Development of a Prediction Model for Atherosclerotic Cardiovascular Disease in the Elderly Based on Traditional Chinese Medicine Constitution: A Postprint

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Abstract

Background The most effective prevention strategy for atherosclerotic cardiovascular disease (ASCVD) is implementing primary care management, with risk assessment as its core measure. Existing ASCVD prediction models for the elderly cannot effectively guide TCM primary care management. Therefore, it is necessary to integrate TCM elements into the development of prediction models to guide the integrated Chinese and Western medicine primary care management of ASCVD.

Objective To construct and validate an ASCVD prediction model for the elderly based on TCM constitution.

Methods A total of 1,418 elderly individuals who underwent health examinations in 2017 at Huayuan Street Community Health Service Center, Chentangzhuang Street Community Health Service Center, Xiangyang Road Street Community Health Service Center, and Daqiuzhuang Town Central Hospital were enrolled as study subjects. General data of the subjects were collected, and constitution identification was performed. The incidence of ASCVD (clinical outcome) was followed up from 2017 to 2022. The subjects' data were randomly split into training and validation sets at an 8 2 ratio. In the training set, a conventional ASCVD prediction model for the elderly (Model 1) and a conventional + constitution ASCVD prediction model for the elderly (Model 2) were constructed using forward stepwise selection. A nomogram of the ASCVD prediction model for the elderly based on TCM constitution was plotted. Calibration curves were plotted and Hosmer-Lemeshow goodness-of-fit test was performed to evaluate model calibration. Receiver operating characteristic curves were plotted and area under the curve (AUC) was calculated to evaluate model discrimination. AUC, net reclassification improvement (NRI), integrated discrimination

improvement (IDI), and decision curve analysis (DCA) were used to compare Model 2 with Model 1 and assess improvement efficacy.

Results There was no statistically significant difference in general data between the training and validation sets (P>0.05). Multivariate analysis results showed that Model 1 included seven predictive variables: sex, age, waist circumference, systolic blood pressure, triglycerides, BMI, and systolic blood pressure × history of hypertension medication; Model 2 included eight predictive variables: sex, age, waist circumference, systolic blood pressure, triglycerides, BMI, systolic blood pressure × history of hypertension medication, and constitution type. The Hosmer-Lemeshow goodness-of-fit test indicated good fit for Model 2. Delong' s test results showed that the AUC of Model 2 was higher than that of Model 1 (Z=2.741, P=0.006), NRI=0.511 [95%CI= (0.359~0.663), P<0.001] , IDI=0.038 [95%CI=(0.024~0.051),P<0.001], suggesting that adding constitution predictive variables could improve model prediction accuracy. Clinical utility comparison results showed that the net benefit of using Model 2 to predict severe ASCVD events in the elderly was superior to Model 1 at threshold probabilities of 5~74%.

Conclusion This study constructed an ASCVD prediction model for the elderly comprising eight predictive variables: sex, age, waist circumference, systolic blood pressure, total cholesterol, body mass index, systolic blood pressure × history of hypertension medication, and constitution type. After validation, the model demonstrated good discrimination and calibration, outperforming conventional prediction models, and can be applied to individualized risk assessment of ASCVD in the elderly and guide integrated Chinese and Western medicine primary care management of ASCVD.

Full Text

Development and Validation of an Atherosclerotic Cardiovascular Disease Prediction Model for the Elderly Based on Traditional Chinese Medicine Constitution

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Abstract

Background: The most effective prevention strategy for atherosclerotic cardiovascular disease (ASCVD) is primary management, with risk assessment as

its core component. Existing ASCVD prediction models for elderly populations cannot adequately guide Traditional Chinese Medicine (TCM)-based primary management. Therefore, integrating TCM elements into prediction model development is necessary to guide integrated TCM-Western medicine primary management of ASCVD.

Objective: To construct and validate an ASCVD prediction model for the elderly based on TCM constitution.

Methods: A total of 1,418 elderly individuals who underwent health examinations in 2017 at Huayuan Street Community Health Service Center, Chentangzhuang Street Community Health Service Center, Xiangyang Road Street Community Health Service Center, and Daqiuzhuang Town Central Health Center were enrolled as study subjects. General demographic and clinical data were collected, and TCM constitution identification was performed. ASCVD incidence (clinical outcomes) was followed up from 2017 to 2022. The dataset was randomly split into a training set and validation set at an 8:2 ratio. Using forward stepwise selection, a conventional ASCVD prediction model for the elderly (Model 1) and a conventional plus constitution prediction model (Model 2) were constructed in the training set. A nomogram for the TCM constitution-based ASCVD prediction model was developed. Model calibration was assessed using calibration curves and the Hosmer-Lemeshow goodness-of-fit test. Model discrimination was evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC). Model 2 was compared against Model 1 using AUC, Net Reclassification Index (NRI), Integrated Discrimination Improvement (IDI), and Decision Curve Analysis (DCA) to evaluate improvement in predictive performance.

Results: No significant differences were observed in baseline characteristics between the training and validation sets ($P>0.05$). Multivariate analysis revealed that Model 1 included seven predictors: gender, age, waist circumference, systolic blood pressure, triglycerides, BMI, and the interaction term systolic blood pressure × hypertension medication history. Model 2 included eight predictors: the aforementioned variables plus constitution type. The Hosmer-Lemeshow test indicated good fit for Model 2. Delong' s test showed that Model 2' s AUC was significantly higher than Model 1' s ($Z=2.741$, $P=0.006$). The NRI was 0.511 [95%CI=(0.359-0.663), $P<0.001$] and IDI was 0.038 [95%CI=(0.024-0.051), $P<0.001$], demonstrating that adding constitution as a predictor improved model accuracy. Clinical utility comparison showed that Model 2 provided better net benefit than Model 1 for predicting severe ASCVD events in the elderly across threshold probabilities of 5% to 74%.

Conclusion: This study developed an ASCVD prediction model for the elderly comprising eight predictors: gender, age, waist circumference, systolic blood pressure, total cholesterol, body mass index, systolic blood pressure × hypertension medication history, and constitution type. The model demonstrated good discrimination and calibration, outperforming conventional prediction models. It can be applied to individualized risk assessment for ASCVD in the elderly

and guide integrated TCM-Western medicine primary management of ASCVD.

Keywords: Coronary disease; Atherosclerosis; Constitutional type (TCM); Aged; Risk prediction model

1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) represents the foremost threat to public health in China [1-2]. Currently, the most effective prevention strategy for ASCVD is implementing primary management, with risk assessment as its core measure. Based on assessment results, risk stratification and individualized prevention and treatment plans can be implemented [3]. Clinical prediction models (CPM) serve as crucial tools for comprehensive risk assessment and personalized health management. By analyzing the combined effects of multiple variables (such as patient demographics, laboratory indicators, and treatment measures), CPMs can accurately predict disease risk in target populations [4]. In addition to facilitating screening of high-risk groups, CPMs analyze risk factors affecting disease occurrence and prognosis along with their effect sizes, providing healthcare professionals and patients with more objective and intuitive information for decision-making [5]. Applying well-performing CPMs in clinical practice can improve disease prevention and treatment levels while enhancing cost-effectiveness.

TCM constitution possesses characteristics of holism, objectivity, differentiation, and modifiability. The relationship between constitution and disease provides new perspectives and evidence for disease prevention and treatment. Numerous studies have demonstrated that TCM constitution is closely associated with ASCVD onset and prognosis [6-8], suggesting that high-risk groups for ASCVD can be identified from a constitutional perspective to facilitate precise prediction of disease occurrence, progression, and prognosis. Moreover, constitution is modifiable—it exhibits both relative stability and dynamic variability. Throughout an individual' s life cycle, constitution can change under the influence of various internal and external environmental factors [9]. Research has shown that comprehensive constitution-based interventions in ASCVD management can significantly improve risk factor profiles and reduce event incidence [10-11].

Integrating TCM constitution into CPMs can provide targeted individualized constitution-based intervention guidance, help standardize primary TCM health management, and thereby enhance ASCVD primary management levels. However, current ASCVD prediction models for the elderly lack TCM constitution elements. Therefore, this study aims to develop a TCM-characteristic ASCVD prediction model for the elderly by incorporating TCM constitution elements based on the China-PAR model [13] recommended in the *Guidelines for Comprehensive Management of Cardiovascular Disease in Primary Care 2020* [12] and combined with primary care clinical practice. This model is expected to

provide an excellent risk assessment tool for ASCVD primary management and promote integrated TCM-Western medicine primary management of ASCVD.

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2. Methods

2.1 Study Subjects

This retrospective cohort study enrolled elderly individuals who underwent health examinations in 2017 at four community health centers in Tianjin: Huayuan Street, Chentangzhuang Street, Xiangyang Road Street, and Daqiuzhuang Town Central Health Center. After excluding individuals with missing constitution identification data, a simple random sampling method was used to select 30% of eligible individuals from each primary care institution as study subjects. Inclusion criteria were: (1) age $\geq$ 65 years; (2) permanent Tianjin residents (residence duration $\geq$ 10 years) willing to participate in follow-up surveys. Exclusion criteria were: (1) existing ASCVD at enrollment; (2) severely missing data for key study indicators. Ultimately, 1,418 subjects were included. The enrollment flowchart is shown in [Figure 1: see original paper].

2.2 Data Collection

2.2.1 General Data Collection: General information collected included age, gender, waist circumference, BMI, systolic blood pressure, hypertension medication use, diabetes history, smoking history (defined as $ $1 cigarette/day for $ $6 months), ASCVD family history, total cholesterol (TC), and triglycerides (TG). Laboratory test results including serum TC and TG were also collected.

2.2.2 Constitution Identification: The "TCM Constitution Identification Questionnaire" from the Tianjin Community Health Service System was administered to identify subjects' constitution types. This questionnaire references the *Classification and Determination of TCM Constitution (Elderly Version)* standard issued by the National Administration of Traditional Chinese Medicine, classifying constitution into nine types: balanced, qi-deficient, yang-deficient, yin-deficient, phlegm-dampness, damp-heat, blood-stasis, qi-stagnation, and special diathesis. For individuals with mixed constitution types, the constitution type with the highest score was used for analysis.

2.3 Follow-up Data Collection

A combination of telephone follow-up and community health service system queries was employed. Tianjin' s family doctor teams conduct comprehensive health assessments for enrolled residents annually and update their electronic health records. Our research team performed telephone follow-up from February to November 2022, focusing on ASCVD occurrence (clinical outcomes). Self-reported information was cross-verified with residents' electronic health records, and verified information was entered into our research database by investigators.

Clinical outcome diagnosis followed the China-PAR study criteria: ASCVD was defined as non-fatal acute myocardial infarction, coronary heart disease death, and fatal or non-fatal stroke [13]. Acute myocardial infarction was defined by changes in biochemical markers of myocardial necrosis accompanied by ischemic symptoms, pathological Q waves, ST-segment elevation or depression, or coronary intervention. Coronary heart disease death included all fatal events caused by myocardial infarction or other coronary artery diseases. Stroke included ischemic stroke, hemorrhagic stroke (including subarachnoid hemorrhage), and unclassified stroke, but excluded minor stroke (TIA) and cerebrovascular disease from other causes. If an individual experienced multiple events (myocardial infarction, coronary death, or stroke) during follow-up, only one ASCVD event was recorded.

2.4 Candidate Predictor Variables

Based on the China-PAR model [13] and clinical practice, conventional predictors were selected and TCM constitution type was added as a new candidate predictor. Conventional predictors included: age, gender, waist circumference, BMI, systolic blood pressure, hypertension medication use, diabetes history, smoking history, ASCVD family history, TC, and TG (11 variables total). Constitution type was included as one predictor variable encompassing nine constitution categories.

2.5 Sample Size Calculation

The criterion of $ 10 $ $ events per variable (EPV) has been widely adopted to minimize over fitting, meaning the numb $ where a represents the number of independent variables and b represents disease incidence. The final training set included 1,127 eligible subjects, and the validation set included 291 subjects.

2.6 Statistical Methods

SPSS 26.0 was used for outlier and missing value processing, dataset splitting (random 8:2 ratio for training and validation sets), and statistical analysis. Categorical variables were expressed as frequencies and compared using ^{2} tests. In the training set, univariate logistic regression analysis ($P<0.1$) was used for initial predictor screening, with significant variables entered into multivariate analysis. Forward stepwise selection ($P<0.05$) was used to construct the conventional ASCVD prediction model (Model 1) and the conventional plus constitution prediction model (Model 2) for the elderly. The R package "rms" was used to develop the nomogram for the TCM constitution-based ASCVD prediction model. Model calibration was assessed using calibration curves and the Hosmer-Lemeshow goodness-of-fit test. Model discrimination was evaluated using ROC curves and AUC. Model 2 was compared against Model 1 using AUC, NRI, IDI, and DCA to assess improvement in predictive performance. $P<0.05$ was considered statistically significant. AUC differences were analyzed using MedCalc (V20.0.22.0), while NRI and IDI were analyzed using R (V4.2.2).

3. Results

3.1 Baseline Characteristics

A total of 1,418 subjects were included, comprising 777 females (54.80%) and 641 males (45.20%). No statistically significant differences were found between the training and validation sets in terms of gender, age, smoking history, ASCVD family history, diabetes history, systolic blood pressure, hypertension medication use, waist circumference, BMI, TC, TG, constitution type, or ASCVD events (P>0.05), as shown in .

3.2 Predictor Selection Through Univariate and Multivariate Logistic Regression

Using ASCVD event occurrence (yes=1, no=0) as the dependent variable and gender, age, smoking history, ASCVD family history, diabetes history, systolic blood pressure, hypertension medication use, waist circumference, BMI, TC, TG, and constitution type as independent variables, univariate logistic regression analysis identified gender, age, ASCVD family history, waist circumference, systolic blood pressure, TC, TG, BMI, constitution type, and the interaction term systolic blood pressure × hypertension medication history as candidates for multivariate analysis (P<0.1), as presented in .

Multivariate analysis incorporating these variables revealed that Model 1 included seven predictors: gender, age, waist circumference, systolic blood pressure, TC, BMI, and systolic blood pressure × hypertension medication history. Model 2 included eight predictors: the aforementioned variables plus constitution type, as detailed in .

3.3 Nomogram Development and Model Evaluation

Variables selected through multivariate logistic regression were incorporated into a nomogram prediction model with ASCVD event occurrence as the outcome variable [Figure 2: see original paper]. The Hosmer-Lemeshow goodness-of-fit test indicated good calibration for Model 2 [training set (^{2}=7.602, df=8, P=0.473); validation set (^{2}=3.756, df=8, P=0.878)], and the nomogram demonstrated accurate prediction of ASCVD event probability , [Figure 4: see original paper].

ROC curves were plotted to assess Model 2' s discrimination. The AUC was 0.818 (95%CI=0.787-0.848) in the training set and 0.794 (95%CI=0.761-0.826) in the validation set, indicating good discriminative ability [Figure 4: see original paper]. Calibration curves for Model 2 are shown in [Figure 3: see original paper].

3.4 Comparison Between TCM Constitution-Based Model and Conventional Model

Likelihood ratio testing showed Model 2' s Nagelkerke R^2 exceeded Model 1' s (0.342 vs. 0.277), suggesting improved model fit after adding constitution predictors. Delong' s test demonstrated Model 2' s AUC was significantly higher than Model 1' s (Z=2.741, P=0.006). The NRI was 0.511 [95%CI=(0.359-0.663), P<0.001] and IDI was 0.038 [95%CI=(0.024-0.051), P<0.001], confirming that adding constitution predictors enhanced prediction accuracy. Clinical decision curve analysis indicated Model 2 provided superior net benefit for predicting severe ASCVD events in the elderly across threshold probabilities of 5% to 74% compared to Model 1 [Figure 5: see original paper].

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4. Discussion

Currently, the most effective ASCVD prevention strategy is primary management centered on risk assessment, which enables risk stratification and individualized prevention and treatment plans [3]. Clinical prediction models are essential tools for comprehensive risk assessment and personalized health management. TCM constitution represents a modifiable risk factor for ASCVD and serves as an excellent predictor for CPM development. This study integrated TCM constitution elements into CPM construction, developing an integrated TCM-Western medicine ASCVD prediction model for the elderly. Evaluation of discrimination and calibration demonstrated that the model enables individualized and precise prediction of ASCVD onset in the elderly, with superior performance compared to conventional models, and can guide integrated TCM-Western medicine primary management of ASCVD.

CPMs primarily include diagnostic prediction models (estimating current disease probability) and prognostic prediction models (estimating future disease or outcome probability). CPM development involves identifying data sources, selecting predictors, establishing modeling strategies, and evaluating model performance [5]. Characteristics, predictors, and clinical outcomes recorded in residents' electronic health records exhibit broader data distributions that align with clinical practice [15], and CPMs developed from such data tend to have better generalizability [16]. China' s electronic health records have been implemented for nearly 20 years with continuous updates during follow-up, providing long follow-up duration and sufficient sample sizes that offer ideal high-quality data for prediction model development. Since our CPM is intended for elderly ASCVD primary management, we selected residents' electronic health records from Tianjin' s community health service system as our data source.

Predictor variables are fundamental components of CPMs and must possess practicality, clinical relevance, and appropriate accuracy [17]. Suitable predictors are essential for developing well-performing CPMs [4]. When selecting predictors, comprehensive literature review should first identify disease-related

factors, with risk factors commonly used as predictors [18]. Practical feasibility, accessibility, and testing costs must be considered to ensure measurement is simple, economical, stable, and reliable [19]. Statistical testing combined with clinical significance and expert discussion then determines final predictor inclusion. China' s ASCVD risk prediction research began gradually in the 1980s [20], and multiple assessment tools have been developed, among which the widely influential China-PAR model based on large-scale prospective Chinese cohorts [13] can predict 10-year and lifetime ASCVD risk and has been incorporated into the *Guidelines for Comprehensive Management of Cardiovascular Disease in Primary Care 2020* [12]. However, this model includes only conventional Western medicine predictors and cannot adequately guide TCM health management. Numerous studies have confirmed that TCM constitution types are closely associated with ASCVD onset and prognosis [21]. Therefore, we selected conventional predictors based on the China-PAR model and added TCM constitution type as a new candidate predictor.

No consensus exists regarding optimal CPM modeling methods. Traditional statistical models mainly include regression models, classification models, and neural network models [22]. Regression models (e.g., logistic regression, Cox regression) are most widely used in medicine, as exemplified by the U.S. Framingham model [23] and China' s China-PAR model [13]. Machine learning methods have recently gained attention, including classification models, neural networks, and methods requiring fewer assumptions [16], such as cardiovascular disease prediction models [24] and elderly stroke prediction models [25] developed in recent years. Generally, when candidate predictors are limited ($ 25)$and sample size is sufficient($20 times the number of candidate predictors), non-machine learning and machine learning approaches achieve comparable accuracy. However, machine learning algorithms may suffer from poor interpretability [16]. As research progresses, studies increasingly incorporate more predictors—for instance, omics research generates extremely complex data with numerous candidate predictors (>10,000), where machine learning models offer accuracy advantages but require larger sample sizes [16]. Since our study included fewer than 25 candidate predictors, we employed logistic regression modeling.

Prediction model performance must be quantitatively evaluated and validated, primarily assessing discrimination and calibration [26]. To determine whether added predictors improve model performance, incremental value must be evaluated using metrics such as likelihood ratio tests, AUC, and NRI [27]. For binary outcome models with nested structures (as in our study, where the new model adds only constitution type), likelihood ratio tests can evaluate model improvement and identify better-fitting models [28-29]. AUC is an overall discrimination measure that helps determine new predictors' utility and whether the new model offers better discrimination [30]. NRI is a risk reclassification metric that categorizes probabilities into clinically meaningful risk strata, showing the proportion of correctly reclassified individuals and whether the new model improves prediction accuracy [31]. Therefore, we evaluated model discrimination and validation

using ROC curves and AUC; assessed calibration using Hosmer-Lemeshow tests and calibration curves; and evaluated constitution predictors' incremental value using likelihood ratio tests, AUC comparison, and NRI calculation. Our model demonstrated good performance, with constitution predictors enhancing model performance.

This study has several limitations: (1) As a retrospective study using 2017 health examination data from electronic health records, missing data were addressed through baseline data verification and supplementation during final follow-up, which may introduce recall bias; (2) Model validation was based on internal data only, demonstrating reproducibility but not external generalizability; (3) Due to sample size constraints, sex-specific models were not developed. Future research should expand sample sizes, conduct prospective studies, obtain data from different temporal or spatial sources for external validation, and perform impact studies to evaluate the model' s effectiveness in integrated TCM-Western medicine ASCVD primary management.

In summary, we developed a TCM constitution-based ASCVD prediction model for the elderly that demonstrated good discrimination and calibration, outperforming conventional models. This model can be applied to individualized ASCVD risk assessment and risk stratification in the elderly, guiding integrated TCM-Western medicine primary management of ASCVD.

Author Contributions: GAO Ying was responsible for conceptualization and design, data collection and analysis, and manuscript drafting. XU Xinyi and LIU Yang contributed to data organization and manuscript revision. YANG Xiaokun supervised the overall project, revised the final manuscript, and provided oversight.

Conflict of Interest Statement: The authors declare no conflicts of interest.

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References

[1] GBD DISEASES AND INJURIES COLLABORATORS. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019[J]. Lancet, 2020, 396(10258): 1204-1222. DOI: 10.1016/S0140-6736(20)30925-9.

[2] XIANG Xianglong, WANG Qiqi, LI Junqi, et al. Trend analysis of cardiovascular and cerebrovascular disease mortality in China from 2009 to 2019[J]. Chinese Preventive Medicine Journal, 2021, 22(11): 811-818. DOI: 10.16506/j.1009-6639.2021.11.001.

[3] Chronic Disease Management Group, Chinese Society of General Practice, Chinese Medical Association. Expert consensus on the primary care pathway for

atherosclerotic cardiovascular disease in Chinese adults (draft)[J]. Chinese General Practice, 2017, 20(3): 251-261. DOI: 10.3969/j.issn.1007-9572.2017.03.001.

[4] RANSTAM J, COOK J A, COLLINS G S. Clinical prediction models[J]. Br J Surg, 2016, 103(13): 1886. DOI: 10.1002/bjs.10242.

[5] GU Hongqiu, ZHOU Zhirui, ZHANG Zhongheng, et al. Clinical prediction models: basic concepts, application scenarios, and research ideas[J]. Chinese Journal of Evidence-Based Cardiovascular Medicine, 2018, 10(12): 1454-1456, 1462. DOI: 10.3969/j.issn.1674-4055.2018.12.04.

[6] BAI Minghua, WANG Ji, ZHENG Yanfei, et al. Analysis of distribution characteristics of TCM constitution types in Chinese population based on 108,015 samples[J]. Journal of Beijing University of Traditional Chinese Medicine, 2020, 43(6): 498-507. DOI: 10.3969/j.issn.1006-2157.2020.06.010.

[7] XIE Qin, HE Huaqin. Investigation and analysis of cardiovascular disease risk factors in populations with different TCM constitutions[J]. Journal of Traditional Chinese Medicine Management, 2021, 29(5): 48-49. DOI: 10.16690/j.cnki.1007-9203.2021.05.020.

[8] WANG Sijia, ZHANG Zhe. Discussion on prevention and treatment strategies based on the correlation between coronary atherosclerotic heart disease and TCM constitution[J]. Journal of Practical Traditional Chinese Internal Medicine, 2022, 36(5): 70-72. DOI: 10.13729/j.issn.1671-7813.Z20211288.

[9] WANG Qi. Response and advantages of TCM constitution theory in major health issues[J]. Journal of Beijing University of Traditional Chinese Medicine, 2021, 44(3): 197-202. DOI: 10.3969/j.issn.1006-2157.2021.03.001.

[10] LIU Donggui, WANG Xiaolei, YANG Lihua, et al. Application value of comprehensive TCM constitution intervention in cardiovascular disease prevention among hyperuricemia patients[J]. China Modern Medicine, 2019, 26(22): 41-44. DOI: 10.3969/j.issn.1674-4721.2019.22.012.

[11] HUANG Juming. Clinical efficacy analysis of "constitution differentiation treatment" combined with chronic disease management in atherosclerosis intervention[D]. Guangzhou: Guangzhou University of Chinese Medicine, 2016.

[12] Beijing Hypertension Prevention and Treatment Association, Beijing Diabetes Prevention and Treatment Association, Beijing Chronic Disease Prevention and Health Education Research Association, et al. Guidelines for comprehensive management of cardiovascular disease in primary care 2020[J]. Chinese Journal of the Frontiers of Medical Science: Electronic Version, 2020, 12(8): 1-73. DOI: 10.12037/YXQY.2020.08-01.

[13] YANG X L, LI J X, HU D S, et al. Predicting the 10-year risks of atherosclerotic cardiovascular disease in Chinese population: the china-PAR project (prediction for ASCVD risk in China)[J]. Circulation, 2016, 134(19): 1430-1440. DOI: 10.1161/CIRCULATIONAHA.116.022367.

[14] RILEY R D, ENSOR J, SNELL K I E, et al. Calculating the sample size required for developing a clinical prediction model[J]. BMJ, 2020, 368: m441. DOI: 10.1136/bmj.m441.

[15] YANG Song, MA Longteng, ZHANG Jingjing. Implementation specifications for real-world studies in Chinese clinical medicine[J]. Medical Journal of Chinese People' s Liberation Army, 2018, 43(1): 1-6. DOI: 10.11855/j.issn.0577-7402.2018.01.01.

[16] STEYERBERG E W. Clinical prediction models: a practical approach to development, validation, and updating[M]. Switzerland: Springer Nature, 2019: 37-57.

[17] HEMANN B A, BIMSON W F, TAYLOR A J. The Framingham Risk Score: an appraisal of its benefits and limitations[J]. Am Heart Hosp J, 2007, 5(2): 91-96. DOI: 10.1111/j.1541-9215.2007.06350.x.

[18] HAN Zesen, LAI Lihong. Overview of clinical prediction model research for coronary atherosclerotic heart disease[J]. Advances in Cardiovascular Diseases, 2020, 41(6): 638-641. DOI: 10.16806/j.cnki.issn.1004-3934.2020.06.019.

[19] WOLFF R F, MOONS K G M, RILEY R D, et al. PROBAST: a tool to assess the risk of bias and applicability of prediction model studies[J]. Ann Intern Med, 2019, 170(1): 51-58. DOI: 10.7326/M18-1376.

[20] WU Xigui, LAI Shenghan, GAO Hong, et al. Multivariate analysis of coronary heart disease risk factors in 988 male workers of Capital Iron and Steel Company[J]. Chinese Journal of Cardiology, 1983, 11(1): 28-32.

[21] LIANG X, WANG Q, JIANG Z Q, et al. Clinical research linking Traditional Chinese Medicine constitution types with diseases: a literature review of 1639 observational studies[J]. Chung I Tsa Chih Ying Wen Pan, 2020, 40(4): 690-702. DOI: 10.19852/j.cnki.jtcm.2020.04.019.

[22] FRANKLIN J. The elements of statistical learning: data mining, inference and prediction[J]. Math Intell, 2005, 27(2): 83-85. DOI: 10.1007/BF02985802.

[23] MAHMOOD S S, LEVY D, VASAN R S, et al. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective[J]. Lancet, 2014, 383(9921): 999-1008. DOI: 10.1016/S0140-6736(13)61752-3.

[24] QUESADA J A, LOPEZ-PINEDA A, GIL-GUILLÉN V F, et al. Machine learning to predict cardiovascular risk[J]. Int J Clin Pract, 2019, 73(10): e13389. DOI: 10.1111/ijcp.13389.

[25] WU Y F, FANG Y. Stroke prediction with machine learning methods among older Chinese[J]. Int J Environ Res Public Heath, 2020, 17(6): 1828. DOI: 10.3390/ijerph17061828.

[26] DEBRAY T P, DAMEN J A, SNELL K I, et al. A guide to systematic review and meta-analysis of prediction model performance[J]. BMJ, 2017, 356: i6460. DOI: 10.1136/bmj.i6460.

[27] MOONS K G, KENGNE A P, WOODWARD M, et al. Risk prediction models: I. Development, internal validation, and assessing the incremental value of a new (bio)marker[J]. Heart, 2012, 98(9): 683-690. DOI: 10.1136/heartjnl-2011-301246.

[28] STEYERBERG E W, PENCINA M J, LINGSMA H F, et al. Assessing the incremental value of diagnostic and prognostic markers: a review and illustration[J]. Eur J Clin Invest, 2012, 42(2): 216-228. DOI: 10.1111/j.1365-2362.2011.02562.x.

[29] WEN Lingzi, WANG Junfeng, GU Hongqiu. Clinical prediction models: incremental predictive value of new predictors[J]. Chinese Journal of Evidence-Based Cardiovascular Medicine, 2020, 12(6): 655-659. DOI: 10.3969/j.issn.1674-4055.2020.06.04.

[30] COOK N R. Quantifying the added value of new biomarkers: how and how not[J]. Diagn Progn Res, 2018, 2: 14. DOI: 10.1186/s41512-018-0037-2.

[31] PICKERING J W, ENDRE Z H. New metrics for assessing diagnostic potential of candidate biomarkers[J]. Clin J Am Soc Nephrol, 2012, 7(8): 1355-1364. DOI: 10.2215/CJN.09590911.

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