograms are currently widely used as diagnostic and prognostic devices in medicine. Nomograms are highly valuable visualization tools for predictive models. They provide graphical representations that integrate intricate mathematical equations with relevant clinical information to accurately estimate the specific numerical probability of a clinical outcome.[33] Nomograms have numerous advantages, including good accuracy, user-friendliness, and comprehensibility, that fulfill the need to comprehensively facilitate numerous applications in clinical practice.[34] Based on these advantages of nomogram, we developed and validated the risk prediction model for MetS using a nomogram. Similar to previous studies, the nomogram in our study yielded six indicators: BMI, DBP, SBP, hyper lipidaemia, hyperglycemia, and abdominal obesity. In a previous cohort study, a clinical decision tree for MetS screening based on waist-to-height ratio and BP with high sensitivity (91.6%) and specificity (95.7%) was proposed; workers with a waist-to-height ratio ≥0.55 and blood pressure ≥128/85 mmHg had a 61.7% probability of developing MetS.[35] Although this study was not evaluated for clinical utility and calibration and only some anthropometric data, it also showed that their model had good predictive power. Similarly, in a birth cohort study, researchers found that BMI, waistline, and BP could predict the occurrence of MetS in young adults.[36] In addition, in a study that aimed to predict MetS based on anthropometry in a Spanish working population, the researchers used anthropometric data to develop predictive model, and the model shows good discriminative power with

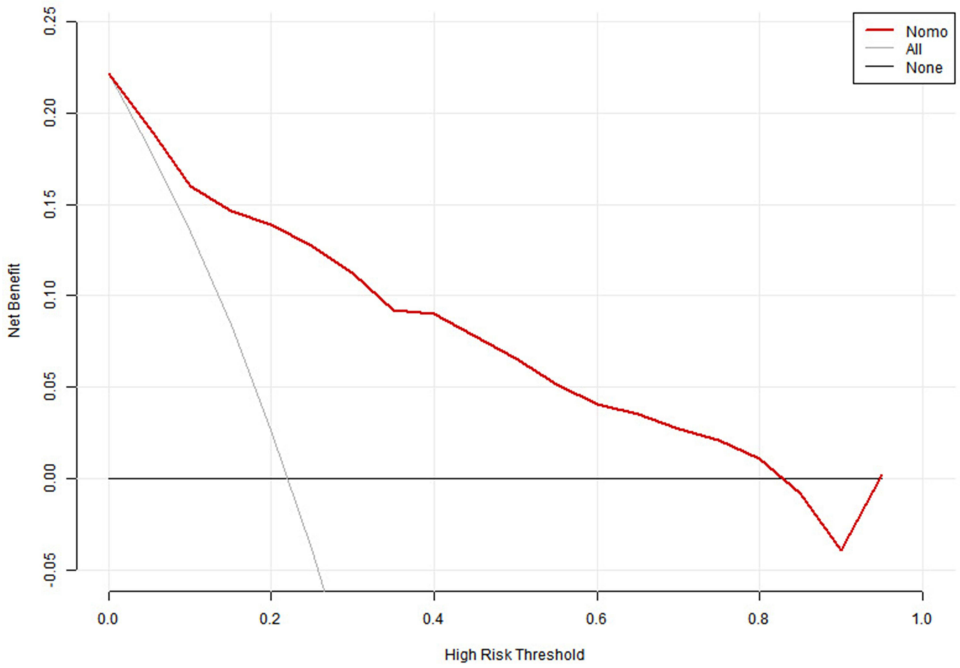

Figure 5 The decision curve analysis (DCA) for the MetS risk nomogram.
Notes: The y-axis measures the net benefit. The red line represents the risk nomogram. The DCA is used for assessing if nomogram-assisted decisions improve patient outcome.

sufficient power (AUC 0.901; 95% CI 0.895–0.906) and a well-calibrated (Emax 0.081, Eavg 0.005, P>0.05), and similar predictors are included in this prediction model.[18] Furthermore, some variables such as waist-to-height ratio, body fat percentage, and genetic and environmental factors, were found to be risk factors for MetS in some studies.[18,37,38] The nomogram we present demonstrates outstanding discriminatory and classification abilities (0.918 (95% CI: 0.9064–0.9302) for the training set and 0.925 (95% CI:0.9085–0.9423) for the validation set). The calibration plots and DCA curves drawn using the validation set data also prove that the MetS risk prediction model established in this paper has high reliability and clinical applicability. Additionally, there is a limited amount of research on using nomogram to predict the risk of MetS in high-altitude areas of Qinghai Province.

This study differs from some previous research in terms of population selection and statistical research methods. Previous studies often employed univariate analysis to validate multivariate analysis results or used stepwise regression and logistic regression analyses to identify predictor variables in the model. For example, Yan Zhang etal[24] used a multivariate logistic regression analysis and decision tree to establish MetS risk prediction models, their data set was preprocessed with a multiple imputation method, and between-group comparisons and multivariate analyses were then performed to determine the independent variables, their results showed that high SBP, high DBP, fatty liver, high BMI, smoking status, previous diabetes, previous hypertension, and age were risk factors. In another study, a risk prediction model of MetS for oil workers was reported; although the authors established three models, their method for building these models and screening independent variables was to first conduct a single factor analysis and then a multivariate logistics regression analysis.[39] However, during this process, various confounding factors must be considered as variables, and there is the problem of multicollinearity. Considering the multiple collinearities among variables and the large number of variables, our study utilized innovative statistical methods, namely, LASSO regression analysis and 10-fold cross-validation, to determine the potential risk factors for MetS.

The early identification and diagnosis of MetS have been crucial. However, without a real-world diagnosis for MetS, it is easy to neglect disease prevention. Consequently, having a quantitative tool for predicting MetS is crucial. The risk factors identified by our nomogram indicate that obesity is the primary factor influencing the occurrence of MetS. However, determining obesity cannot be based solely on a person's BMI index or abdominal obesity. These two, or more

indicators, should be considered to be used to make the most accurate assessment. This finding is similar to the research findings of Solam Lee[40] and Junho Kim.[41] In contrast, Yan Zhang et al[24] identified walking and running as factors protective against MetS, but our model does not include these. We did filter out these factors in our LASSO regression analysis. We speculate that the reason for the difference is that physical exercise may affect MetS development indirectly through its effects on factors such as obesity and blood glucose. This is similar to the research finding of the Zhou J et al,[42] they found mediation effects of diet and physical activity. But what is undeniable, lifestyle modifications and risk factor treatment remain the primary remain the primary choices for the prevention and management of MetS.[43]

However, these aforementioned studies have all focused on constructing MetS risk prediction models based on solely low-altitude populations; limited attention has been focused on high-altitude populations. In contrast, our study targets individuals residing specifically in Qinghai Province at altitudes ranging from 1900 m to 3100 m, can provide some methodological references for the future research on the risk prediction model of MetS in high altitude areas. Compared to the recently reported nationwide prevalence rates in China (27.9% for hypertension, 11.2% for diabetes, and 40.4% for dyslipidemia)[44], the incidence rate of high blood glucose in our studied population is relatively lower, while the incidence rate of dyslipidemia is significantly higher. This finding is consistent with the conclusion from Sherpa LY et al's study, [45] which stated that although the overall prevalence of MetS is low in high-altitude areas, the incidence of certain components may be high. Although researchers are increasingly concerned about the prevalence of metabolic syndrome in people living at high altitudes. However, until now, research has been lacking regarding risk prediction models for MetS specifically tailored to the population residing in high-altitude areas of Qinghai Province. Based on this situation, our research can provide some reference for future prevention and management of MetS in high-altitude areas of Qinghai Province.

There are also several limitations to this study that need to be noted. First, our study lacks external validation, and the nomogram is constructed based on the plateau population of Qinghai Province, further verification is needed to determine its applicability to other regions. Second, due to the lack of detailed recording of the altitude of each participants' place of residence during the data collection process, it was not possible to incorporate the factor of altitude into our study. We hope that more detailed, extensive and geographically diverse studies can be carried out in future studies. Third, as this is a cross-sectional study, our results and observed correlations do not imply causality. Despite these limitations, this study developed a useful nomogram for predicting the risk of developing MetS with high accuracy.

Conclusions

The nomogram developed in our study exhibits high discriminative power and strong clinical applicability. The indicators of this nomogram can affect the early screening of MetS and the timely prevention of related complication progression. As a result, this nomogram could serve as a valuable methodological reference for the prevention and control of MetS in the plateau areas of Qinghai Province.

Abbreviations

MetS, metabolic syndrome; NCDs, non-communicable diseases; LASSO, least absolute shrinkage and selection operator; ROC, receiver operating characteristic; DCA, decision curve analysis; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, Fasting plasma glucose; TC, total cholesterol; TG, fasting triglycerides; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol; UA, uric acid; AUC, area under the curve; AUROC, area under the receiver operating characteristic; WHR, Waist-to-hip ratio; H-L test, Hosmer-Lemeshow test.

Ethics Approval

The study was approved by the Ethics Committee of Qinghai University.

Consent to Participate

All individual participants included in the study gave their informed consent.

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.

Funding

This work was supported by "Kunlun Talents High-end Innovation and Entrepreneurial Talents in Qinghai province" project and Foundation for Young Scientists of in Qinghai University(2020-QSY-3).

Disclosure

The authors declare that there is no conflicts of interest in this work.

References

1. Fahed G, Aoun L, BouZerdan M, et al. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. International journal of molecular sciences. 2022;23(2)doi:10.3390/ijms23020786
2. Cornier M-A, Dabelea D, Hernandez TL, et al. The Metabolic Syndrome. Endocrine reviews. 2008;29(7):777-822. doi:10.1210/er.2008-0024
3. Gharipour M, Nezafati P, Sadeghian L, Eftekhari A, Rothenberg I, Jahanfar S. Precision medicine and metabolic syndrome. ARYA atherosclerosis. 2022;18(4):1–10. doi:10.22122/arya.2022.26215
4. Saklayen MG. The Global epidemic of the metabolic syndrome. *Curr Hypertens Rep*. 2018;20(2):12. doi:10.1007/s11906-018-0812-z
5. Hirode G, Wong RJ. Trends in the prevalence of metabolic syndrome in the United States, 2011-2016. *JAMA*. 2020;323(24):2526–2528. doi:10.1001/jama.2020.4501
6. Yao F, Bo Y, Zhao L, et al. Prevalence and influencing factors of metabolic syndrome among adults in China from 2015 to 2017. *Nutrients*. 2021;13(12):4475. doi:10.3390/nu13124475
7. TEAM W. World Health Organization, ed. World health statistics 2023: monitoring health for the SDGs, sustainable development goals. 2023:119.
8. Mili N, Paschou SA, Goulis DG, Dimopoulos MA, Lambrinoudaki I, Psaltopoulou T. Obesity, metabolic syndrome, and cancer: pathophysiological and therapeutic associations. *Endocrine*. 2021;74(3):478–497. doi:10.1007/s12020-021-02884-x
9. Silveira Rossi JL, Barbalho SM, Reverete de Araujo R, Bechara MD, Sloan KP, Sloan LA. Metabolic syndrome and cardiovascular diseases: going beyond traditional risk factors. *Diabetes Metab Res Rev*. 2022;38(3):e3502. doi:10.1002/dmrr.3502
10. Moulignier A, Costagliola D. Metabolic syndrome and cardiovascular disease impacts on the pathophysiology and phenotype of HIV-associated neurocognitive disorders. *Curr Top Behav Neurosci*. 2021;50:367–399. doi:10.1007/7854_2019_123
11. Lemieux I, Després JP. Metabolic syndrome: past, present and future. *Nutrients*. 2020;12(11):3501. doi:10.3390/nu12113501
12. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998;15(7):539–553. doi:10.1002/(sici)1096-9136(199807)15:7<539::Aid-dia668>3.0.Co;2-s
13. Expert Panel on Detection E, Adults ToHBCi. 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
14. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome--A new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med*. 2006;23(5):469–480. doi:10.1111/j.1464-5491.2006.01858.x
15. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation*. 2009;120(16):1640–1645. doi:10.1161/CIRCULATIONAHA.109.192644
16. Chinese Elderly Type 2 Diabetes Prevention and Treatment of Clinical Guidelines Writing Group; Geriatric Endocrinology and Metabolism Branch of Chinese Geriatric Society; Geriatric Endocrinology and Metabolism Branch of Chinese Geriatric Health Care Society; Geriatric Professional Committee of Beijing Medical Award Foundation; National Clinical Medical Research Center for Geriatric Diseases (PLA General Hospital) [Clinical guidelines for prevention and treatment of type 2 diabetes mellitus in the elderly in China (2022 edition)]. Zhonghua nei ke za zhi. 2022;61(1):12–50. doi:10.3760/cma.j.cn112138-20211027-00751
17. Myers J, Kokkinos P, Nyelin E. Physical Activity, Cardiorespiratory Fitness, and the Metabolic Syndrome. *Nutrients*. 2019;11(7):1652. doi:10.3390/nu11071652
18. 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
19. Mathew TM, Sharma S. High Altitude Oxygenation. StatPearls. StatPearls Publishing Copyright © 2024, StatPearls Publishing LLC; 2024.
20. Zhao L, Li T, Wang H, et al. Association of co-exposure to metal(loid)s during pregnancy with birth outcomes in the Tibetan plateau. Chemosphere. 2023;342:140144. doi:10.1016/j.chemosphere.2023.140144
21. Mallet RT, Burtscher J, Richalet JP, Millet GP, Burtscher M. Impact of High Altitude on Cardiovascular Health: Current Perspectives. Vascular health and risk management. 2021;17:317–335. doi:10.2147/vhrm.S294121
22. Sanchez-Samaniego G, Mäusezahl D, Carcamo C, Probst-Hensch N, Verastegui H, Maria Hartinger S. Metabolic syndrome in rural Peruvian adults living at high altitudes using different cookstoves. *PLoS One*. 2022;17(2):e0263415. doi:10.1371/journal.pone.0263415

23. Peng W, Wang YX, Wang HJ, Li K, Sun XM, Wang YF. The prevalence and associated factors of metabolic syndrome among Tibetan pastoralists in transition from nomadic to settled urban environment. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2022;43(4):533–540. doi:10.3760/cma.j.cn112338-20211118-00900
24. Zhang Y, Razbek J, Li D, et al. Construction of Xinjiang metabolic syndrome risk prediction model based on interpretable models. *BMC Public Health*. 2022;22(1):251. doi:10.1186/s12889-022-12617-y
25. National Health and Health Commission of the People's Republic of China,Dietary guidelines for adults with hyperlipemia (2023 edition), Clinical Education of General Practice,2023,21(07):581–583.
26. Zhang Z. Univariate description and bivariate statistical inference: the first step delving into data. *Ann Transl Med*. 2016;4(5):91. doi:10.21037/atm.2016.02.11
27. Palmer MK, Toth PP. Trends in lipids, obesity, metabolic syndrome, and diabetes mellitus in the United States: an NHANES analysis (2003-2004 to 2013-2014). *Obesity*. 2019;27(2):309–314. doi:10.1002/oby.22370
28. Ranasinghe P, Mathangasinghe Y, Jayawardena R, Hills AP, Misra A. Prevalence and trends of metabolic syndrome among adults in the Asia-pacific region: a systematic review. *BMC Public Health*. 2017;17(1):101. doi:10.1186/s12889-017-4041-1
29. Huang X, Hu Y, Du L, et al. Metabolic syndrome in native populations living at high altitude: a cross-sectional survey in Derong, China. *BMJ open*. 2020;10(1):e032840. doi:10.1136/bmjopen-2019-032840
30. Lopez-Pascual A, Arévalo J, Martínez JA, González-Muniesa P. Inverse association between metabolic syndrome and altitude: a cross-sectional study in an adult population of Ecuador. *Front Endocrinol*. 2018;9:658. doi:10.3389/fendo.2018.00658
31. Tibshirani R. The lasso method for variable selection in the Cox model. *Stat Med Feb*. 1997;16(4):385–395. doi:10.1002/(sici)1097-0258-(19970228)16:4
32. Jiang Y, He Y, Zhang H. Variable selection with prior information for generalized linear models via the prior LASSO method. *J Am Stat Assoc*. 2016;111(513):355–376. doi:10.1080/01621459.2015.1008363
33. Grimes DA. The nomogram epidemic: resurgence of a medical relic. *Ann Intern Med*. 2008;149(4):273–275. doi:10.7326/0003-4819-149-4-200808190-00010
34. Balachandran VP, Gonen M, Smith JJ, DeMatteo RP. Nomograms in oncology: more than meets the eye. *Lancet Oncol Apr*. 2015;16(4):e173–80. doi:10.1016/s1470-2045(14)71116-7
35. 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
36. 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
37. Alzeidan R, Fayed A, Rabiee F, Hersi A, Elmorshedy H. Diagnostic performance of waist-to-height ratio in identifying cardiovascular risk factors and metabolic syndrome among adult Saudis. A cross-sectional study. *Saudi Med J*. 2020;41(3):253–260. doi:10.15537/smj.2020.3.24915
38. Zhu Y, Zhang D, Zhou D, et al. Susceptibility loci for metabolic syndrome and metabolic components identified in Han Chinese: a multi-stage genome-wide association study. *J Cell Mol Med*. 2017;21(6):1106–1116. doi:10.1111/jcmm.13042
39. Wang J, Li C, Li J, et al. Development and internal validation of risk prediction model of metabolic syndrome in oil workers. *BMC Public Health*. 2020;20(1):1828. doi:10.1186/s12889-020-09921-w
40. Lee S, Lee H, Choi JR, Koh SB. Development and validation of prediction model for risk reduction of metabolic syndrome by body weight control: a prospective population-based study. *Sci Rep*. 2020;10(1):10006. doi:10.1038/s41598-020-67238-5
41. Kim J, Mun S, Lee S, Jeong K, Baek Y. Prediction of metabolic and pre-metabolic syndromes using machine learning models with anthropometric, lifestyle, and biochemical factors from a middle-aged population in Korea. *BMC Public Health*. 2022;22(1):664. doi:10.1186/s12889-022-13131-x
42. Zhou J, He R, Shen Z, et al. Altitude and metabolic syndrome in China: beneficial effects of healthy diet and physical activity. *J Glob Health*. 2023;13:04061. doi:10.7189/jogh.13.04061
43. Samson SL, Garber AJ. Metabolic syndrome. *Endocrinol Metab Clin North Am*. 2014;43(1):1–23. doi:10.1016/j.ecl.2013.09.009
44. In China T, Hu SS. Report on cardiovascular health and diseases in China 2021: an updated summary. Journal of geriatric cardiology : JGC. 2023;20(6):399–430. doi:10.26599/1671-5411.2023.06.001
45. Sherpa LY, Deji, Stigum H, Chongsuvivatwong V, Nafstad P, Bjertness E, Bjertness E. Prevalence of metabolic syndrome and common metabolic components in high altitude farmers and herdsmen at 3700 m in Tibet. *High Alt Med Biol*. 2013;14(1):37–44. doi:10.1089/ham.2012.1051