Menopause or Aging? A Prospective Cohort Study on Risk Factors for Coronary Heart Disease in Middle-aged Women (Postprint)

Authors: Yang Mukun, Jia Xiaoxiang, Ren Zhenghong, Gu Bei, Bai Wenpei, Bai Wenpei

Date: 2023-08-23T00:00:00+00:00

Abstract

Background Menopause induces a series of pathophysiological changes and long-term complications (coronary heart disease, cerebrovascular disease, osteoporosis, etc.), among which coronary heart disease is the leading threat to health. Objective To investigate the effects of changes in menopausal status and aging on common risk factors for coronary heart disease in middle-aged women, including carotid intima-media thickness (CIMT) thickening, hypertension, dyslipidemia, diabetes mellitus, and obesity. Methods A total of 556 healthy premenopausal women aged 45-54 years who underwent regular health check-ups at the Physical Examination Center of Beijing Shijitan Hospital, Capital Medical University in 2018 were selected. According to relevant criteria, 89 were excluded, and 467 women were finally included as study subjects. Based on whether menopause occurred during the 3-year follow-up period, the subjects were divided into a premenopausal group (176) and a postmenopausal group (291). Changes in BMI, waist circumference, blood glucose, blood pressure, blood lipids, and other indicators were monitored in both groups, and inter-group and intra-group comparisons were performed before and after follow-up. Multivariate logistic regression analysis was used to explore the effects of menopausal status and age on the incidence of risk factors for coronary heart disease (CIMT thickening, hypertension) in middle-aged women. Results The mean age of the 467 subjects was (47.6$±$2.3) years. Compared with baseline, waist circumference, uric acid (UA), total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) levels increased after 3 years, while fasting blood glucose (FBG) levels decreased ($P<0.05$). Inter-group comparison: After 3 years, there were no statistically significant differences in waist circumference, BMI, TG, FBG, or high-density lipoprotein cholesterol (HDL-C) levels between the two groups ($P>0.05$); UA, TC, and LDL-C levels in the postmenopausal group were

higher than those in the premenopausal group, with statistically significant differences (P<0.05). Intra-group comparison: Waist circumference in both groups increased after 3 years compared with baseline levels (P<0.05). UA, TC, and TG levels in the premenopausal group were higher after 3 years than at baseline (P<0.05). UA, TC, TG, and LDL-C levels in the postmenopausal group were higher after 3 years than at baseline (P<0.05). Multivariate logistic regression analysis showed that age $ $50 years was a risk factor for CIMT thickening in middle-aged women (OR=2.475, 95%CI=1.049-5.838, P=0.038). Conclusion Changes in waist circumference and TG in middle-aged women were mainly influenced by aging, changes in LDL-C were mainly influenced by menopausal status, and changes in TC and UA were influenced by both menopausal status and aging. Age $ $50 years is a risk factor for CIMT thickening in middle-aged women, and changes in metabolic indicators such as UA, TC, and LDL-C after menopause precede changes in CIMT.

Full Text

Menopause or Chronologic Aging? A Prospective Cohort Study on Risk Factors for Coronary Heart Disease in Middle-aged Women

YANG Mukun[1], JIA Xiaoxiang[2], RENG Zhenghong[3], GU Bei[1], BAI Wenpei[1]*

[1]Department of Obstetrics and Gynecology, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China
[2]Department of Obstetrics and Gynecology, Tongzhou Maternal and Child Health Hospital, Beijing 101101, China
[3]School of Public Health, Peking University Health Science Center, Beijing 100191, China

Corresponding author: BAI Wenpei, Chief physician/Professor; E-mail: Baiwp@bjsjth.cn

Abstract

Background: Menopause causes a series of pathophysiologic changes and long-term complications (coronary heart disease, cerebrovascular disease, osteoporosis, etc.), among which coronary heart disease is the leading cause of mortality. **Objective:** To investigate the effects of menopausal status changes and aging on common risk factors for coronary heart disease in middle-aged women, including increased carotid intima-media thickness (CIMT), hypertension, dyslipidemia, diabetes, and obesity. **Methods:** A total of 556 healthy premenopausal women aged 45-54 years who underwent regular physical examinations at the Physical Examination Center of Beijing Shijitan Hospital affiliated with Capital Medical University in 2018 were initially selected. After excluding 89 women according to relevant criteria, 467 women were finally included as study sub-

jects. Based on whether they became menopausal during the 3-year follow-up period, subjects were divided into a premenopausal group (n=176) and a postmenopausal group (n=291). Changes in BMI, waist circumference, blood glucose, blood pressure, blood lipids, and other indicators were monitored, and inter-group and intra-group comparisons were performed before and after follow-up. Multivariate logistic regression analysis was used to explore the effects of menopausal status and age on the incidence of coronary heart disease risk factors (CIMT thickening, hypertension) in middle-aged women. **Results:** The average age of the 467 subjects was (47.6$±$2.3) years. Compared with baseline, waist circumference, uric acid (UA), total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels increased, while fasting blood glucose (FBG) levels decreased after 3 years (P<0.05). Inter-group comparison showed no significant differences in waist circumference, BMI, TG, FBG, or high-density lipoprotein cholesterol (HDL-C) levels between the two groups after 3 years (P>0.05). UA, TC, and LDL-C levels in the postmenopausal group were significantly higher than those in the premenopausal group (P<0.05). Intra-group comparison revealed that waist circumference in both groups increased after 3 years compared with baseline (P<0.05). UA, TC, and TG levels in the premenopausal group were higher after 3 years than at baseline (P<0.05). UA, TC, TG, and LDL-C levels in the postmenopausal group were higher after 3 years than at baseline (P<0.05). Multivariate logistic regression analysis showed that age $ $50 years was a high-risk factor for increased CIMT in middle-aged women (OR=2.475, 95%CI=1.049-5.838, P=0.038). **Conclusions:** Changes in waist circumference and TG in middle-aged women are mainly affected by age, changes in LDL-C are mainly affected by menopausal status, and changes in TC and UA are affected by both menopausal status and age. Age $ $50 years is a high-risk factor for increased CIMT in middle-aged women, and changes in metabolic indicators such as UA, TC, and LDL-C precede changes in CIMT after menopause.

Keywords: Coronary disease; Menopause; Age; Obesity; Middle-aged women; Risk factors; Prospective studies; Cohort studies

Introduction

After age 40, women gradually experience ovarian function decline, and complete ovarian exhaustion marks the onset of menopause. In addition to reproductive system changes, menopause is accompanied by a series of pathophysiologic changes across multiple systems and organs, including alterations in physical function, cardiovascular system changes, and metabolic shifts, which also increase the risk of various chronic diseases such as coronary heart disease, cerebrovascular disease, and osteoporosis. Coronary heart disease has gradually become the leading cause of death in both developed and developing countries. Epidemiological reports indicate that menopause, age, family history of early-onset coronary heart disease, hypertension, hypercholesterolemia, diabetes, obe-

sity, and smoking are all common risk factors for coronary heart disease.

With increasing age and changes in menopausal status, some modifiable risk factors for coronary heart disease (such as hypertension, hypercholesterolemia, diabetes, and obesity) may also be affected, further increasing the incidence of coronary heart disease. This prospective cohort study explores the influence patterns of age and menopausal status on coronary heart disease-related risk factors in middle-aged women, providing guidance for health management and intervention strategies for menopausal women.

1.1 Study Subjects

Healthy premenopausal women aged 45-54 years who underwent regular physical examinations at the Physical Examination Center of Beijing Shijitan Hospital affiliated with Capital Medical University in 2018 were selected. **Inclusion criteria:** (1) Women with regular menstrual cycles; (2) Age 45-54 years. **Exclusion criteria:** (1) Pregnancy; (2) Hysterectomy; (3) Use of hormone replacement therapy (including estrogen, progesterone, sequential or combined estrogen-progesterone therapy); (4) Smoking; (5) Family history of early-onset coronary heart disease; (6) Malignant tumors, increased carotid intima-media thickness, hypertension, diabetes, coronary heart disease, hyperlipidemia, or hyperuricemia. **Elimination criteria:** (1) Unable to complete follow-up on schedule; (2) Uncertain menopausal status at follow-up end (irregular menstruation or amenorrhea not meeting menopause diagnostic criteria). This study was approved by the Ethics Committee of Beijing Shijitan Hospital affiliated with Capital Medical University (2018 Research Review No. 46), complied with the ethical standards of the Declaration of Helsinki, and all subjects signed informed consent forms.

1.2 Study Methods

This was a prospective cohort study. Follow-up began at enrollment and ended after 3 years, concluding in February 2022. Subjects who became menopausal during the 3-year follow-up period entered the experimental group (postmenopausal group). Those who remained premenopausal after 3 years entered the control group (premenopausal group). Subjects with uncertain menopausal status at the 3-year follow-up end (irregular menstruation or amenorrhea not meeting menopause diagnostic criteria) were eliminated from the study. At the start and end of follow-up, medical history was collected (new diseases and surgical conditions, etc.) and relevant examinations were performed for each group, including: physical examination (height, weight, waist circumference, systolic pressure, diastolic pressure, etc.), laboratory tests [uric acid (UA), total cholesterol (TC), triglyceride (TG), fasting blood glucose (FBG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)], and carotid intima-media thickness (CIMT) measurement. Differences in examination indicators during the 3-year follow-up

period were analyzed, with further intra-group and inter-group comparisons conducted according to postmenopausal and premenopausal groups.

1.3 Diagnostic Criteria

1.3.1 Menopause: In women over 40 years of age, after excluding pregnancy, 12 consecutive months of amenorrhea constitutes a retrospective clinical diagnosis.

1.3.2 CIMT thickening: Subjects were placed in a supine position with the head turned to the side opposite the examination area. The same professional physician used a Philips IE 33 ultrasound machine (linear array probe, frequency 4-11 MHz) to scan the transverse and longitudinal axes of both common carotid arteries, internal carotid arteries, and carotid bifurcations. The arterial posterior wall showed a "double-line" image with boundaries between the intima and lumen and between the media and adventitia; the distance between them was defined as CIMT. When the vascular wall was smooth and CIMT<0.9 mm, it was considered normal; when CIMT$ $0.9 mm, it was considered thickened.

1.3.3 Hypertension: In the absence of antihypertensive medication, hypertension can be diagnosed when systolic pressure$ $140 mmHg and/or diastolic pressure$ $90 mmHg are measured on three different days.

1.4 Statistical Methods

SPSS 26.0 software was used for statistical analysis. Measurement data with normal distribution were expressed as ($\bar{x}\pm s$). Independent samples t-test was used for inter-group comparisons, and paired t-test was used for intra-group comparisons before and after follow-up. Count data were expressed as relative numbers, and inter-group comparisons used ^{2} test. Multivariate logistic regression analysis was used to explore the effects of menopausal status and age on the incidence of coronary heart disease risk factors (CIMT thickening, hypertension) in middle-aged women. P<0.05 was considered statistically significant.

Results

2.1 Follow-up Results

A total of 556 premenopausal healthy women were enrolled. At the end of the 3-year follow-up, 89 women were excluded: 85 developed amenorrhea or oligomenorrhea but did not meet menopause criteria; 2 were unable to complete follow-up and related examinations due to personal reasons (1 due to job transfer, 1 lost to follow-up); and 2 used sex hormone therapy due to menopause-related symptoms [Figure 1: see original paper]. Finally, 467 women were included as study subjects. At follow-up end, 291 women who had become menopausal were included in the postmenopausal group (n=291), and 176 women who remained premenopausal were included in the premenopausal group (n=176). The average age of study subjects was (47.6$±$2.3) years. Compared with baseline,

waist circumference, UA, TC, TG, and LDL-C levels increased after 3 years, while FBG levels decreased (P<0.05). There were no significant differences in BMI or HDL-C levels before and after follow-up (P>0.05) .

TABLE:1 shows the follow-up results of research subjects (n=467, $\bar{x}\pm s$).

2.2 Comparison of Waist Circumference and BMI Between the Two Groups

Inter-group comparison showed no significant differences in waist circumference or BMI between the two groups at baseline or after 3 years (P>0.05). Intra-group comparison revealed that waist circumference in both groups increased after 3 years compared with baseline (P<0.05) .

2.3 Comparison of Laboratory Examination Indexes Between the Two Groups

Inter-group comparison showed no significant differences in UA, TC, TG, FBG, HDL-C, or LDL-C levels between the two groups at baseline (P>0.05). After 3 years, there were no significant differences in TG, FBG, or HDL-C levels between the two groups (P>0.05). However, UA, TC, and LDL-C levels in the postmenopausal group were significantly higher than those in the premenopausal group (P<0.05) .

Intra-group comparison showed no significant differences in FBG, HDL-C, or LDL-C levels in the premenopausal group before and after follow-up (P>0.05), while UA, TC, and TG levels after 3 years were significantly higher than baseline (P<0.05). In the postmenopausal group, there were no significant differences in FBG or HDL-C levels before and after follow-up (P>0.05), while UA, TC, TG, and LDL-C levels after 3 years were significantly higher than baseline (P<0.05) .

2.4 Comparison of CIMT Thickening and Hypertension Incidence Between the Two Groups

After 3 years, there was no significant difference in the incidence of CIMT thickening between the two groups (P>0.05). However, the incidence of hypertension in the postmenopausal group was significantly higher than that in the premenopausal group (P<0.05) .

2.5 Multivariate Logistic Regression Analysis of the Effects of Menopause and Age on the Incidence of Increased CIMT and Hypertension in Middle-aged Women

Using new-onset CIMT thickening and hypertension as dependent variables (assignment: yes=1, no=0), and menopausal status (assignment: menopausal=1, premenopausal=0) and age (assignment: $ $50 years=1, <50 years=0) as independent variables, multivariate logistic regression analysis showed that age $ $50

years was a risk factor for CIMT thickening in middle-aged women (OR=2.475, 95%CI=1.049-5.838, P=0.038) .

Discussion

3.1 Changes in Menopausal Status and Metabolic Disorders

The essence of menopause is the change in estrogen levels caused by ovarian failure. During the transition of menopausal status, women experience a transition from normal to low estrogen levels, a period also known as the menopausal transition. Estrogen has multiple physiological functions, participating in the regulation of protein synthesis, water-electrolyte balance, and lipid metabolism. Do the obvious fluctuations in estrogen levels during the menopausal transition also cause a series of metabolic disorders?

The postmenopausal group in this study precisely experienced the transition from premenopause to menopause during the 3-year follow-up period (menopausal transition). Studying this population helps explore relevant changes in women's bodies before and after the menopausal transition. Therefore, the "effects of menopause" discussed in this study specifically refer to the short-term effects of menopausal status changes on the body.

The average age of menopause is 49-51 years, with menopause before age 45 defined as early menopause and after age 55 as late menopause. This study selected women aged 45-54 years to minimize interference from age span on the results. According to baseline data comparisons between the two groups (Tables 2 and 3), there were no significant differences in any indicators at enrollment (P>0.05).

3.2 Menopause, Age, and Obesity

Obesity is closely related to various chronic diseases in the elderly, particularly coronary heart disease, diabetes, and hypertension. Women tend to develop obesity in middle age, and traditional concepts attribute this change to both aging and menopausal status changes. In a cross-sectional study—the Study of Women's Health Across the Nation (SWAN)—16,065 middle-aged women were followed by telephone, finding that naturally menopausal women had similar BMI to premenopausal women, while surgically menopausal women had higher BMI than premenopausal women. Our study results showed that postmenopausal women, who experienced menopausal status changes during the 3-year follow-up period, had no significant BMI changes compared with premenopause [baseline $(23.29\$\pm3.17)kg/m^{\{2\},3yearslater(23.34\pm3.19)kg/m\{2\}\$}$; P=0.722], consistent with SWAN findings. Since this study did not include surgically menopausal patients, we could not evaluate BMI changes in that population.

In addition to BMI, waist circumference is also an important indicator reflecting obesity. Also in a SWAN study, 543 middle-aged women un-

dergoing menopause were observed, showing a 6% increase in waist circumference over 6 years of follow-up. In our study, the average waist circumference of all subjects significantly increased during the 3-year follow-up period [baseline $(76.31\$\pm7.25)cm, 3years later(77.91\pm\$7.62)$ cm; P<0.001]. Specifically, postmenopausal subjects' average waist circumference increased from $(76.66\$\pm7.53)cm to(78.09\pm7.72)cm(P < 0.001), while premenopausal subjects' average waist circumference increased from(75.76\pm6.78)cm to(77.62\pm\$7$ cm (P<0.001). However, there were no significant differences between the two groups before or after follow-up (P=0.235 at baseline; P=0.566 at 3 years). Therefore, we speculate that menopausal status changes have minimal impact on waist circumference, and that changes in waist circumference in middle-aged women are mainly affected by age.

In a study on body fat distribution detection, 8 middle-aged women underwent MRI evaluation before and after menopause (8-year interval), finding that menopausal status changes did not cause waist circumference changes [premenopause $(92.1\$\pm4.6)cm, postmenopause(93.4\pm\$3.7)$ cm], but subcutaneous and visceral fat distribution did change. Therefore, adding body fat distribution detection to future studies could help further understand changes in fat distribution in middle-aged women.

3.3 Menopause, Age, and Blood Lipids

Lipid metabolism disorders are closely related to cardiovascular disease occurrence, and menopause is closely related to body fat changes. SWAN results showed that after menopause, middle-aged women's serum TC, LDL-C, and apolipoprotein B levels all significantly increased and were associated with carotid plaque formation in the long term. Our study results showed that after 3 years of follow-up, average TC and TG levels in all subjects significantly increased compared with baseline (P<0.001). In further group comparisons, postmenopausal women's TC levels after 3 years significantly increased compared with baseline (P<0.001) and were significantly higher than those in the premenopausal group at the same time point (P<0.001), while premenopausal women's TC levels also significantly increased compared with baseline (P=0.004). We speculate that TC changes in middle-aged women are affected by both menopausal status and age. After 3 years, TG levels in both postmenopausal and premenopausal women significantly increased compared with baseline (postmenopausal P<0.001; premenopausal P=0.001), with no significant difference between groups (P=0.422). We speculate that TG changes in middle-aged women are mainly affected by age.

Additionally, our results showed that after 3 years of follow-up, LDL-C levels in all subjects increased compared with baseline (P=0.039). In further group comparisons, postmenopausal women's LDL-C levels significantly increased compared with baseline (P=0.005) and were significantly higher than those in the premenopausal group at the same time point (P=0.005), while premenopausal women's LDL-C levels showed no significant change compared with baseline

(P=0.664). We speculate that LDL-C changes in middle-aged women are mainly affected by menopausal status.

3.4 Age, Menopause, and UA

Elevated UA levels are positively correlated with cardiovascular disease occurrence, possibly because UA crystals deposit on vascular walls, stimulate vascular smooth muscle cell proliferation, and induce inflammatory responses that promote arterial plaque formation. In the SONIC study, a cross-sectional study of 1,115 elderly subjects found that elevated serum UA might be an independent risk factor for CIMT thickening in women around 70 years old and could serve as an alternative predictive indicator for atherosclerosis. In our study, after 3 years of follow-up, UA levels in all subjects significantly increased compared with baseline (P<0.001). Further group comparisons showed that postmenopausal women's UA levels significantly increased compared with baseline (P<0.001) and were significantly higher than those in the premenopausal group at the same time point (P=0.001), while premenopausal women's UA levels also significantly increased compared with baseline (P=0.004). We speculate that UA levels in middle-aged women are affected by both menopausal status and age.

3.5 Age, Menopause, and CIMT Thickening/Hypertension

A recent meta-analysis of 119 randomized controlled trials including 100,667 patients found that interventions slowing CIMT progression might simultaneously reduce cardiovascular disease incidence, demonstrating the positive correlation between CIMT and cardiovascular risk and indicating that CIMT detection can serve as an early prediction method for coronary heart disease. A cross-sectional study by IEAMTAIRAT et al. (including 61 premenopausal and 61 postmenopausal women) showed that postmenopausal women had significantly higher mean common carotid artery CIMT than premenopausal women, indicating that menopause is an important risk factor for CIMT thickening.

Based on the average menopausal age of 49-51 years, this study used age $ $50 years and <50 years as assignment variables. Results showed that age $ $50 years was a high-risk factor for CIMT thickening, with women $ $50 years having 2.475 times higher incidence of CIMT thickening than those <50 years (P=0.038). However, we did not find an effect of menopause on CIMT thickening, speculating that changes in metabolic indicators such as UA, TC, and LDL-C after menopause precede changes in CIMT.

A prospective cohort study by ZHANG Ying et al. found that monitoring CIMT thickening combined with hypertension could more efficiently predict coronary heart disease occurrence and improve prevention efficiency. However, this study did not find effects of menopause and age on hypertension incidence, possibly because our observation window (3 years) may be too short to observe the full development of coronary heart disease. Therefore, future studies should extend follow-up time to obtain complete observation of cardiovascular events during

the menopausal transition in middle-aged women.

Summary and Outlook

In summary, this study found that changes in waist circumference and TG in middle-aged women are mainly affected by age, changes in LDL-C are mainly affected by menopausal status, and changes in TC and UA are affected by both menopausal status and age. Age $ $50 years is a high-risk factor for CIMT thickening in middle-aged women, and changes in metabolic indicators such as UA, TC, and LDL-C after menopause precede changes in CIMT.

Coronary heart disease is a ruthless killer of human health, and tertiary prevention and early prediction of coronary heart disease remain hot research topics. Regarding controllable high-risk factors for coronary heart disease, the Chinese Society of Cardiology clearly outlined management measures in the 2018 edition of the "Guidelines for the Diagnosis and Treatment of Stable Coronary Artery Disease," including lipid management, blood pressure management, blood glucose management in diabetic patients, physical exercise, weight management, smoking cessation, psychosocial factor management, and alcohol management.

Based on our study results, LDL-C, TC, and UA are all affected by menopausal status, and their changes precede CIMT changes. Therefore, for postmenopausal women, monitoring of LDL-C, TC, and UA levels should be emphasized, and effective management through diet, exercise, lifestyle modifications, and pharmacological control should be implemented to combat abnormal elevations in these indicators, thereby achieving the goal of preventing long-term cardiovascular disease. Additionally, for middle-aged women aged $ $50 years, regular CIMT monitoring is recommended to enable early identification and management of high-risk factors for coronary heart disease.

Author Contributions: YANG Mukun proposed the main research objectives, was responsible for study design and implementation, data statistics and figure/table production, and manuscript writing. JIA Xiaoxiang was responsible for data collection and management. RENG Zhenghong provided guidance on statistical methods and participated in study design. GU Bei was responsible for follow-up implementation and manuscript revision. BAI Wenpei was responsible for quality control and review of the article, took overall responsibility for the article, and provided supervision and management.

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

References

[1] THURSTON R C, KARVONEN-GUTIERREZ C A, DERBY C A, et al. Menopause versus chronologic aging: their roles in women's health[J]. Menopause, 2018, 25(8): 849-854. DOI: 10.1097/GME.0000000000001143.

[2] Chinese Menopause Society, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Chinese guidelines for menopause management

and menopausal hormone therapy (2023 edition)[J]. Chinese Journal of Obstetrics and Gynecology, 2023, 58(1): 4-21. DOI: 10.3760/cma.j.cn112141-20221118-00706.

[3] MALAKAR A K, CHOUDHURY D, HALDER B, et al. A review on coronary artery disease, its risk factors, and therapeutics[J]. J Cell Physiol, 2019, 234(10): 16812-16823. DOI: 10.1002/jcp.28350.

[4] Interventional Cardiology Group, Chinese Society of Cardiology, Chinese Medical Association; Atherosclerosis and Coronary Heart Disease Group, Chinese Society of Cardiology, Chinese Medical Association; Thrombosis Prevention and Treatment Committee, Chinese College of Cardiovascular Physicians, et al. Guidelines for the diagnosis and treatment of stable coronary artery disease[J]. Chinese Journal of Cardiology, 2018, 46(9): 680-694. DOI: 10.3760/cma.j.issn.0253-3758.2018.09.004.

[5] CHEN Zhongguo, ZHU Xiaoli, WAN Yuting, et al. Correlation analysis between carotid intima-media thickness and coronary heart disease[J]. Chinese Journal of Interventional Radiology (Electronic Edition), 2019, 7(1): 31-34. DOI: 10.3877/cma.j.issn.2095-5782.2019.01.006.

[6] LUO Lan, NIU Min, GAO Zhengnan. Correlation between central obesity, abnormal glucose metabolism and carotid intima-media thickness[J]. Chinese Journal of Diabetes, 2019, 11(3): 196-200. DOI: 10.3760/cma.j.issn.1674-5809.2019.03.007.

[7] CHEN Bo, YANG Wanyong, SHI Xinnian, et al. Discussion on the preventive role of carotid intima-media thickness detection in health checkups[J]. International Medicine and Health Guidance News, 2020, 26(3): 314-317. DOI: 10.3760/cma.j.issn.1007-1245.2020.03.006.

[8] Bureau of Disease Prevention and Control, National Health Commission; National Center for Cardiovascular Diseases; Fuwai Hospital, Chinese Academy of Medical Sciences, et al. Chinese hypertension health management specifications (2019)[J]. Chinese Journal of Cardiology, 2020, 48(1): 10-46. DOI: 10.3760/cma.j.issn.0253-3758.2020.01.004.

[9] CUI Linlin, CHEN Zijiang. Physiological effects and applications of estrogen[J]. Journal of Practical Obstetrics and Gynecology, 2010, 26(9): 641-643. DOI: 10.3969/j.issn.1003-6946.2010.09.001.

[10] Chinese Menopause Society, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Expert consensus on diagnosis and treatment of abnormal uterine bleeding in perimenopausal period[J]. Medical Journal of Peking Union Medical College Hospital, 2018, 9(4): 313-319. DOI: 10.3969/j.issn.1674-9081.2018.04.006.

[11] POWELL-WILEY T M, POIRIER P, BURKE L E, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association[J]. Circulation, 2021, 143(21): e984-e1010. DOI:

10.1161/CIR.0000000000000973.

[12] MATTHEWS K A, ABRAMS B, CRAWFORD S, et al. Body mass index in mid-life women: relative influence of menopause, hormone use, and ethnicity[J]. Int J Obes Relat Metab Disord, 2001, 25(6): 863-873. DOI: 10.1038/sj.ijo.0801618.

[13] SOWERS M, ZHENG H Y, TOMEY K, et al. Changes in body composition in women over six years at midlife: ovarian and chronological aging[J]. J Clin Endocrinol Metab, 2007, 92(3): 895-901. DOI: 10.1210/jc.2006-1393.

[14] FRANKLIN R M, PLOUTZ-SNYDER L, KANALEY J A. Longitudinal changes in abdominal fat distribution with menopause[J]. Metabolism, 2009, 58(3): 311-315. DOI: 10.1016/j.metabol.2008.09.030.

[15] YU W, CHENG J D. Uric acid and cardiovascular disease: an update from molecular mechanism to clinical perspective[J]. Front Pharmacol, 2020, 11: 582680. DOI: 10.3389/fphar.2020.582680.

[16] TANAKA K, KABAYAMA M, SUGIMOTO K, et al. Association between uric acid and atherosclerosis in community-dwelling older people: the SONIC study[J]. Geriatr Gerontol Int, 2021, 21(1): 94-101. DOI: 10.1111/ggi.14081.

[17] WILLEIT P, TSCHIDERER L, ALLARA E, et al. Carotid intima-media thickness progression as surrogate marker for cardiovascular risk: meta-analysis of 119 clinical trials involving 100,667 patients[J]. Circulation, 2020, 142(7): 621-642. DOI: 10.1161/CIRCULATIONAHA.120.046361.

[18] IEAMTAIRAT P, SOONTRAPA S, KAEWRUDEE S, et al. Difference in carotid intima-media thickness between pre and postmenopausal women[J]. Menopause, 2019, 26(1): 39-44. DOI: 10.1097/GME.0000000000001159.

[19] ZHANG Ying, DU Xin, LI Jie, et al. Correlation analysis between serum high-sensitivity C-reactive protein level and carotid intima-media thickness[J]. Clinical Medicine of China, 2021, 37(1): 26-30. DOI: 10.3760/cma.j.cn101721-20200712-00010.

(Received: June 1, 2023; Revised: August 2, 2023)
(This article was edited by KANG Yanhui)

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