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ORIGINAL RESEARCH

Constructing a Predictive Model to Evaluate the Risk of CHD Based on New Metabolic Indicators

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Objective: Constructing a predictive model to evaluate the risk of coronary heart disease (CHD) for early identification of patients with CHD risk based on new metabolic indicators.

Methods: A retrospective analysis was conducted based on NHANES databases. Collect general information, cardiovascular comorbidities, new metabolic indicators (BMI, Triglycerides/Glucose, Waist Circumference-to-Height ratio, Cholesterol/HDL, Triglycerides/HDL, Cardiometabolic index, Neutrophil percentage-to-albumin ratio, etc). The least absolute shrinkage and selection operator (LASSO) regression model and multivariate logistic regression were performed to analyze the risk factors of CHD and develop a CHD risk predictive model using R software.

Results: A total of 3741 individuals were included and 160 (4.3%) individuals had CHD. According to the results of the LASSO regression model and multivariate logistic regression, 9 factors were related to CHD such as Hypertension (Yes), Cardiometabolic index (≥0.672), Mean arterial pressure (<70 mmHg), Gender (male), COPD (Yes), Age (>69), Neutrophil percentage-to-albumin ratio (≥1.465), Thyroid problem (Yes) and Stroke (Yes), which were developed a CHD risk prediction nomogram. The nomogram presented good discrimination with a C-index value of 0.869 (95% confidence interval: 0.82196–0.91604), AUC (0.868) and good calibration. Based on the maximum point of the Youden index, the individuals with a score greater than 136.5 are at high risk for CHD.

Conclusion: A risk prediction model for CHD has been developed based on new metabolic indicators in this study and boasts a relatively high accuracy in the early identification of patients with CHD risk. It may help clinicians develop strategies to prevent CHD and improve care quality.

Keywords: CHD, risk factors, predictive model, metabolic indicators

Introduction

Cardiovascular diseases are the leading cause of disease burden in the world, the global prevalence of cardiovascular diseases is nearly 523 million.[1] According to the 2022 statistics in the United States, heart disease remains the leading cause of mortality among Americans,[2] approximately one-quarter of all deaths in the US are attributed to coronary heart disease (CHD) annually,[3] and expenditures on cardiovascular diseases healthcare have reached $ 89.3 billion, exerting considerable pressure on healthcare resources.[4] Current therapeutic options for CHD predominantly encompass pharmacological thrombolysis and endovascular interventional surgery, which substantially enhance the short-term quality of life for CHD patients.[5] However, these treatments also brought a heavy burden to patients and public healthcare. Simultaneously, the morbidity, disability, and mortality rates of CHD continue to rise year after year, ranking among the highest globally.[6]

The development of CHD is a gradual process phenomenon from incremental chronic inflammation, suggesting a susceptible timeframe exists for the modulation of CHD risk before its full expression.[5] Early detection of key factors before CHD lesions and timely intervention may effectively prevent the occurrence of CHD. Patients with dyslipidemia

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are more likely to increase the risk of atherosclerosis, and atherosclerosis was also significantly associated with a worse prognosis for cardiovascular disease.[7] Obesity such as central obesity is frequently accompanied by abnormal lipid metabolism, which substantially increases the risk of developing cardiovascular disease.[8] According to literature reports, an increase per 5 kg/m2 in Body Mass Index (BMI) was related to a 1.9 higher risk of cardiometabolic multimorbidity.[9] A potential limitation of BMI is its inability to differentiate between muscle and fat accumulation. The gold-standard imaging assessments of visceral adipose tissue (VAT), such as computed tomography (CT) and magnetic resonance imaging (MRI), have drawbacks including the high costs, radiation exposure, and the time consumption involved.[10]

Identifying practical and helpful markers that allow early intervention in metabolic factors in individuals at high risk of CHD. The cardiometabolic index (CMI), Triglycerides/HDL-C, WHtR (Waist Circumference/Height), and neutrophil percentage-to-albumin ratio (NPAR) are novel metabolism-related indexes, and metabolic syndrome plays a significant role in the development of CHD.[7] However, the relationship between CMI levels and the risk of developing CHD have not been fully explored and requires further research. The NPAR represents an emerging biomarker that encompasses two vital factors: the percentage of neutrophils, which indicates systemic inflammation, and albumin, a marker of nutritional status.[11] A study has indicated that NPAR could potentially be clinically beneficial in forecasting long-term health outcomes and mortality rates among individuals with hypertension.[12] However, the association between NPAR and CHD needs further confirmation. Mean arterial pressure (MAP) is the average arterial pressure throughout one cardiac cycle, systole, and diastole.[13] The literature suggests that CHD elevates the risk of perioperative ischemic stroke within the subgroup characterized by a preoperative MAP $\geq$ 94.2 mmHg.[14] However, the relationship between MAP and the risk of CHD remains uncertain.

Given its profound impact on public health and the global economy, early identification and prediction of CHD are essential. Thus, our research aimed to screen the risk factors for CHD with novel metabolism-related indexes and construct a CHD risk prediction tool for early identification of patients with CHD risk.

Methods

Data Collection

Data were collected from the National Health and Nutrition Examination Survey (NHANES) database from January 2015 to December 2018. The National Center for Health Statistics Research Ethics Review Board has approved all methodologies utilized in the NHANES study. Additionally, the Ethics Committee of Nanchong Central Hospital has also endorsed this research endeavor. The individuals were categorized into two distinct groups: the case group, comprising individuals with CHD, and the control group, consisting of individuals without CHD.

Data were collected from the NHANES database from January 2015 to December 2018, including CHD, BMI, Triglycerides/Glucose, Cholesterol/HDL, Triglycerides/HDL, Waist Circumference-to-Height ratio (WHtR), Cardiometabolic index (CMI), Mean arterial pressure (MAP), Hypertension, Gender, Age, Race, drinks, neutrophil percentage-to-albumin ratio (NPAR), AST, ALT, BUN, Calcium, Serum creatinine, Potassium, Sodium, Osmolality, Diabetes, LDL, Gout, Stroke, Thyroid problem, COPD, increasing exercise, reducing salt in diet, reducing fat in diet, trouble sleeping, Smoked at least 100 cigarettes,25 (OH) D3, red blood cell distribution width (RDW), and PLT. The inclusion criteria were 1) aged $\geq$ 18 years and 2) diagnosed with or without CHD. The exclusion criteria were 1) incomplete data records in the NHANES database.

Statistical Analysis

All features were assessed using SPSS software and R software. The categorical variables were articulated in terms of frequencies and percentages, alongside the grade data, which were also presented in frequencies and percentages. Meanwhile, the continuous variables pertaining to normal distribution data were disclosed as mean and standard deviation. Predictors were selected utilizing the least absolute shrinkage and selection operator (LASSO) regression method using R software. Multivariate logistic regression analysis was conducted to identify risk factors for CHD. P values below 0.05 were deemed to signify statistical significance. Then, develop a predictive nomogram for CHD using these risk factors, which have P values below 0.05, using R software. The nomogram was assessed using the C-index

(higher than 0.7, indicating the good discriminating ability of the nomogram), Receiver operating characteristic (ROC) curve, and calibration. Bootstrapping with 1000 resamples was done to calculate a relatively accurate C-index for internal cross-validation. The cutoff values for low-risk and high-risk in the prediction model are determined by the Youden index. The maximum point of the Youden index is determined by the Area Under Curve (AUC) of its ROC curve and the nearest point in the upper left corner.

Results

Initially, 19225 individuals were enrolled in the National Health and Nutrition Examination Survey (NHANES) database conducted from January 2015 to December 2018. After excluding those participants with incomplete data, our comprehensive final analysis encompassed a total of 3741 respondents aged from 20 to 80 years, with a mean age of 50.39 ±17.408 years (Table 1). Among them, 160 (4.3%) had CHD. According to the results of the LASSO regression model for CHD (Figure 1), 26 of the 35 features were considered potential predictors, which included, "NPAR", "AST", "BMI",

Table 1 Baseline Characteristics of Participants According to CHD

Characteristics	Without CHD n =3581	With CHD n =160
Age (year)	49.57 ± 17.221	68.7 ± 9.906
Gender		
Male	1730(48.3%)	108(67.5%)
Female	1851(51.7%)	52(32.5%)
Race		
Mexican American	576(16.1%)	16(10.0%)
Other Hispanic	424(11.8%)	16(10.0%)
Non-Hispanic White	1217(34.0%)	87(54.4%)
Non-Hispanic Black	765(21.4%)	24(15.0%)
Non-Hispanic Asian	437(12.2%)	9(5.6%)
Other Race-Including Multi-Racial	162(4.5%)	8(5.0%)
LDL	2.91± 0.924	2.33 ± 0.865
AST	23.74± 18.52	22.78 ± 7.13
ALT	23.8 ± 16.15	21.3 ± 10.31
BMI	29.58 ± 7.055	29.35 ± 5.94
Triglycerides/Glucose	0.245 ± 0.14	0.23 ± 0.119
Cholesterol/HDL	3.74± 1.34	3.48 ± 1.12
Triglycerides/HDL	1.14 ± 0.959	1.32 ± 0.943
Waist Circumference/Height	0.602 ± 0.101	0.631 ± 0.08
MAP	88.92 ± 12.41	87.08 ± 13.62
NPAR	1.378 ± 0.272	1.498 ± 0.344
Blood urea nitrogen	5.15 ± 1.95	6.85 ± 2.88
Calcium	2.31 ± 0.08	2.32 ± 0.09

(*Continued*)

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Table 1 (Continued).

Characteristics	Without CHD n =3581	With CHD n =160
Serum creatinine	76.01 ± 28.24	96.79 ± 42.49
Potassium	2.55 ± 1.45	2.58 ± 1.54
Sodium	139.61± 2.47	139.67 ± 2.89
25 (OH) D3	63.17 ± 30.57	66.0 ± 28.26
RDW	13.81 ± 1.31	14.26 ± 1.46
PLT	237.18 ± 62.45	201.15 ± 49.81
Osmolality	279.41± 5.44	282.28 ± 6.76
Increasing exercise		
Yes	2130(59.5%)	85(53.1%)
No	1451(40.5%)	75(46.9%)
Drink		
Yes	2875(80.3%)	134(83.8%)
No	706(19.7%)	26(16.3%)
CMI		
<0.672	2212(61.8%)	75(46.9%)
≥0.672	1369(38.2%)	85(53.1%)
Gout		
No	3400(94.9%)	131(81.9%)
Yes	181(5.1%)	29(18.1%)
Stroke		
No	3466(96.8%)	134(83.8%)
Yes	115(3.2%)	26(16.3%)
Thyroid problem		
No	3177(88.7%)	122(76.3%)
Yes	404(11.3%)	38(23.8%)
Diabetes		
Yes	517(14.4%)	61(38.1%)
No	2962(82.7%)	96(60.0%)
Borderline	102(2.8%)	3(1.9%)
COPD		
No	3457(96.5%)	129(80.6%)
Yes	124(3.5%)	31(19.4%)

(*Continued*)

Table 1 (Continued).

Characteristics	Without CHD n =3581	With CHD n =160
Hypertension		
No	2331(65.1%)	39(24.4%)
Yes	1250(34.9%)	121(75.6%)
Reducing salt in diet		
Yes	1885(52.6%)	112(70.0%)
No	1696(47.4%)	48(30.0%)
Reducing fat in diet		
Yes	2071(57.8%)	111(69.4%)
No	1510(42.2%)	49(30.6%)
Trouble sleeping		
Yes	988(27.6%)	67(41.9%)
No	2593(72.4%)	93(58.1%)
Smoked at least 100 cigarettes		
Yes	1562(43.6%)	95(59.4%)
No	2019(56.4%)	65(40.6%)

Abbreviations: CMI, Cardiometabolic Index; MAP, Mean Arterial Pressure; BMI, Body Mass Index; RDW, Red blood cell distribution width; NPAR, Neutrophil Percentage to Albumin Ratio.

"CMI", "hypertension", "MAP", "Gender", "Age", "drinks", "gout", "ALT", "stroke", "Calcium", "BUN", "Serum creatinine", "Sodium", "Diabetes", "LDL", "thyroid problem", "COPD", "increasing exercise", "reducing salt in diet", "reducing fat in diet", "trouble sleeping", "X25OHD3" and "PLT".

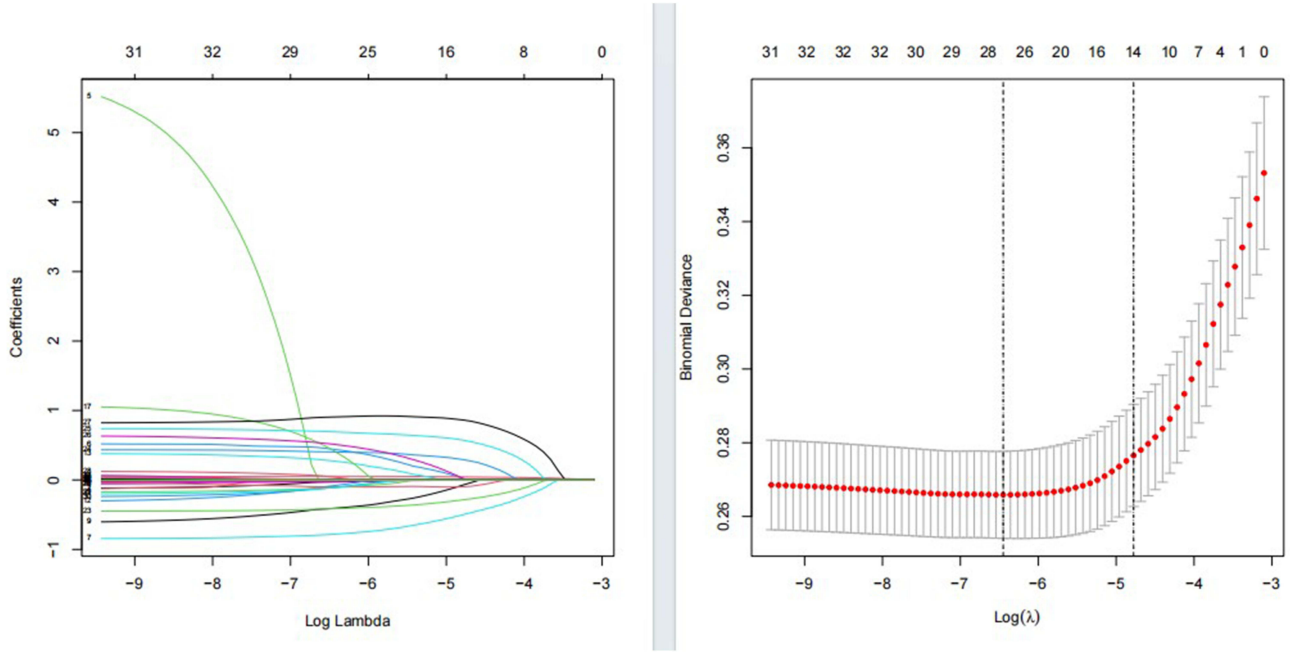

Figure 1 Predictors was selected using LASSO regression.
Abbreviation: LASSO, the least absolute shrinkage and selection operator.

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Table 2 Predictors of Risk Models for CHD

Variable	Multivariate Analysis		
	β	Odds Ratio (95% CI)	P
Hypertension (Yes)	0.88	2.41(1.59–3.72)	<0.001
CMI (≥0.672)	0.46	1.59(1.07–2.35)	0.019
MAP (70–105mmHg)	−0.75	0.46(0.23–0.99)	0.038
MAP (>105mmHg)	−1.15	0.31(0.12–0.78)	0.012
Gender (Female)	−0.69	0.49(0.32–0.74)	<0.001
Age (40–55 year)	1.68	5.37(1.43–34.89)	0.029
Age (56–69 year)	2.84	17.19(5.14–106.88)	<0.001
Age (>69 year)	3.301	27.15(7.98–170.12)	<0.001
Stroke (Yes)	0.77	2.16(1.25–3.64)	0.004
COPD (Yes)	0.95	2.59(1.54–4.25)	<0.001
NPAR (≥1.465)	0.42	1.53(1.06–2.22)	0.022
Thyroid problem (Yes)	0.53	1.71(1.08–2.66)	0.019

Abbreviations: CMI, Cardiometabolic Index; MAP, Mean Arterial Pressure; NPAR, Neutrophil Percentage to Albumin Ratio.

These 26 potential predictors analyzed by multivariate logistic regression and indicated significant differences in Hypertension (Yes, P < 0.001), CMI (≥0.672, P = 0.019), MAP (>105 mmHg, P = 0.012), Gender (Female, P < 0.001), COPD (Yes, P < 0.001), Age (>69, P < 0.001), NPAR (≥1.465, P = 0.022), Thyroid problem (Yes, P = 0.019), Stroke (Yes, P = 0.004), between the two groups (Table 2), and these factors were developed a CHD risk prediction nomogram (Figure 2). The C-index and the area under the ROC curve range higher than 0.7, indicating the good discriminating ability of the nomogram. The area under the ROC curve (Figure 3), the calibration results (Figure 3) and the C-index values (0.869; 95% confidence interval: 0.82196–0.91604) showed that the nomogram was very reliable. The C-index value of internal cross-validation was 0.8617938 (95% confidence interval: 0.8147538–0.9088338).

Based on the maximum point of the Youden index, the individuals with a score greater than 136.5 are at high risk for CHD based on CHD risk prediction nomogram. The scores from the nomogram are displayed in Table 3. Comparison of CHD risk prediction nomogram and metabolic indicators in predicting CHD, the Area Under the Curve (AUC, 0.868) of the CHD risk prediction nomogram exceeds that of other metabolic indicators (Figure 4). Among various metabolic indicators, the AUC of NPAR is 0.606, which is higher than other metabolic indicators. The AUC values of WHtR, Triglycerides/HDL, CMI, and BMI for predicting CHD are 0.597, 0.577, 0.574, and 0.507, respectively.

Discuss

CHD is a classic type of cardiovascular disease characterized by a decreased oxygenated blood supply to the heart.[15] CHD remains a leading global cause of mortality, despite the advances in coronary revascularization and significant progress in secondary preventive treatments.[16] Considering the increasing prevalence and difficulty treatment of CHD, traditional cardiovascular risk factors are no longer sufficient to predict the occurrence of CHD.[17] Thus, there is an urgent need for novel indexes to predict the occurrence of CHD. First introduced in 2015, CMI was an indicator initially devised to forecast diabetes mellitus risk.[18] As clinical inquiry plumbs more profound depths, studies found that CMI was positively associated with risks of metabolic syndrome, and individuals with high CMI may encounter elevated systemic inflammation, which could potentially aggravate cardiovascular disease.[4] CMI is calculated as follows: [(triglycerides/

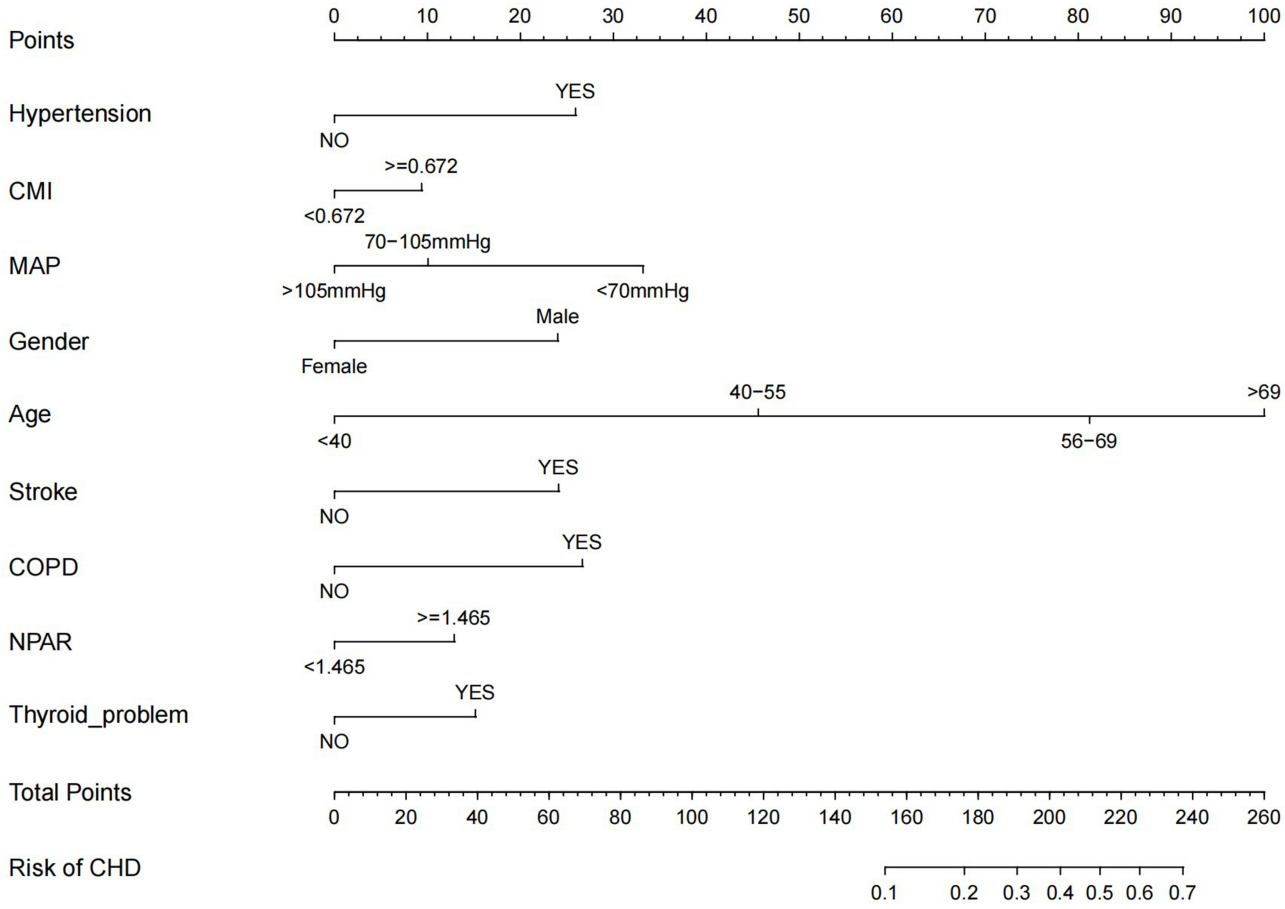

Figure 2 Developed CHD risk predictive nomogram.
Notes: The probability of CHD is calculated by drawing a line to the point on the axis for each of the following features. The points for each feature are summed and located on the total point line. Next, a vertical line is projected from the total point line to the predicted probability-scale line to obtain the elderly people's probability of CHD.
Abbreviations: CHD, Coronary Heart Disease; CMI, Cardiometabolic Index; MAP, Mean Arterial Pressure; NPAR, Neutrophil Percentage-to-Albumin Ratio.

HDL-C) × (waist circumference/height)]. Compared with triglycerides/HDL-C and waist circumference/height, CMI is more correlated with the risk of CHD occurrence. Our findings suggested that CMI ≥ 0.672 is a risk factor for CHD, getting a risk score of 9 points. The mechanism of CMI in cardiovascular health will be further explored in the next step to provide a scientific basis for the early prevention of CHD. BMI is a potential predictor for CHD by the LASSO regression model, but not a risk factor for CHD compared with other factor by multivariate logistic regression analysis.

Studies have demonstrated that the neutrophil percentage-to-albumin ratio (NPAR) serves as a valuable prognostic biomarker for predicting cardiogenic shock and myocardial infarction.[19] NPAR encompasses the percentage of neutrophils and albumin, which can reflect the dynamic balance of immunity, inflammation, and disease activity. During inflammation, activated neutrophils lead to oxidative stress and impair endothelial function, thereby promoting atherosclerosis and thrombosis,[20] atherosclerosis is a risk factor for CHD. Albumin with lower levels can increase the risk of mortality from cardiovascular disease.[21] NPAR ≥ 1.465 was identified as a risk factor for CHD in our research and get the risk score of 13 points. And among various metabolic indicators, the AUC of NPAR is 0.606, which is higher than other metabolic indicators. Our next step is to study the mechanisms between NPAR and CHD in the future.

MAP is impacted by cardiac output and systemic vascular resistance, both of which are in turn influenced by a variety of factors.[13] Literature reports that patients with heart failure who have a MAP less than 80 mmHg are at a higher risk of 28-day and 6-month all-cause mortality.[22] In our study, MAP < 70 mmHg is associated with CHD and get the risk score

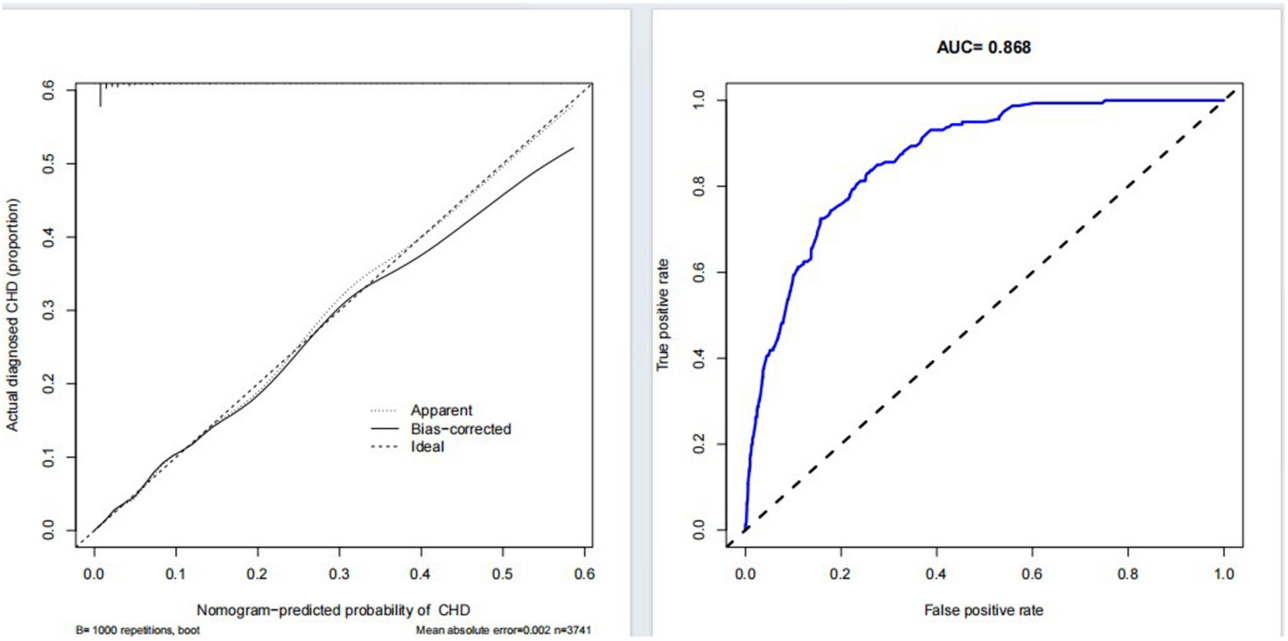

Figure 3 Calibration and receiver operating characteristic (ROC) curve of the CHD risk predictive nomogram.
Notes: The x-axis represents in calibration curve predicted CHD risk. The y-axis represents the actual diagnosed CHD. The solid-line close to the 45 degrees diagonal line represents a better prediction.
Abbreviation: CHD, Coronary Heart Disease.

of 33 points. Studies have demonstrated a significant correlation between red blood cell distribution width (RDW) and CHD among patients with rheumatoid arthritis.[23] In this study, RDW is not a risk factor with CHD. This study also found that men have a higher risk of CHD than women, which may be due to the role of sex hormones in young women.

Accompanied by hyperthyroidism, the consequent overproduction of thyroid hormones, there may be an elevation in heart rate and myocardial contractility, over time, this could impose a greater workload on the heart and heighten the risk of CHD.[24] On the contrary, when accompanied by hypothyroidism, the secretion of thyroid hormones decreases,

Table 3 Risk Scores for CHD According to Predictive Nomogram

Risk Factor	Score
Hypertension	
No	0
Yes	26
CMI	
<0.672	0
≥0.672	9
MAP	
<70mmHg	33
70–105mmHg	10
>105mmHg	0

(*Continued*)

Table 3 (Continued).

Risk Factor	Score
Gender	
Male	24
Female	0
Age	
<40year	0
40–55 year	46
56–69 year	81
>69 year	100
Stroke	
No	0
Yes	24
COPD	
No	0
Yes	27
NPAR	
<1.465	0
≥1.465	13
Thyroid problem	
No	0
Yes	15

Notes: Low Risk: Score≤136.5. High Risk: Score>136.5.
Abbreviations: CMI, Cardiometabolic Index; MAP, Mean Arterial Pressure; NPAR, Neutrophil Percentage to Albumin Ratio.

potentially resulting in a slower heart rate, reduced myocardial contractility, weakened cardiac pumping function, and an elevated risk of CHD. Furthermore, thyroid disorders can impact blood lipid levels, and aberrant lipid metabolism constitutes a risk factor for CHD. Consistent with our study, in this study, thyroid problem is associated with CHD and get the risk score of 15 points. Therefore, for patients suffering from thyroid diseases, regular cardiovascular health check-ups are essential to promptly identify and address any potential cardiovascular risks.

Hypertension is closely associated with CHD.[25] Chronic hypertension can lead to damage in the blood vessel walls, elevating the risk of arteriosclerosis and consequently increasing the risk of CHD. Consistent with our study, in this study, hypertension is associated with CHD and get the risk score of 26 points. Therefore, when managing hypertension, it is imperative to closely monitor the patient's coronary artery status. If required, diagnostic procedures like coronary angiography should be conducted to evaluate the extent of coronary artery disease.

Both stroke and CHD involve the narrowing or blockage of blood vessels, the underlying mechanisms, such as atherosclerosis (the buildup of plaques in the arteries), are similar in both conditions. This is consistent with our research findings, in

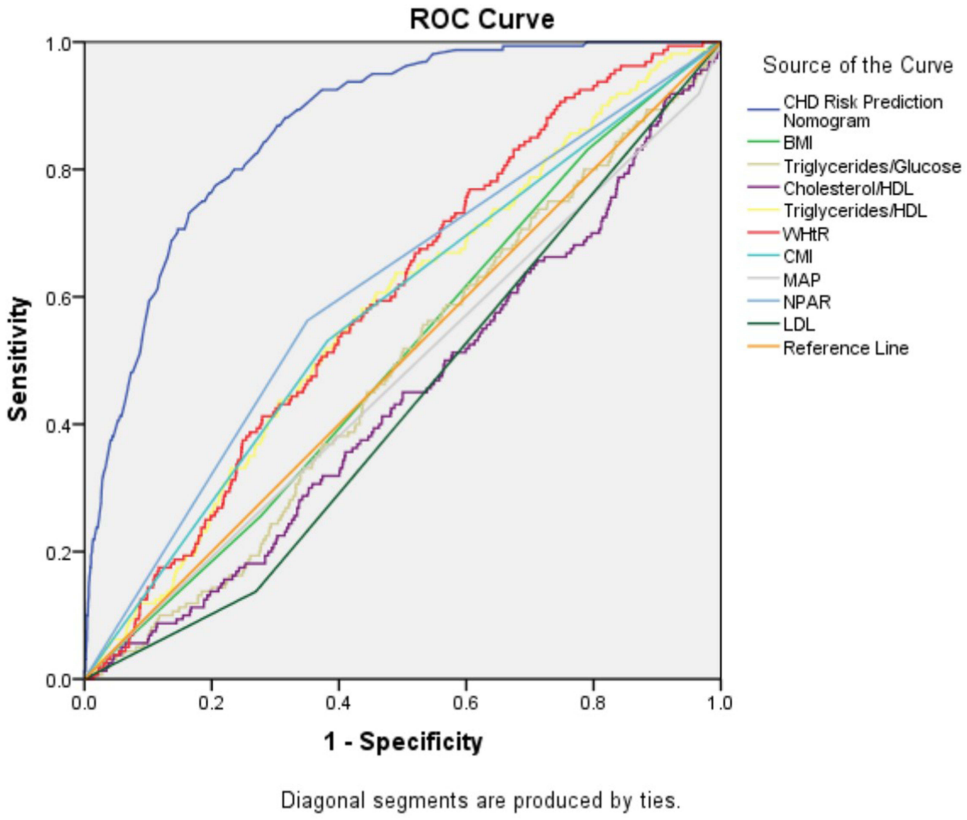

Figure 4 Comparison of metabolic Indicators and prediction nomogram for CHD Prediction.
Abbreviations: CMI, Cardiometabolic Index; BMI, Body Mass Index; LDL, Low-density Lipoprotein; MAP, Mean Arterial Pressure; NPAR, Neutrophil Percentage-to-Albumin Ratio; WHtR, Waist Circumference/Height.

our research, stroke is associated with CHD and gets the risk score of 24 points. The relationship between stroke and CHD is characterized by shared pathophysiological mechanisms. This interplay highlights the importance of a comprehensive approach to cardiovascular health, where preventing and managing one condition can significantly impact the other.

One study found that individuals with COPD have a higher risk of developing CHD.[26] This increased risk is attributed to the systemic inflammation caused by COPD, which can lead to atherosclerosis, the primary cause of CHD. Our research also found that COPD is a risk factor for CHD and gets the risk score of 64 points. In the future, further research is needed to better understand the mechanisms behind COPD and CHD, the strategies for preventing and managing both conditions.

In addition, this study also found that increasing exercise, reducing salt in diet, reducing fat in diet, and trouble sleeping are potential risk factors for CHD through the LASSO regression model. However, after multivariate logistic regression analysis, these factors are not risk factors for CHD, the reason may related to the frequency and duration. The next step is to explore the correlation between these factors and CHD.

Limitations

This research does not use an independent NHANES dataset or other datasets for external validation to enhance the model's generalizability. The next step is to use clinical data to externally validate the prediction model for CHD.

Conclusion

CHD stands as one of the leading causes of mortality globally. The treatment of CHD has been increasingly challenging. We developed a risk prediction model based on new metabolic indicators for CHD which include 9 factors such as

Hypertension, CMI, MAP, Gender, COPD, Age, NPAR, Thyroid problem and Stroke in this study, which boasts relatively high accuracy in early identification of patients at risk for CHD. It may assist clinicians in devising strategies to prevent CHD and enhance the quality of care.

The Ethics Statement

The full name of the ethics committee that reviewed my study is Nanchong Central Hospital.

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Disclosure

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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