Development and Validation of an Early Aortic Stiffness Risk Screening Model: Postprint

Authors: Zhou Zhensen, Huangyan, Cheng Siwei, Zhang Xiaoyu, Zhang Xiaoyu, Sun Ting, Yang Xianjun, Xie Hui, Ma Zuchang, Ma Zuchang

Date: 2024-07-02T00:00:00+00:00

Abstract

Background: In cardiovascular risk assessment, aortic stiffness is recognized as a key predictive indicator, and carotid-femoral pulse wave velocity (cfPWV) is considered the gold standard for noninvasive assessment of aortic stiffness risk. However, due to technical challenges and other obstacles, cfPWV testing has not been widely implemented in China.

Objective: This study aimed to develop and validate an early aortic stiffness risk screening model based on cardiovascular risk factors, to replace the complex measurement process of cfPWV and reduce dependence on traditional measurement methods.

Methods: A total of 878 subjects recruited from the Health Examination Center of the First Affiliated Hospital of Anhui Medical University between May and November 2023 were randomly divided into a model development group (n=703) and a validation group (n=175) at an 8:2 ratio. General information, laboratory test results, and cfPWV were collected. Based on cfPWV examination results and relevant guidelines, subjects in the model development group were categorized into no aortic stiffness risk (n=503) and aortic stiffness risk (n=240). Multivariate Logistic regression analysis was employed to screen variables and establish a nomogram evaluation model. Receiver operating characteristic (ROC) curves were plotted to predict aortic stiffness risk, with area under the ROC curve (AUC) and Hosmer-Lemeshow test used to evaluate model discrimination and calibration, DeLong test used to compare AUCs among models, decision curve analysis (DCA) used to evaluate clinical utility, and Bootstrap method with 1000 repeated samplings used for internal validation.

Results: In the model development group, subjects with aortic stiffness risk exhibited higher age, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), urea, fasting blood glucose (FBG),

low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), hemoglobin (Hb), alcohol consumption, dyslipidemia, and diabetes mellitus prevalence, and lower glomerular filtration rate (GFR) and platelet count (PLT) compared to those without aortic stiffness risk (P<0.05). Multivariate Logistic regression analysis revealed that age (OR=1.112, 95%CI=1.082~1.143), MAP (OR=1.146, 95%CI=1.107~1.188), Hb (OR=1.026, 95%CI=1.004~1.049), and FBG (OR=1.353, 95%CI=1.076~1.701) were independent risk factors for aortic stiffness (P<0.05). Prediction model I was constructed incorporating indicators with statistically significant differences in multivariate Logistic regression analysis (age, MAP, Hb, FBG), while smoking, gender, and dyslipidemia were separately incorporated to construct model II, model III, and model IV. ROC curves for models I-IV yielded AUCs of 0.941 (95%CI=0.923~0.964, P<0.05), 0.941 (95%CI=0.922~0.962, P<0.05), 0.941 (95%CI=0.922~0.963, P<0.05), and 0.939 (95%CI=0.919~0.962, P<0.05), respectively. DeLong test results showed no statistically significant differences in AUCs among models I, II, III, and IV (P>0.05). Based on multivariate Logistic regression analysis results, a nomogram model was constructed with age, heart rate, FBG, and Hb as predictors. The AUC of the prediction model training set was 0.941 (95%CI=0.920~0.962), with sensitivity of 0.832 and specificity of 0.917. The validation set AUC was 0.961 (95%CI=0.914~1.000), with sensitivity of 0.872 and specificity of 0.964. DCA results demonstrated that using the early aortic stiffness screening model could provide clinical benefit to subjects.

Conclusion: This study established an early aortic stiffness risk screening model based on four simple indicators (age, MAP, Hb, and FBG), providing a convenient and efficient method for early vascular function screening.

Full Text

Construction and Validation of a Screening Model for Early Atherosclerosis Risk in the Aorta

ZHOU Zhensen[1,2], **HUANG Yan**[2], **CHENG Siwei**[3], **ZHANG Xiaoyu**[2], **ZHANG Xiaoyu**[4], **SUN Ting**[1], **YANG Xianjun**[2], **XIE Hui**[1], **MA Zuchang**[2,3*]

[1]Department of Nursing, Bengbu Medical University, Bengbu 233030, China
[2]Institute of Intelligent Machines, Hefei Institutes of Physical Science, Chinese Academy of Sciences, Hefei 230031, China
[3]University of Science and Technology of China, Hefei 230026, China
[4]The First Affiliated Hospital of Anhui Medical University, Hefei 230022, China

Corresponding author: MA Zuchang, Researcher; E-mail: zuchangma_{zcm}@163.com

Abstract

Background In the field of cardiovascular risk assessment, aortic stiffness is considered a key predictive indicator, and carotid-femoral pulse wave velocity (cfPWV) is recognized as the gold standard for non-invasive assessment of atherosclerotic risk in the aorta. Due to challenges such as technical difficulty, cfPWV testing has not been widely implemented in China. **Objective** This study aimed to develop and validate a screening model for early atherosclerotic risk in the aorta based on cardiovascular risk factors, with the intention of replacing the complex measurement process of cfPWV and reducing reliance on traditional measurement methods. **Methods** A total of 878 participants recruited from the Health Checkup Center of the First Affiliated Hospital of Anhui Medical University between May and November 2023 were selected as research subjects, randomly divided into a model-building group (n=703) and a validation group (n=175) in an 8:2 ratio. Patient general information, laboratory test results, and cfPWV were collected. Based on the cfPWV examination results and relevant guidelines, participants in the model-building group were divided into those without atherosclerotic risk in the aorta (n=503) and those with atherosclerotic risk in the aorta (n=240). Multifactorial logistic regression analysis was used to screen variables and establish a nomogram assessment model. The receiver operating characteristic curve (ROC curve) for predicting the risk of atherosclerosis in the aorta was plotted for the model, and the model's discriminative ability and calibration were assessed using the area under the ROC curve (AUC) and the Hosmer-Lemeshow test, respectively. The Delong test was used to compare the AUCs of different models, and decision curve analysis (DCA) was used to assess the clinical utility of the model. Internal validation of the model was performed using the bootstrap method with 1,000 resampling iterations. **Results** Participants with atherosclerotic risk in the model-building group were older, had higher BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), urea, fasting blood glucose (FBG), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), hemoglobin (Hb), and a higher proportion of alcohol consumption, dyslipidemia, and diabetes than those without atherosclerotic risk in the aorta. The glomerular filtration rate (GFR) and platelet count (PLT) were lower in those with atherosclerotic risk (P<0.05). Multifactorial logistic regression analysis showed that age (OR=1.112, 95%CI=1.082-1.143), MAP (OR=1.146, 95%CI=1.107-1.188), Hb (OR=1.026, 95%CI=1.004-1.049), and FBG (OR=1.353, 95%CI=1.076-1.701) were independent risk factors for atherosclerosis in the aorta (P<0.05). A predictive Model I was constructed using statistically significant indicators from the multifactorial logistic regression analysis (age, MAP, Hb, FBG), and Models II, III, and IV were constructed by additionally including smoking, gender, and dyslipidemia, respectively. The AUCs for Models I to IV were 0.941 (95%CI=0.923-0.964, P<0.05), 0.941 (95%CI=0.922-0.962, P<0.05), 0.941 (95%CI=0.922-0.963, P<0.05), and 0.939 (95%CI=0.919-0.962, P<0.05), respectively. The Delong test showed no

statistically significant difference in AUCs among Models I, II, III, and IV (P>0.05). A nomogram model was constructed using age, heart rate, FBG, and Hb as predictive factors, with an AUC of 0.941 (95%CI=0.920-0.962) for the training set, sensitivity of 0.832, and specificity of 0.917. The AUC for the validation set was 0.961 (95%CI=0.914-1.000), with sensitivity of 0.872 and specificity of 0.964. DCA results indicated that the use of the early atherosclerosis screening model could benefit participants in clinical practice. **Conclusion** Based on four simple indexes of age, mean arterial pressure, hemoglobin, and fasting blood glucose, a screening model for early aortic sclerosis risk was established, which provides a convenient and efficient method for early vascular function screening.

Keywords Arteriosclerosis; Aortic stiffness; Carotid-femoral pulse wave velocity; Prediction model; Early screening

Introduction

Driven by rapid population aging and unhealthy lifestyles in China, the prevalence and mortality of cardiovascular disease (CVD) continue to rise among Chinese populations. According to the "Summary of the China Cardiovascular Health and Disease Report 2022" [1], CVD has become the leading disease threatening residents' health. Statistics indicate that approximately 330 million people in China currently suffer from CVD, with 2 out of every 5 deaths attributed to CVD, representing an extremely serious situation.

In the field of cardiovascular risk assessment, aortic stiffness is considered a key predictive indicator [2]. Increased arterial stiffness leads to elevated systolic pressure, causing increased left ventricular afterload. Simultaneously, decreased diastolic pressure results in insufficient blood perfusion, leading to myocardial ischemia [3-4]. Currently, the main non-invasive screening methods for aortic sclerosis include imaging techniques such as color ultrasound, CT scanning, and magnetic resonance imaging, which focus on vascular structure assessment. In contrast, carotid-femoral pulse wave velocity (cfPWV) detection emphasizes vascular function evaluation. cfPWV is recognized as the gold standard for non-invasive assessment of aortic sclerosis risk [5], showing the most significant correlation with CVD among various pulse wave velocity measurements [6]. Since functional vascular changes typically precede structural changes, cfPWV measurement is crucial for reflecting early vascular function.

However, cfPWV measurement still faces several challenges: expensive equipment, requirement for professional operators, and potential privacy concerns when measuring the femoral artery. To address these issues, this study successfully constructed an early aortic sclerosis risk screening model that effectively replaces the complex measurement process of cfPWV, enabling residents to independently monitor their aortic sclerosis risk levels and implement targeted prevention and management measures.

Methods

Study Subjects

A total of 878 participants recruited from the Health Checkup Center of the First Affiliated Hospital of Anhui Medical University between May and November 2023 were selected as research subjects. Inclusion criteria were: (1) age ≥ 18 years; (2) conscious with good Chinese reading and writing communication abilities; (3) good compliance and voluntary participation. Exclusion criteria were: (1) mental illness; (2) severe cardiovascular, cerebrovascular, liver, or kidney diseases; (3) severe peripheral arterial occlusive disease involving left/right carotid, upper limb, iliac, or femoral arteries preventing cfPWV measurement; (4) frequent premature contractions, atrial fibrillation, or other conditions preventing regular sinus rhythm during detection; (5) acute pain, severe distress, or agitation; (6) physical or emotional restlessness or non-cooperation; (7) refusal to participate for any reason; (8) other disqualifying conditions determined by researchers, including pregnant women and those with impalpable arterial pulses at measurement sites.

Sample size was calculated using the events per variable (EPV) method for logistic regression sample size estimation. To ensure robust regression analysis results, EPV should be 10-20 [7]. A preliminary survey of 100 cases found a 30% detection rate of aortic sclerosis. Assuming EPV=10 and with 21 study factors included, the required number of positive events was 21$×$10=210 cases, necessitating a total sample size of 210÷30%=700 cases. According to the principle that external validation sample size for risk prediction models should generally be 1/4 to 1/2 of the modeling group sample size [8], the validation group should comprise 175-350 cases. This study included 878 total samples, randomly divided in an 8:2 ratio, with 703 cases in the modeling group and 175 cases in the validation group.

Data Collection Methods

1.2.1 General Data Collection Participants fasted for 8 hours before measurement and abstained from caffeine or smoking for 3 hours prior. Two standardized operators performed measurements at a fixed morning time each day with ambient temperature controlled at (25$±$2)°C. Data collected included age, gender, height, weight, hypertension, diabetes, medication history, systolic blood pressure (SBP), diastolic blood pressure (DBP), smoking history (defined as smoking $ $1 cigarette/day within 30 days before the survey$ [9]), and alcohol consumption history (defined as drin
($SBP + 2×$DBP)/3.

1.2.2 Laboratory Indicators Collection After 8 hours of fasting, participants underwent elbow venous blood collection the following morning to determine total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting blood glucose (FBG), glomerular filtration rate (GFR), urea, uric acid (UA),

hemoglobin (Hb), alanine aminotransferase (ALT), aspartate aminotransferase (AST), platelet count (PLT), and creatinine levels. According to the "Chinese Guidelines for Blood Lipid Management (2023)" [11], dyslipidemia was defined as TC $ $5.2 mmol/L, LDL-C $ $3.4 mmol/L, HDL-C $ $1.0 mmol/L, or TG $ $1.7 mmol/L.

1.2.3 cfPWV Detection This study used the Sphygmocor XCEL device. After participants rested in supine position for 10 minutes, the strongest pulsation points of the right carotid and femoral arteries were located for each participant [2] to measure cfPWV. Participants were not allowed to talk or sleep during measurement. A tape measure was used to measure the distance (m) between the most prominent points of carotid and femoral pulsations as the actual distance, which was entered into the analysis system. The distance between carotid and femoral arteries = actual distance (m) × 0.8 to correct measurement error [2]. After collecting 10 stable waveforms, the system calculated cfPWV as cfPWV (m/s) = L$×$0.8/Δt, where L is the distance between carotid and femoral arteries (m) and Δt is pulse wave transit time (s) [12], using the average of two measurements. If the difference between two cfPWV calculations exceeded 0.5 m/s, a third measurement was performed.

1.2.4 Participant Grouping According to European expert consensus [2], this study used 10 m/s as the cfPWV cutoff value to divide participants into no aortic sclerosis risk (n=503) and aortic sclerosis risk (n=240) groups. The modeling group comprised 703 members, with 200 having aortic sclerosis risk, while the validation group comprised 175 members, with 40 having aortic sclerosis risk.

This study followed the Declaration of Helsinki and was approved by the Science and Technology Ethics Committee of Hefei Institutes of Physical Science, Chinese Academy of Sciences (YXLL-2023-46). All participants provided informed consent.

Statistical Methods

Data analysis was performed using R4.1.0 and SPSS 26.0 statistical software. Normally distributed measurement data were expressed as ($\bar{x}\pm s$) and compared between groups using independent samples t-test; non-normally distributed measurement data were expressed as M(P25, P75) and compared using Mann-Whitney U test; count data were expressed as [cases (%)] and compared using ^{2} test. Multifactorial logistic regression analysis was used to screen variables. The R 3.6.1 software package combined with rms package was used to establish a nomogram assessment model. ROC curves were plotted, and model discrimination and calibration were evaluated using AUC and Hosmer-Lemeshow test. The Delong test was used to compare AUCs among models, decision curve analysis (DCA) was used to assess clinical utility, and bootstrap resampling with 1,000

iterations was used for internal validation. P<0.05 was considered statistically significant.

Results

Comparison of Baseline Clinical Data in the Modeling Group

The modeling group included 703 participants (349 males, 354 females) with a median age of 51 (30, 61) years, ranging from 18 to 91 years. Participants with aortic sclerosis risk showed significantly higher age, BMI, SBP, DBP, MAP, urea, FBG, LDL-C, TG, TC, ALT, AST, Hb, and higher proportions of alcohol consumption, dyslipidemia, and diabetes compared to those without risk (P<0.05). GFR and PLT were significantly lower in the aortic sclerosis risk group (P<0.05). No significant differences were found between groups in gender, heart rate, creatinine, UA, HDL-C, or smoking proportion (P>0.05) .

Univariate and Multivariate Logistic Regression Analysis of Aortic Sclerosis Influencing Factors

Univariate logistic regression analysis was performed with aortic sclerosis occurrence (no=0, yes=1) as the dependent variable and gender (female=0, male=1), dyslipidemia (no=0, yes=1), age, MAP, BMI, AST, GFR, UA, FBG, TG, TC, and Hb (all assigned as actual measured values) as independent variables. Results showed that gender, age, MAP, BMI, AST, GFR, UA, FBG, TG, TC, Hb, and dyslipidemia were influencing factors for aortic sclerosis (P<0.05). Significant results from univariate analysis were further included in multivariate logistic regression analysis (assignments same as above). Results showed that age (OR=1.112, 95%CI=1.082-1.143), MAP (OR=1.146, 95%CI=1.107-1.188), Hb (OR=1.026, 95%CI=1.004-1.049), and FBG (OR=1.353, 95%CI=1.076-1.701) were independent risk factors for aortic sclerosis (P<0.05) .

Performance Evaluation of Aortic Sclerosis Prediction Models

Predictive Model I was constructed using indicators with statistically significant differences in multivariate logistic regression analysis (age, MAP, Hb, FBG). Models II, III, and IV were constructed by additionally including smoking, gender, and dyslipidemia, respectively. ROC curves for Models I-IV showed AUCs of 0.941 (95%CI=0.923-0.964, P<0.05), 0.941 (95%CI=0.922-0.962, P<0.05), 0.941 (95%CI=0.922-0.963, P<0.05), and 0.939 (95%CI=0.919-0.962, P<0.05), respectively. Delong test results showed no statistically significant differences in AUCs among Models I, II, III, and IV (P>0.05) [Figure 1: see original paper].

Construction of the Nomogram Model

Based on multivariate logistic regression analysis results, a nomogram model was constructed using age, heart rate, FBG, and Hb as predictive factors [Figure 2: see original paper]. The total score was obtained by adding corresponding

scores of predictive factors, with the corresponding probability representing the likelihood of aortic sclerosis occurrence.

Internal and External Validation of the Model

Internal Validation: Bootstrap method was used for internal validation. After 1,000 resampling iterations of the modeling group, the C-index was 0.939, indicating good model discrimination with 86.8% accuracy. The Hosmer-Lemeshow test result was ^{2}=14.500 (P=0.070), showing good agreement between the prediction model curve and reference line, suggesting good calibration. The ROC curve showed an AUC of 0.941 (95%CI=0.920-0.962), sensitivity of 0.832, specificity of 0.917, and Youden index of 0.267 [Figure 3: see original paper]A.

External Validation: In the validation group, the C-index was 0.922, and the calibration curve showed good agreement between actual and ideal curves. The AUC was 0.961 (95%CI=0.914-1.000), sensitivity 0.872, specificity 0.964, and prediction accuracy 93.9%. The Hosmer-Lemeshow test was ^{2}=1.547 (P=0.992) [Figure 3: see original paper]B.

In the DCA curve, Line A assumed intervention for all participants with aortic sclerosis risk, showing negative net benefit with a negative slope; Line B assumed no intervention, with net benefit of 0. Using the early atherosclerosis screening model could provide clinical benefit to participants [Figure 4: see original paper].

Discussion

Study Results and Significance

Through comprehensive analysis of data from 703 participants in the modeling group, this study revealed significant associations between aortic sclerosis and multiple physiological indicators, providing important scientific evidence for early identification and prevention of cardiovascular disease. Results showed that the aortic sclerosis group had significantly higher age, BMI, heart rate, SBP, DBP, MAP, urea, FBG, TG, TC, AST, PLT, and proportions of alcohol consumption, dyslipidemia, and diabetes, while GFR levels were significantly lower than the normal group. These findings not only deepen understanding of aortic sclerosis pathological mechanisms but also provide new biomarkers for clinical diagnosis of aortic sclerosis. Furthermore, regression analysis results indicated that age, MAP, Hb, and FBG were independent predictors of aortic sclerosis. Based on these risk factors, the constructed early aortic sclerosis risk screening model can accurately identify individuals with early vascular dysfunction, offering a simple and efficient assessment tool for cardiovascular disease prevention and management with promising clinical applications.

Analysis of Atherosclerosis Risk Factors

Logistic regression analysis revealed that increased age and elevated MAP were independent risk factors for aortic sclerosis. Age showed positive correlation with aortic sclerosis risk, as aging causes gradual loss of vascular wall elasticity, intimal changes, and lipid plaque accumulation [13], progressively increasing individual aortic sclerosis risk. Hypertension also plays a critical role in aortic sclerosis pathogenesis by increasing vascular wall pressure, causing intimal damage, increasing arterial wall permeability to lipoproteins, and accelerating cholesterol plaque formation [14]. Current hypertension definitions are based on SBP and DBP levels, though research suggests [15] that long-term stroke risk in Asians should be assessed using both SBP and DBP or through MAP. Liu et al. [16] found that baseline MAP and MAP elevation during 10-year follow-up were important factors affecting atherosclerosis progression in non-hypertensive populations. Benetos et al. [17] found that higher MAP correlated with lower arterial distensibility ($r=-0.36$, $P<0.01$).

This study found that elevated Hb was an independent risk factor for aortic sclerosis, consistent with findings from Zhang et al. [18] and Liang et al. [19]. Hb primarily affects peripheral vascular resistance by influencing blood viscosity and small arterial caliber [20]. Elevated Hb levels may increase pulse wave velocity through several mechanisms: (1) elevated Hb correlates with increased blood pressure, which accelerates atherosclerosis; (2) Hb can cause insulin resistance, which is associated with arterial stiffness [21]; (3) heme oxygenase-1 (HO-1) is a rate-limiting enzyme for hemoglobin degradation with vasodilatory effects. Excessive free Hb in blood causes oxidative stress, activating HO-1 degradation. Reduced HO-1 cannot regulate vascular endothelial growth factor to alleviate oxidative stress and inflammation in hypertension [22-23].

FBG is an important risk factor for aortic sclerosis and an inexpensive, convenient method for glucose metabolism measurement. Hyperglycemia is closely associated with the presence and severity of coronary artery disease. Research shows hyperglycemia induces excessive mitochondrial reactive oxygen species production in cardiovascular cells, promoting atherosclerosis through multiple pathways [24]. Additionally, hyperglycemia may accelerate atherosclerosis by inducing endothelial dysfunction, reducing nitric oxide bioavailability, promoting vasoconstriction, creating procoagulant states, and enhancing nuclear factor- B expression [25]. A 5-year prospective study of Chinese community populations found that elevated FBG was an independent influencing factor for increased cfPWV [26], consistent with our findings.

Smoking and dyslipidemia are widely recognized cardiovascular disease risk factors. Nicotine in cigarettes activates NOD-like receptor thermal protein domain associated protein 3 inflammasomes through reactive oxygen species production, causing endothelial cell pyroptosis and adipose tissue abnormalities, thereby accelerating atherosclerosis progression [27-28]. Dyslipidemia refers to elevated plasma cholesterol and/or TG levels or reduced HDL-C levels, causing

lipid deposition in vascular intima and atherosclerotic plaque formation [29]. While smoking and dyslipidemia appear to cause arterial stiffness, Cecelja et al. [30] conducted a meta-analysis of 65 studies showing only individual studies reported significant independent correlations between smoking, TC, LDL-C, HDL-C, and cfPWV. Our study also found that after adjusting for other potential confounders, smoking and dyslipidemia were not independent risk factors for aortic sclerosis, consistent with Vlachopoulos et al. [31]. This may be because cfPWV evaluates early vascular function, and these risk factors may have minimal impact on arterial wall stiffness in early atherosclerosis stages, though they may increase arterial stiffness with disease progression, particularly when calcified plaques appear.

Establishment of Early Atherosclerosis Risk Screening Model

Nomogram modeling is a powerful and highly interpretable statistical tool for binary classification problems that can predict the probability of clinical events [32]. During model construction, logistic regression analysis identified significant factors for aortic sclerosis risk, including age, MAP, Hb, and FBG. By assigning scores to these factors and calculating total scores, corresponding risk prediction values were obtained. The validated model can effectively screen populations with early vascular dysfunction. External validation showed a C-index of 0.922 and AUC>0.9, indicating good discrimination [33]. The calibration curve showed good agreement between curves, and Hosmer-Lemeshow test indicated good consistency between predicted and observed results. Additionally, external validation accuracy of 93.9% further demonstrated high accuracy between predicted and observed results. In model performance evaluation, when considering only age, MAP, Hb, and FBG, the model showed superior AUC, specificity, and accuracy compared to models incorporating dyslipidemia, smoking, and gender, which were therefore not included in the final model.

Conclusion

This study successfully constructed an early aortic sclerosis risk screening model using age, MAP, Hb, and FBG as predictive factors. The model demonstrated high efficiency and accuracy in identifying populations with early vascular abnormalities, providing a convenient and efficient screening tool for community residents. However, this study employed a cross-sectional design, preventing inference of causal relationships or temporal sequences between variables. Additionally, the study did not consider other potential risk factors such as genetic predisposition, environmental exposure, or personal lifestyle, which may significantly influence aortic sclerosis development. Given that aortic sclerosis is a dynamic pathological process, future studies should incorporate long-term follow-up and multidimensional factors including genetics, environment, and lifestyle for more comprehensive risk assessment.

Author Contributions: ZHOU Zhensen contributed to study design, data analysis, and manuscript writing; ZHOU Zhensen, HUANG Yan, and ZHANG

Xiaoyu were responsible for data collection; CHENG Siwei was responsible for data verification and entry; ZHANG Xiaoyu, SUN Ting, YANG Xianjun, and XIE Hui were responsible for manuscript review; MA Zuchang was responsible for final version revision and overall responsibility for the manuscript.

Conflict of Interest: The authors declare no conflict of interest.

References

[1] Chinese Cardiovascular Health and Disease Report Writing Group. Summary of the China Cardiovascular Health and Disease Report 2022 [J]. Chinese Circulation Journal, 2023, 38(6): 583-612. DOI:10.3969/j.issn.1000-3614.2023.06.001.

[2] VAN BORTEL L M, LAURENT S, BOUTOUYRIE P, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity [J]. J Hypertens, 2012, 30(3): 445-448. DOI:10.1097/HJH.0b013e32834fa8b0.

[3] BENETOS A, WAEBER B, IZZO J, et al. Influence of age, risk factors, and cardiovascular and renal disease on arterial stiffness: clinical applications [J]. Am J Hypertens, 2002, 15(12): 1101-1108. DOI:10.1016/s0895-7061(02)03029-7.

[4] LIANG Y L, TEEDE H, KOTSOPOULOS D, et al. Non-invasive measurements of arterial structure and function: repeatability, interrelationships and trial sample size [J]. Clin Sci, 1998, 95(6): 669-679. DOI:10.1042/cs0950669.

[5] LAURENT S, COCKCROFT J, VAN BORTEL L, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications [J]. Eur Heart J, 2006, 27(21): 2588-2605. DOI:10.1093/eurheartj/ehl254.

[6] KIM E D, BALLEW S H, TANAKA H, et al. Short-term prognostic impact of arterial stiffness in older adults without prevalent cardiovascular disease [J]. Hypertension, 2019, 74(6): 1373-1382. DOI:10.1161/HYPERTENSIONAHA.119.13496.

[7] COURVOISIER D S, COMBESCURE C, AGORITSAS T, et al. Performance of logistic regression modeling: beyond the number of events per variable, the role of data structure [J]. J Clin Epidemiol, 2011, 64(9): 993-1000. DOI:10.1016/j.jclinepi.2010.11.012.

[8] TAKUMA Y, SHOTA I, MIYATAKE H, et al. Nomograms to predict the disease-free survival and overall survival after radiofrequency ablation for hepatocellular carcinoma [J]. J Hepatol, 2012, 56(6): 1369-1375. DOI:10.1016/j.jhep.2012.01.011.

[9] MCCLAVE A K, MCKNIGHT-EILY L R, DAVIS S P, et al. Smoking characteristics of adults with selected lifetime mental illnesses: results from the 2007 National Health Interview Survey [J]. Am J Public Health, 2010, 100(12): 2464-2472. DOI:10.2105/AJPH.2009.188136.

[10] XU Wenchao, QIN Yu, SU Jian, et al. Interaction between alcohol consumption and obesity on diabetes prevalence among community residents aged $ $35 years in Jiangsu Province [J]. Chinese Journal of Public Health, 2020, 36(12): 1776-1779. DOI:10.11847/zgggws1123881.

[11] WANG Zengwu, LIU Jing, LI Jianjun, et al. Chinese Guidelines for Blood Lipid Management (2023) [J]. Chinese Circulation Journal, 2023, 38(3): 237-271.

[12] REFERENCE VALUES FOR ARTERIAL STIFFNESS' COLLABORATION. Determinants of pulse wave velocity in healthy people and in the presence of cardiovascular risk factors: 'establishing normal and reference values' [J]. Eur Heart J, 2010, 31(19): 2338-2350. DOI:10.1093/eurheartj/ehq165.

[13] CECELJA M, CHOWIENCZYK P. Role of arterial stiffness in cardiovascular disease [J]. JRSM Cardiovasc Dis, 2012, 1(4): cvd.2012.012016. DOI:10.1258/cvd.2012.012016.

[14] RAFIEIAN-KOPAEI M, SETORKI M, DOUDI M, et al. Atherosclerosis: process, indicators, risk factors and new hopes [J]. Int J Prev Med, 2014, 5(8): 927-946.

[15] MIURA K, SOYAMA Y, MORIKAWA Y, et al. Comparison of four blood pressure indexes for the prediction of 10-year stroke risk in middle-aged and older Asians [J]. Hypertension, 2004, 44(5): 715-720. DOI:10.1161/01.HYP.0000145108.23948.7b.

[16] LIU Qian, HAN Xu, MA Yihan, et al. Effect of mean arterial pressure on atherosclerosis progression in non-hypertensive population [J]. Chinese Journal of Hypertension, 2021, 29(8): 733-739. DOI:10.16439/j.issn.1673-7245.2021.08.008.

[17] BENETOS A, LAURENT S, HOEKS A P, et al. Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries [J]. Arterioscler Thromb, 1993, 13(1): 90-97. DOI:10.1161/01.atv.13.1.90.

[18] ZHANG Z Z, WANG P, KONG X L, et al. Association of hemoglobin with arterial stiffness evaluated by carotid-femoral pulse wave velocity among Chinese adults [J]. Chronic Dis Transl Med, 2019, 5(2): 122-128. DOI:10.1016/j.cdtm.2018.06.001.

[19] LIANG J, ZHOU N, TENG F, et al. Hemoglobin A1c levels and aortic arterial stiffness: the Cardiometabolic Risk in Chinese (CRC) study [J]. PLoS One, 2012, 7(8): e38485. DOI:10.1371/journal.pone.0038485.

[20] FOSSUM E, HØIEGGEN A, MOAN A, et al. Whole blood viscosity, blood pressure and cardiovascular risk factors in healthy blood donors [J]. Blood Press, 1997, 6(3): 161-165. DOI:10.3109/08037059709061932.

[21] BARBIERI M, RAGNO E, BENVENUTI E, et al. New aspects of the insulin resistance syndrome: impact on haematological parameters [J]. Diabetolo-

gia, 2001, 44(10): 1232-1237. DOI:10.1007/s001250100634.

[22] CHEN H M, HUA Q, HOU H X. Association of hemoglobin with ambulatory arterial stiffness index in untreated essential hypertensive patients without anemia [J]. Intern Med, 2011, 50(22): 2759-2765. DOI:10.2169/internalmedicine.50.5832.

[23] ANGERMAYR B, MEJIAS M, GRACIA-SANCHO J, et al. Heme oxygenase attenuates oxidative stress and inflammation, and increases VEGF expression in portal hypertensive rats [J]. J Hepatol, 2006, 44(6): 1033-1039. DOI:10.1016/j.jhep.2005.09.021.

[24] SHAH M S, BROWNLEE M. Molecular and cellular mechanisms of cardiovascular disorders in diabetes [J]. Circ Res, 2016, 118(11): 1808-1829. DOI:10.1161/CIRCRESAHA.116.306923.

[25] KING R J, GRANT P J. Diabetes and cardiovascular disease: pathophysiology of a life-threatening epidemic [J]. Herz, 2016, 41(3): 184-192. DOI:10.1007/s00059-016-4414-8.

[26] FU S H, CHEN W J, LUO L M, et al. Roles of fasting and postprandial blood glucose in the effect of type 2 diabetes on central arterial stiffness: a 5-year prospective community-based analysis [J]. Diabetol Metab Syndr, 2017, 9: 33. DOI:10.1186/s13098-017-0231-3.

[27] WU X X, ZHANG H Y, QI W, et al. Nicotine promotes atherosclerosis via ROS-NLRP3-mediated endothelial cell pyroptosis [J]. Cell Death Dis, 2018, 9(2): 171. DOI:10.1038/s41419-017-0257-3.

[28] WANG Z Y, WANG D, WANG Y. Cigarette smoking and adipose tissue: the emerging role in progression of atherosclerosis [J]. J Immunol Res, 2017, 2017: 3102737. DOI:10.1155/2017/3102737.

[29] LI Jianjun. Modern concepts of the relationship between dyslipidemia and atherosclerosis [J]. Chinese Circulation Journal, 2022, 37(3): 212-214. DOI:10.3969/j.issn.1000-3614.2022.03.002.

[30] CECELJA M, CHOWIENCZYK P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review [J]. Hypertension, 2009, 54(6): 1328-1336. DOI:10.1161/HYPERTENSIONAHA.109.137653.

[31] VLACHOPOULOS C, XAPLANTERIS P, ABOYANS V, et al. The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Group on peripheral circulation: endorsed by the Association for Research into Arterial Structure and Physiology (ARTERY) Society [J]. Atherosclerosis, 2015, 241(2): 507-532. DOI:10.1016/j.atherosclerosis.2015.05.007.

[32] TAO Liyuan, ZHANG Hua, ZHAO Yiming. Key points and application of nomogram production [J]. Chinese Journal of Pediatrics, 2017, 55(5): 323.

DOI:10.3760/cma.j.issn.0578-1310.2017.05.002.

[33] WANG Junfeng, ZHANG Zhongheng, ZHOU Zhirui, et al. Clinical prediction model: model validation [J]. Chinese Journal of Evidence-Based Cardiovascular Medicine, 2019, 11(2): 141-144. DOI:10.3969/j.issn.1674-4055.2019.02.04.

(Received: February 7, 2024; Revised: June 20, 2024)

Note: Figure translations are in progress. See original paper for figures.