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Original Article

Pregnancy-Induced Hypertension and Atherosclerotic Cardiovascular Disease Risk Score in China

Honghong He, MM,[a,‡] Junyan Sun, MM,[b,‡] Hongqiu Huo, MB,[a] Yanxiu Wang, MD,[a] Yuntao Wu, MM,[a] Suhua Chen, MB,[c] Yangyang Wang, MM,[c] Xiaoming Zheng, MD,[a] and Haiyan Zhao, MD[a]

[a] *Department of Cardiology, Kailuan General Hospital, Tangshan, China*

[b] *Department of Traditional Chinese Medicine, Kailuan General Hospital, Tangshan, China*

[c] *Department of Obstetrics and Gynecology, Kailuan General Hospital, Tangshan, China*

ABSTRACT

Background: Pregnancy-induced hypertension (PIH) poses a significant threat to maternal health. This study aims to explore the association between PIH and the risk of atherosclerotic cardiovascular disease (ASCVD).

Methods: The cohort comprised 1947 pregnant women delivering a single child between 2004 and 2020 in the Kailuan study. Participants, categorized into PIH and non-PIH (NPIH) groups based on PIH history, completed questionnaires and underwent physical examinations and laboratory assessments within 2 years after delivery. Predicted ASCVD risks used the Atherosclerotic Cardiovascular Disease Risk in China (China-PAR) model, distinguishing lifetime ASCVD risk as "low" (<32.8%) and "high" (≥32.8%). χ^2 tests and logistic regression were used to investigate the association between PIH and high lifetime risk China-PAR categories.

Results: Overall, 6.17% of the PIH group had high lifetime risk, compared with 0.96% in the NPIH group (χ^2 29.59, $P < 0.001$). After adjusting for confounders, PIH was independently associated with high-risk China-PAR categories, with the PIH group having a 5.03 times higher probability than the NPIH group (95% CI 2.20-11.51, $P < 0.01$).

Conclusion: Pregnancy-induced hypertension was associated with increased lifetime risk of ASCVD.

RÉSUMÉ

Contexte : L'hypertension gestationnelle constitue une menace importante pour la santé maternelle. Cette étude vise à évaluer le lien entre l'hypertension gestationnelle et le risque de maladie cardiovasculaire athéroscléreuse (MCVA).

Méthodologie : L'étude Kailuan comprenait une cohorte de 1 947 femmes enceintes d'un seul enfant de 2004 à 2020. Les participantes, classées dans des groupes avec ou sans hypertension gestationnelle selon leurs antécédents d'hypertension gestationnelle, ont répondu à des questionnaires et ont été soumises à des examens physiques et des analyses de laboratoire au cours des 2 années ayant suivi l'accouchement. Les risques prédits de MCVA faisaient appel au modèle China-PAR (*Atherosclerotic Cardiovascular Disease Risk in China* [risque de MCVA en Chine]), qui distingue le risque à vie de MCVA comme étant soit « faible » (< 32,8 %) soit « élevé » (≥ 32,8 %). Les tests χ^2 et la régression logistique ont été utilisés pour évaluer le lien entre l'hypertension gestationnelle et un risque à vie élevé selon les catégories China-PAR.

Résultats : Globalement, 6,17 % du groupe avec hypertension gestationnelle affichait un risque à vie élevé, comparativement à 0,96 % dans le groupe sans hypertension gestationnelle (χ^2 29,59; $p < 0,001$). Après correction pour les facteurs de confusion, l'hypertension gestationnelle a été liée de manière indépendante aux catégories à risque élevé de China-PAR, la probabilité étant 5,03 fois plus élevée dans le groupe avec hypertension gestationnelle que dans le groupe sans hypertension gestationnelle (intervalle de confiance [IC] à 95 % : 2,20-11,51; $p < 0,01$).

Conclusion : L'hypertension gestationnelle a été associée à une augmentation du risque à vie de MCVA.

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‡These authors are equally contributing first authors.

Corresponding author: Dr Haiyan Zhao, Department of Cardiology, Kailuan General Hospital, No. 57 Xinhua East Road, Tangshan 063000, China. Tel.: +86-15081645885.

E-mail: hanyan7922@163.com

See page 440 for disclosure information.

Pregnancy-induced hypertension (PIH) complicates 6% to 10% of pregnancies, posing a major threat to maternal and neonatal health.[1,2] Beyond its short-term impact, PIH has implications for long-term maternal health. Observational studies demonstrate that women experiencing PIH have a higher long-term risk of cardiovascular events compared to

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those with normotensive pregnancies.[3,4] In addition, a cohort study revealed that women with hypertensive disorders of pregnancy, including PIH, had a significantly higher rate of atherosclerosis in the years following pregnancy.[5]

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of premature death worldwide, imposing a significant burden in China.[6] There are important sex differences in ASCVD between women and men that contribute to risk prevention and diagnostic and treatment uncertainty, resulting in insufficient ASCVD care in women. PIH poses substantial challenges to the maternal cardiovascular system, which have longer-term effects on maternal health for decades after pregnancy. The China-PAR project, a risk prediction model, has been developed based on contemporary Chinese adult cohorts but does not include pregnancy-related variables.[7,8] This study aims to explore the relationship between PIH and ASCVD risk evaluated by the China-PAR model.

Methods

Study design and population

The Kailuan study (registration number: ChiCTR-TNC-11001489) is an ongoing, large-scale, community-based, prospectively designed cohort that aims to investigate the risk factors for cardiometabolic diseases. All residents of the Kailuan community (n=155,418) are current or retired employees of the Kailuan coal mining company and were invited to participate in the study. Female employees did not engage in underground mining but were involved in administrative or support roles. Approved by the Kailuan General Hospital Ethics Committee, China (2006−05), the Kailuan study has issued health examinations every 2 years since 2006. All participants gave their written informed consent. Details of the Kailuan study have been previously described.[9] For the current sub-analysis, 5057 participants from the Kailuan cohort who delivered a single child between 2004 and 2020 were recruited. Among them, we excluded individuals who missed the health examinations within 2 years after delivery (n = 2965), had incomplete delivery data (n = 42), had incomplete data for China-PAR equation (n = 86), had pre-existing hypertension or secondary hypertension (n = 10), or had undergone induced abortion or miscarriage (n = 7), leaving a total of 1947 participants for the current analysis. Figure 1 displays the flowchart of the participants.

Inclusion and exclusion criteria

Inclusion criteria comprised (1) female employees who had delivered a single child in a hospital of the Kailuan Medical Group (including Kailuan Hospital, Kailuan Fanjiazhuang Hospital, Kailuan Zhaojiazhuang Hospital, Kailuan Linxi Hospital, Kailuan Linancang Hospital, Kailuan Lujatuo Hospital, Kailuan Majiagou Hospital, Kailuan Tangjiazhuang Hospital, Kailuan Jingjiazhuang Hospital, Kailuan Qianying Hospital) between 2004 and 2020 with complete delivery records, (2) women who experienced their first pregnancy resulting in a live birth and underwent a health check within 2 years postpartum, and (3) women who voluntarily signed the informed consent to participate in the study. Exclusion criteria included (1) women who had pre-existing hypertension before pregnancy, (2) women who had undergone induced abortion or miscarriage, (3) women with secondary hypertension, and (4) women with incomplete China-PAR model data.

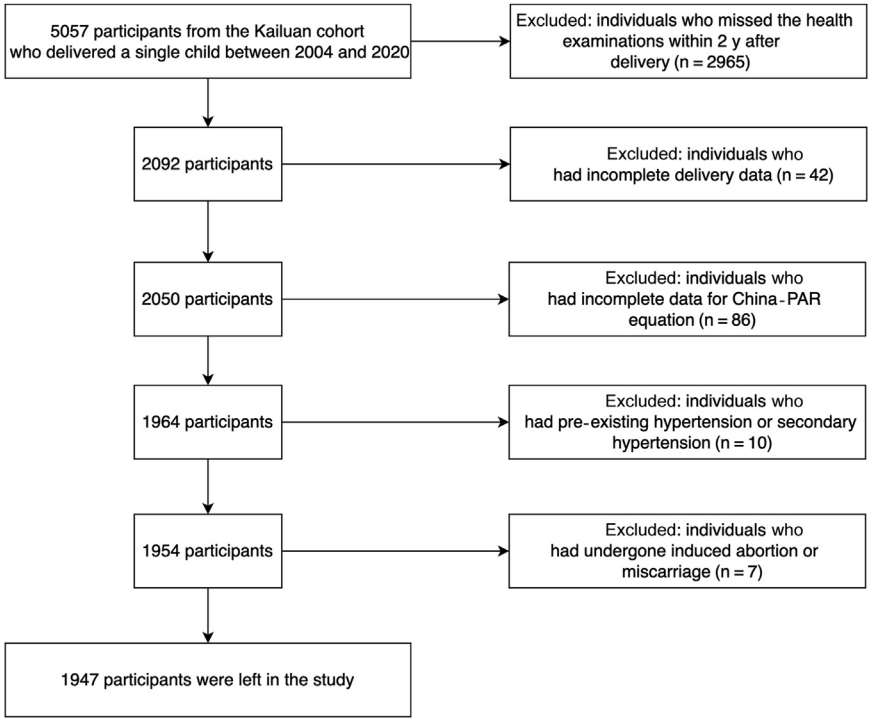

Figure 1. Flowchart showing the exclusion process for selecting eligible participants.

Epidemiologic questionnaire design

A standardized questionnaire was administered by a trained interviewer to collect information on age, history of hypertension, diabetes, stroke, and myocardial infarction; smoking and alcohol consumption; level of physical activity, educational background, and income status, as well as family histories of myocardial infarction and stroke.

Physical examination procedure

Physical examinations were performed by trained nurses, following standard procedures. Weight and height were obtained according to a standardized protocol, and body mass index (BMI) calculated as weight (kg) divided by height (m) squared. The details were described in the published literature of the research group.[10]

Laboratory tests

Blood samples were obtained from the participants in the morning after a 12-hour fasting period. Serum were separated and analyzed for including creatinine, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting plasma glucose (FPG), and triglyceride (TG) levels. In addition, the estimated glomerular filtration rate (eGFR) was computed, using serum creatinine, sex, and age, according to the Chronic Kidney Disease Epidemiology Collaboration equation, as detailed elsewhere.[10,11]

Delivery data collection

Delivery data were extracted from medical records, encompassing a comprehensive data set that included the age of delivery, mode of delivery, delivery times, as well as pre- and postdelivery blood pressure.

Diagnostic criteria for PIH

The diagnostic criteria for PIH were established according to the Chinese Guidelines for the Prevention and Control of Hypertension (2005 Revision) and characterized as follows: after 20 weeks of pregnancy, a pregnant woman is considered to have PIH if her blood pressure is $\geq$140/90 mm Hg (1 mm Hg = 0.133 kPa), or if there is an increase of $\geq$25/15 mm Hg compared with her prepregnancy or early pregnancy baseline, with measurements taken at least twice during a 6-hour interval. PIH does not include hypertension present before pregnancy or before 20 weeks of gestation and is, therefore, distinct from hypertensive disorders of pregnancy.

ASCVD risk score

The 10-year and lifetime risks of ASCVD were estimated for each participant using the China-PAR algorithms, accessible through the evaluation tool on the website https://www.cvdrisk.com.cn. ASCVD was defined as nonfatal acute myocardial infarction or coronary heart disease death or fatal or nonfatal stroke. The China-PAR risk assessment models encompassed factors such as sex, age, current residence (urban or rural), geographical area (North or South, bound by the Yangtze River), waist circumference, total cholesterol, HDL-C, blood pressure, history of hypertension, diabetes, smoking, and family history of cardiovascular disease (CVD).

Based on the predicted ASCVD 10-year risk, participants were categorized into 3 groups: low risk (<5.0%), medium risk (5.0%−9.9%), and high risk ($\geq$10.0%). Additionally, participants were classified into 2 groups based on predicted lifetime risk: low risk (<32.8%) and high risk ($\geq$32.8%).

Statistical analysis

We used multiple imputation techniques to account for missing data under the missing-at-random assumption. Baseline characteristics were described as the mean with standard deviation, or numbers and percentages (%), when appropriate. Intergroup comparisons were conducted by 1-way analyses of variance or Kruskal-Wallis tests for continuous variables and Pearson χ^2 tests for categorical variables.

Logistic regression was employed to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the variables influencing the China-PAR category. The frequency of the high lifetime risk category was used as the dependent variable, with adjustments made for age, age at delivery, FPG, and overweight status based on BMI.

All statistical analyses were performed with SPSS 13.0 (SPSS, Chicago, IL) and SAS 9.4 (SAS Institute, Cary, NC). A 2-tailed P value <0.05 was considered statistically significant.

Result

Baseline characteristics

Table 1 provides a snapshot of the baseline characteristics of the study participants. A total of 1947 participants were selected, with an average age of 30.48 $\pm$ 3.84 years. Among them, the PIH group comprised 162 participants, whereas the NPIH group included 1785 participants.

Compared with the NPIH group, the PIH group exhibited notable differences. Specifically, the PIH group showed significantly higher values in waist circumference, systolic and diastolic blood pressure, fasting blood glucose, delivery age, and BMI. Additionally, the PIH group had significantly lower levels of HDL-C and a lower likelihood of alcohol consumption. Interestingly, no significant differences were observed between the PIH and NPIH groups in terms of age, HDL-C, eGFR, education level, and family history of ASCVD. Individuals without complete data for the China-PAR equation and delivery information were excluded. Therefore, the following variables do not have missing data: delivery age, age, current residence, geographical area, waist circumference, total cholesterol, HDL-C, systolic blood pressure, history of hypertension, diabetes, smoking, and family history of CVD. The amount of missing data for other variables is provided in Supplemental Table S1.

PIH and 10-year ASCVD risk stratification

In accordance with the China-PAR 10-year risk stratification, all 162 subjects in the PIH group were assigned to the low-risk category. Within the NPIH group, the majority, totaling 1783 subjects, were also categorized as low risk, with only 1 subject identified as medium risk and another as high risk. Importantly, no statistically significant difference

Table 1. Baseline characteristics of the PIH and NPIH groups

	PIH (n = 162)	NPIH (n = 1785)	Total (N = 1947)	*P* value
Age, y	31.24±4.42	30.41±3.77	30.48±3.84	0.059
Waist circumference, cm	80.78±10.39	78.34±9.26	78.54±9.38	0.002
SBP, mm Hg	115.10±14.26	110.15±12.52	110.93±12.73	0.001
DBP, mm Hg	76.05±10.35	71.58±7.62	71.95±7.98	<0.001
LDL-C, mmol/L	2.53±0.91	2.41±0.98	2.42±0.97	0.131
HDL-C, mmol/L	1.44±0.32	1.51±0.39	1.51±0.38	0.040
FPG, mmol/L	5.31±1.55	4.93±1.40	4.96±1.41	0.002
eGFR, mL/min/1.73 m^2	106.98±22.89	108.63±22.53	108.49±22.55	0.383
Delivery age, y	29.66±4.23	28.77±3.61	28.84±3.67	0.017
BMI overweight, n (%)	75 (46.3)	526 (29.47)	601 (30.87)	<0.001
Antihypertension medication, n (%)	7 (4.32)	3 (0.17)	10 (0.51)	<0.001
Alcohol consumption, n (%)	7 (4.32)	215 (12.04)	222 (11.40)	0.003
Current smoker, n (%)	1 (0.62)	7 (0.39)	8 (0.41)	0.668
Education >9 y, n (%)	93 (57.41)	966 (54.12)	1059 (54.39)	0.421
High-income level, n (%)	34 (20.99)	324 (16.64)	358 (18.39)	0.372
Family history of ASCVD, n (%)	160 (98.77)	1730 (96.92)	1890 (97.07)	0.182

ASCVD, atherosclerotic cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, high-density lipoprotein cholesterol; NPIH, non−pregnancy-induced hypertension; PIH, pregnancy-induced hypertension; SBP, systolic blood pressure.

A high-income level was defined as the average family income >800 yuan per person per month. One US dollar equals approximately 7.1 Chinese yuan. Overweight was defined as a BMI of 24 or more.

emerged between the PIH and NPIH groups in terms of their 10-year ASCVD risk categories.

PIH and lifetime ASCVD risk stratification

Table 2 illustrates a notable distinction: 6.7% of subjects in the PIH group exhibited a high lifetime risk, whereas a mere 0.95% of subjects in the NPIH group shared this classification. The disparity in the proportion of individuals with high lifetime risk between the PIH and NPIH groups was statistically significant, underscoring a substantial difference in risk profiles.

There were 47 individuals diagnosed with pre-eclampsia, accounting for 29.01% of all PIH cases. Among them, 4 are expected to have a high lifetime risk of CVD, whereas the remaining 43 are considered to be at low risk.

Association of PIH and lifetime China-PAR categories

In the univariate analysis of model 1, the PIH group exhibited a heightened probability of falling into the high lifetime risk category.

In the multiple logistic regression analysis of model 2, a significant association between PIH and the high lifetime risk category emerged, with the adjusted OR being 5.03 (95% CI 2.20-11.51). Notably, neither age nor delivery age displayed an association with the high-risk category. The adjusted ORs for FPG and BMI overweight were 1.16 (95% CI 1.03-1.30) and 5.05 (95% CI 2.10-12.16), respectively. Further details can be found in Table 3, and Figure 2 illustrates the forest plot of model 2.

Discussion

This study aimed to investigate the association between PIH and ASCVD risk scores, as defined by the China-PAR model. The logistic regression analysis demonstrated that PIH independently acted as a risk factor for high lifetime risk in China-PAR categories, with the probability in the PIH group being 5.03 times higher than that in the NPIH group (95% CI 2.20-11.51, $P < 0.01$). Furthermore, our findings indicated that elevated FPG and BMI overweight were associated with an increased likelihood of being categorized as high lifetime risk according to the China-PAR model. Notably, this study did not identify a significant association between PIH and 10-year ASCVD risk categories.

Our findings are in line with previous research suggesting that hypertensive disorders of pregnancy, including gestational hypertension and pre-eclampsia, are linked to an increased risk of CVD.[5,12,13] Notably, earlier studies predominantly focused on pre-eclampsia, which has been reported to be associated with 8- to 10-fold higher cardiovascular mortality compared with normotensive pregnancies, as opposed to the 2-fold higher cardiovascular mortality noted in our study.[14,15] The American Heart Association recognizes pre-eclampsia as an independent risk factor for CVD, incorporating it into algorithms for assessing CVD risk.[16]

Of significance, our study indicates that PIH is associated with a lifetime ASCVD risk. Additionally, our findings reveal that lower FPG and a BMI below 24 are linked to a reduced lifetime ASCVD risk, consistent with observations from prior studies.[17,18] Our study also found that the PIH group had

Table 2. The lifetime ASCVD risk stratification of PIH group and NPIH group

	PIH	NPIH	Total	χ^2	*P* value
Low risk, n (%)	152 (93.83)	1768 (99.05)	1920 (98.61)	29.59	<0.001
High risk, n (%)	10 (6.17)	17 (0.95)	27 (1.39)		

ASCVD, atherosclerotic cardiovascular disease; NPIH, non−pregnancy-induced hypertension; PIH, pregnancy-induced hypertension.

Table 3. Logistic regression analysis for high lifetime ASCVD risk category

	Variables	*B*	SE	Wald χ^2	OR	95% CI	*P* value
Model 1	PIH	1.92	0.41	22.29	6.84	3.08-15.20	<0.001
Model 2	PIH	1.61	0.42	14.60	5.03	2.20-11.51	<0.001
	Age	0.04	0.07	0.28	1.04	0.90-1.19	0.599
	Delivery age ≥35 y	0.38	0.90	1.78	1.47	0.25-8.56	0.673
	FPG	0.145	0.06	6.30	1.16	1.03-1.30	0.012
	BMI overweight	1.62	0.45	13.07	5.05	2.10-12.16	<0.001

ASCVD, atherosclerotic cardiovascular disease; *B*, regression coefficient; BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; OR, odds ratio; PIH, pregnancy-induced hypertension; SE, standard error.

Overweight was defined as a BMI of 24 or higher.

higher blood pressure, lower HDL-C levels, and larger waist circumferences compared with the NPIH group. These risk factors are included in the China-PAR equation and contribute to the higher lifetime ASCVD risk scores in the PIH group. Women with PIH may benefit from better control of other ASCVD risk factors, such as blood pressure, HDL-C, and waist circumference.

This study uncovered a lack of a significant association between PIH and the 10-year ASCVD risk, potentially linked to the relatively youthful age of the participants. Young women, especially those premenopausal, typically exhibit a lower risk of CVD. Traditional risk prediction models, such as the Framingham Risk Score, the Systematic Coronary Risk Evaluation (SCORE), and the QRISK score, rarely classify women aged ≤65 years as high cardiovascular risk individuals.[19-21] Notably, applying a 30-year CVD risk score model revealed that women with multiple risk factors had a 12% predicted risk of CVD at 25 years of age, escalating to 42% at 45 years of age.[22] Hence, it seems reasonable to include PIH in the lifetime risk prediction model rather than confining it to the 10-year risk prediction model.

Existing models do not include pregnancy-related information, which may be due to several reasons. First, the influence of pregnancy-related factors is relatively small compared with other traditional ASCVD risk factors. Second, these factors have not been widely recognized. Finally, pregnancy-related data can be relatively difficult to obtain.

The current study is not without limitations. First, its single-center design and the exclusive inclusion of participants from a northern Chinese city may limit the generalizability of the findings to a broader geographical context. Second, the sample size, particularly the insufficient number of individuals diagnosed with PIH, poses a limitation. Consequently, the stability of the ORs and 95% CIs derived from the logistic regression analysis may be compromised. To address these constraints and bolster the reliability of the results, future investigations could benefit from a multicenter approach involving larger, more diverse community-based cohorts for a more robust calibration and refinement of the risk assessment models. Third, although our study examined a range of cardiovascular risk factors, we did not collect data on several female-specific obstetric risk factors, such as the number of deliveries, preterm birth, low birth weight, and intrauterine growth restriction. These factors are known to potentially impact cardiovascular health and should be considered in future research. Finally, the main limitation of this study is that the risk of ASCVD events was estimated using a risk score rather than actual recorded events. In future studies, long-term follow-up of the participants could be conducted to validate the accuracy of the risk score.

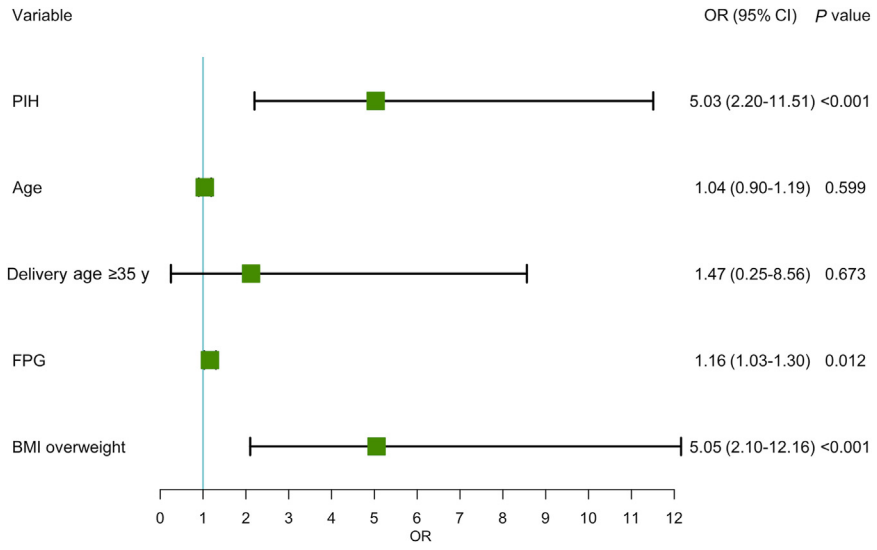

Figure 2. Forest plot of logistic regression for high lifetime atherosclerotic cardiovascular disease risk categories. BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; OR, odds ratio; PIH, pregnancy-induced hypertension.

Conclusion

PIH was associated with increased lifetime risk of ASCVD. Early identification of high-risk individuals in clinical practice is necessary for the prevention of ASCVD in the female population.

Acknowledgments

Ethics Statement

The study was approved by the Kailuan General Hospital Ethics Committee, China (2006-05).

Patient Consent

The authors confirm that patient consent forms have been obtained for this article.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2025.01.006