

Associations of Demographic and Menopause-Related Characteristics with SCORE2 Cardiovascular Risk Among Women Aged 45 to 55 Years: A Retrospective Analysis

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Cite as: Can S, Hocaoglu M, Demircivi E, et al. Associations of Demographic and Menopause-Related Characteristics with SCORE2 Cardiovascular Risk Among Women Aged 45 to 55 Years: A Retrospective Analysis. *J Cukurova Anesth Surg.* 2026;9(3):1148-1154. doi: 10.36516/jocass.2041730

Received: 17.09.2026, **Accepted:** 28.09.2026, **Published:** 30.09.2026, CC BY-NC 4.0

Abstract

Objectives: Menopause-related symptoms and hormonal changes may influence cardiovascular risk. We assessed demographic and menopause-related characteristics associated with SCORE2 risk in women aged 45–55 years. **Materials and Methods:** This retrospective observational study included 192 women. The primary outcome was SCORE2 cardiovascular risk (%). Prespecified predictors were postmenopausal status and vasomotor symptoms, with education modeled as an ordinal variable and BMI, parity, follicle stimulating hormone (FSH), and estradiol (E2) included as covariates. SCORE2 components were not entered as predictors because they are used to calculate SCORE2. Continuous variables were summarized as mean (standard deviation) or median (interquartile range), and categorical variables as n/N (percent%). Multivariable linear regression and Spearman rank correlations were performed using a complete case approach. **Results:** Median age was 50.0 (48.0 to 52.0) years and median SCORE2 risk was 3.2 (2.1 to 5.0). Current smoking was present in 63/192 (32.8%), and 129/192 (67.2%) participants were postmenopausal. SCORE2 risk categories were low to moderate in 117/192 (60.9%), high in 58/192 (30.2%), and very high in 17/192 (8.9%). In multivariable regression, postmenopausal status (beta 0.542, 95% CI –0.633 to 1.717) and vasomotor symptoms (beta 0.689, 95% CI –0.162 to 1.540) were not significantly associated with SCORE2 risk (%). Spearman correlations were weak for vasomotor symptoms (rho 0.154) and postmenopausal status (rho 0.152). **Conclusion:** Among women aged 45 to 55 years, demographic and menopause-related characteristics showed weak crude correlations with SCORE2 risk and were not independently associated with SCORE2 risk in multivariable models.

Keywords: menopause; hot flashes; cardiovascular diseases

1. Introduction

Menopause is a key midlife transition and reflects permanent cessation of menstruation due to loss of ovarian follicular activity. This transition is accompanied by changes in gonadotropins and sex steroid hormones. The timing of menopause is clinically relevant

because the transition may coincide with changes in vascular and metabolic function that can influence cardiovascular risk¹.

Menopause most often occurs around 51 years of age, and most women have their final menstrual period between 45 and 55 years². This places the 45 to 55 age interval within the typical window for the menopausal transition and early postmenopause, a period when menopausal symptoms are common and when cardiometabolic risk factors may begin to cluster³. Vasomotor symptoms, particularly hot flushes and night sweats, are among the most frequent manifestations of the menopausal transition. Recent studies suggest that vasomotor symptoms may be linked to a less favorable cardiovascular profile and to markers of subclinical vascular disease, although reported effects are typically small and depend on how symptoms are measured⁴.

For primary prevention, accurate estimation of future cardiovascular risk is essential to guide intensity of lifestyle and pharmacologic interventions. The European Society of Cardiology 2021 prevention guideline introduced SCORE2 as an updated risk estimation system that predicts the 10 year risk of cardiovascular disease in apparently healthy individuals within the validated age range. SCORE2 uses sex, age, smoking status, systolic blood pressure, total cholesterol, and high-density lipoprotein (HDL) cholesterol, and it is calibrated to regional baseline risk to support risk stratification and clinical decision making⁵.

Despite increasing interest in the cardiovascular implications of menopause related characteristics, data remain limited on how demographic and menopause related characteristics relate to SCORE2 estimated risk specifically in women within the typical menopausal age window. Therefore, we aimed to evaluate associations between demographic and menopause related characteristics, including education level, menopausal status, vasomotor symptoms, and sex hormone levels, and SCORE2 cardiovascular risk among women aged 45 to 55 years.

2. Materials and Methods

We performed a retrospective observational analysis in the gynecology clinic of a tertiary care hospital. The study protocol was reviewed and approved by the Istanbul Medipol University Non-Interventional Clinical Research Ethics Committee (Date: 05.03.2026, Approval No: 405). Informed consent to participate was obtained from all participants. All procedures were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the Declaration of Helsinki.

Women aged 45 to 55 years were eligible for inclusion. Postmenopause was defined as the absence of menstruation for 12 consecutive months. Hormonal levels and STRAW+10 staging were not used as additional criteria for defining postmenopause. In premenopausal women, FSH and E2 levels were measured on day 3 of the menstrual cycle. Participants were excluded if they had a history of systemic disease such as diabetes. Participants receiving any medical treatment, including menopausal hormone therapy, antihypertensive medication, or lipid-lowering medication, were excluded from the study. Participants with systemic conditions such as hypertension, hyperlipidemia, diabetes, thyroid disorders, or cancer were also excluded.

Clinical and laboratory information was retrieved from medical records. We recorded age, body mass index (BMI), parity, smoking status, education level, menopausal status, follicle-stimulating hormone (FSH), estradiol (E2), HDL, total cholesterol, systolic and diastolic blood pressure, SCORE2 cardiovascular risk (%), and SCORE2 risk category. Education was grouped into four ordered levels (illiterate, primary school, high school, and university) and was handled as an ordinal variable in regression models. SCORE2 risk category was classified as low to moderate, high, and very high, based on the SCORE2 percentage category recorded in the dataset.

The primary outcome was SCORE2 cardiovascular risk (%). SCORE2 is derived from sex, age, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, and regional calibration. Because these variables constitute the SCORE2 calculation, they were not entered as predictors in multivariable models where SCORE2 risk (%) was the dependent variable.

Normality of continuous variables was assessed using Shapiro–Wilk and Kolmogorov–Smirnov tests. As normality assumptions were frequently not met, continuous variables were generally summarized as median and interquartile range (IQR), and compared between groups using the Mann–Whitney U test. When normality assumptions were satisfied, mean and standard deviation (SD) were reported and comparisons were performed using the independent samples t test. Categorical variables were summarized as numerator/denominator (percentage%) and compared using the Chi-square test and Fisher exact test.

We used multivariable linear regression with SCORE2 risk (%) as a continuous outcome. The prespecified predictors were postmenopausal status and vasomotor symptoms, and covariates included education level, BMI, parity, FSH, and E2. A complete-case approach was applied ($n = 192$).

Crude associations between SCORE2 risk (%) and candidate predictors were also explored using Spearman rank correlations.

All analyses were conducted using SPSS v27 (SPSS Inc., Chicago, Illinois, USA), and statistical significance was defined as a p value below 0.05.

3. Results

A total of 192 women aged 45 to 55 years were included in the analysis. The median age was 50.0 (48.0 to 52.0) years, and the median BMI was 26.85 (24.0 to 30.0) kg/m^2 . The median parity was 2.0 (2.0 to 3.0). Current smoking was present in 63/192 (32.8%). Education level was distributed as 9/192 (4.7%) illiterate, 100/192 (52.1%) primary school, 37/192 (19.3%) high school, and 46/192 (24.0%) university. Overall, 129/192 (67.2%) participants were postmenopausal. Median FSH was 53.35 (27.78 to 80.18), and median estradiol (E2) was 14.55 (5.32 to 47.15). The median HDL was 56.0 (49.75 to 63.0), and mean total cholesterol was 218.38 (32.0). Median systolic and diastolic blood pressures were 139.0 (132.75 to 144.0) mmHg and 87.0 (84.0 to 90.0) mmHg, respectively. The median SCORE2 risk was 3.2% (2.1% to 5.0%). SCORE2 risk categories were low to moderate in 117/192 (60.9%), high in 58/192 (30.2%), and very high in 17/192 (8.9%) (Table 1).

Table 1. Demographic and Clinical Characteristics of the Participants

Variable	Summary
Age (years)	50.0 (48.0, 52.0)
BMI (kg/m^2)	26.85 (24.0, 30.0)
Parity	2.0 (2.0, 3.0)
Smoking	63/192 (32.8%)
Education Level	
Illiterate	9/192 (4.7%)
Primary school	100/192 (52.1%)
High school	37/192 (19.3%)
University	46/192 (24.0%)
Postmenopausal	129/192 (67.2%)
FSH (mIU/mL)	53.35 (27.78, 80.18)
E2 (pg/mL)	14.55 (5.32, 47.15)

Variable	Summary
HDL (mg/dL)	56.0 (49.75, 63.0)
Total Cholesterol (mg/dL)	218.38 (32.0)
Systolic Blood Pressure (mmHg)	139.0 (132.75, 144.0)
Diastolic Blood Pressure (mmHg)	87.0 (84.0, 90.0)
SCORE2 Risk (%)	3.2 (2.1, 5.0)
Risk Category	
Low to moderate	117/192 (60.9%)
High	58/192 (30.2%)
Very high	17/192 (8.9%)

body mass index (BMI), follicle-stimulating hormone (FSH), estradiol (E2), high-density lipoprotein cholesterol (HDL)

In multivariable linear regression with SCORE2 risk (%) as a continuous outcome, none of the prespecified predictors showed a statistically significant association with SCORE2 risk (Table 2). Postmenopausal status (beta 0.542, 95% CI -0.633 to 1.717, $p=0.3659$) and vasomotor symptoms (beta 0.689, 95% CI -0.162 to 1.540, $p=0.1126$) were not significantly associated with SCORE2 risk. Similarly, education level, BMI, parity, FSH, and estradiol were not significantly associated with SCORE2 risk in the adjusted model.

Table 2. Associations with SCORE2 risk (%) (Multivariable linear regression)

Predictor	Beta	CI	p
Intercept	3,873	(0.536, 7.209)	0.0229
Postmenopausal status	0,542	(-0.633, 1.717)	0.3659
Vasomotor symptom	0,689	(-0.162, 1.54)	0.1126
Education Level	0,052	(-0.419, 0.524)	0.8274
BMI (kg/m ²)	-0,023	(-0.109, 0.064)	0.6087
Parity	0,049	(-0.248, 0.347)	0.7456
FSH (mIU/mL)	-0,003	(-0.016, 0.009)	0.6046
E2 (pg/mL)	-0,002	(-0.009, 0.006)	0.6607

body mass index (BMI), follicle-stimulating hormone (FSH), estradiol (E2)

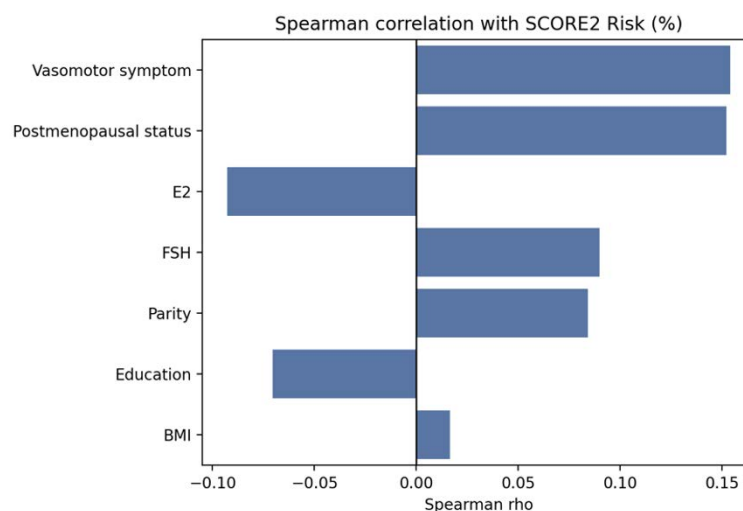


Figure 1. Crude bivariate relationships between SCORE2 risk (%) and candidate predictors (Spearman rank correlation coefficients)

In Spearman correlation analyses (Figure 1), SCORE2 risk (%) showed a weak positive correlation with vasomotor symptoms ($\rho = 0.154$) and with postmenopausal status ($\rho = 0.152$). Estradiol (E2) exhibited a weak inverse correlation with SCORE2 ($\rho = -0.093$), whereas FSH was weakly positively correlated with SCORE2 ($\rho = 0.090$). Parity also demonstrated a weak positive correlation ($\rho = 0.084$). Education level was very weakly negatively correlated with SCORE2 ($\rho = -0.070$). The correlation between BMI and SCORE2 was negligible ($\rho = 0.017$).

4. Discussion

In this retrospective study of 192 women aged 45 to 55 years, SCORE2 cardiovascular risk showed only weak crude correlations with vasomotor symptoms and postmenopausal status. In multivariable linear regression models that included postmenopausal status, vasomotor symptoms, education level, BMI, parity, FSH, and estradiol, none of these variables was independently associated with SCORE2 risk percentage. Overall, our findings suggest that, within this age range, demographic and menopause related characteristics were not strongly associated with SCORE2 risk percentage.

Menopause is linked to cardiometabolic changes, and cardiovascular risk factors often worsen across the menopausal transition. The American Heart Association scientific statement highlights that blood pressure, lipids, body composition, and other risk factors can change during the transition, and that this period may be important for early prevention¹. Our study focused on women in the typical menopausal age window, but we did not observe a clear independent association of menopausal status with SCORE2 in multivariable models. One explanation is that SCORE2 already includes major conventional risk factors and is strongly driven by them, so additional menopause related variables may add limited value, especially in this age range.

Vasomotor symptoms have been linked in several studies and reviews to a less favorable cardiovascular risk factor profile and to subclinical cardiovascular disease, although effect sizes are often modest and findings vary by population and symptom characterization⁴. In population based research, van den Berg et al. examined whether an unfavorable cardiovascular risk profile was a risk factor for later vasomotor symptoms, supporting the concept that symptom reporting and cardiovascular risk can cluster, although the direction of association and causal pathways remain uncertain⁶. Recent reviews that synthesize findings from cohorts such as SWAN and studies including MsHeart and MsBrain suggest that vasomotor symptoms may be associated with a less favorable cardiovascular risk factor profile and with markers of subclinical vascular disease⁷. However, these associations are generally small and appear sensitive to how symptoms are measured. In our data, vasomotor symptoms showed a weak positive crude correlation with SCORE2, but this association did not remain significant in multivariable analyses. This pattern is consistent with a situation where vasomotor symptoms correlate with conventional risk factors that are already included in risk estimation and may not provide a strong independent contribution in this setting.

Armeni and colleagues conducted a systematic review and meta-analysis evaluating the association between vasomotor symptoms and future cardiovascular events in peri- and postmenopausal women⁸. The meta-analysis pooled 11 prospective studies and one key finding was that the association varied by age. The authors reported that vasomotor symptoms were associated with a higher risk of incident cardiovascular events particularly among women younger than 60 years at baseline, whereas the association was not clearly observed in older women. This suggests that vasomotor symptoms may act as a risk marker during the menopausal years, although the magnitude of the association

appears limited and may differ across populations. In our study, we focused on this higher relevance age window; however, we did not identify a statistically significant association between vasomotor symptoms and cardiovascular risk as estimated by SCORE2 in multi-variable models.

In the literature, Zhu and colleagues performed a pooled analysis of six prospective studies to examine vasomotor menopausal symptoms and incident cardiovascular disease⁹. They reported that symptom severity, rather than frequency, showed the most consistent association with cardiovascular disease risk. In adjusted models, frequent hot flashes were not clearly associated with incident cardiovascular disease, whereas more severe symptoms were linked to higher risk, and both early onset and late onset vasomotor symptoms were also associated with increased cardiovascular disease risk. Because symptom severity was not available in our dataset, we were unable to examine whether more severe vasomotor symptoms are more strongly related to cardiovascular risk.

Earlier population-based studies have examined whether vasomotor symptoms are linked to cardiovascular risk factors and whether estradiol levels help explain these links. In a large cohort, women reporting vasomotor symptoms had a less favorable cardiovascular risk profile, and estradiol levels were lower among symptomatic women. However, the difference in cardiovascular risk factors was not fully explained by circulating estradiol, suggesting that estradiol alone is unlikely to be the main pathway and that other factors, such as adiposity, aging, and unmeasured cardiometabolic mechanisms, may contribute¹⁰. In our cohort, crude correlations between SCORE2 risk (%) and vasomotor symptoms as well as postmenopausal status were weakly positive, whereas estradiol was weakly inversely correlated with SCORE2. These directions are broadly consistent with prior observations that menopausal symptoms and hormone levels may track with cardiovascular risk, but the magnitude of associations tends to be small.

This study has several strengths. We examined a clinically relevant age window that covers the usual period of menopausal transition and early postmenopause, and we evaluated multiple menopause related characteristics, including symptoms and hormone levels, together with SCORE2 risk. We also used prespecified models and standardized reporting of categorical variables.

Limitations should be considered. The retrospective design limits control over measurement and completeness of data. The sample size may have limited power to detect small associations. The age range was intentionally narrow, which improves comparability but reduces variability in SCORE2. Additionally, SCORE2 is a risk estimation tool rather than a measure of observed cardiovascular events, so our findings reflect associations with estimated risk, not clinical outcomes. When SCORE2 risk (%) is used as the dependent variable, it is methodologically appropriate not to reintroduce the SCORE2 components into the regression model. However, this approach also makes it more difficult to demonstrate associations of menopause related characteristics with SCORE2, because SCORE2 is already strongly driven by conventional risk factors that are embedded in the score.

5. Conclusion

Among women aged 45 to 55 years, demographic and menopause related characteristics showed only weak crude correlations with SCORE2 risk, and none was independently associated with SCORE2 risk (%) in multivariable models. These findings suggest that, in this midlife age window, menopause related characteristics may have limited additional value for explaining SCORE2 estimated cardiovascular risk beyond the conventional risk factors that SCORE2 already incorporates. Further studies with larger samples, prospective symptom assessment, and longitudinal follow-up are needed to clarify

whether specific menopausal features add predictive value for cardiovascular risk stratification.

Author Contribution: SC was responsible for the conceptualization, study design, data analysis, and manuscript writing. SC and MH participated in the study design, manuscript writing, supervision, and critical review of the manuscript. SC, ED, BK, CSO, NK, and ST contributed to data collection. MH and AT contributed to the critical review of the manuscript. All authors read and approved the final version of the manuscript.

Funding: The authors received no funding for this study.

Conflicts of interests: The authors declare that they have no competing interests.

Ethics approval and consent to participate: The study was approved by the local ethics committee (Date: 05.03.2026, Approval no: 405). The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant guidelines and regulations.

Informed consent statement: Informed consent to participate was obtained from all participants.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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