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Original Article

Association Between Menopause Duration and Lesion Complexity in Chronic Total Occlusion: An Evaluation Using the Japanese-Chronic Total Occlusion Score

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Abstract

Objective: The decline in estrogen levels in menopause accelerates atherosclerosis through endothelial dysfunction, inflammation, and metabolic alterations. This process may contribute to increased cardiovascular risk in the postmenopausal period and to the development of more advanced coronary lesions. The J-CTO score is a widely used tool for assessing chronic total occlusion (CTO) lesion complexity and predicting procedural success. This study aimed to evaluate the association between menopause duration and CTO lesion complexity using the Japanese CTO (J-CTO) score.

Methods: This retrospective observational study included 60 postmenopausal women with known menopausal status who underwent percutaneous coronary intervention for CTO at a tertiary center between January 2021 and December 2025. Patients were categorized into two groups according to J-CTO score: Low complexity (J-CTO <2) and high complexity (J-CTO ≥2). Demographic, clinical, laboratory, and angiographic data were obtained from hospital records. Missing data regarding menopausal age, duration of menopause, and obstetric history were completed by telephone interviews. The relationship between menopausal characteristics and J-CTO score was evaluated.

Results: Of the 60 patients included in the study, 32 (53.3%) had low-complexity CTO lesions and 28 (46.7%) had high-complexity CTO lesions. There were no significant differences between the groups in age, body mass index, menopausal age, duration of menopause, or parity (p>0.05). Although menopause duration tended to be longer in the high-complexity group, the difference did not reach statistical significance (20.5 vs. 15, p=0.094). The high-complexity group had significantly higher rates of diabetes mellitus (p=0.039), hyperlipidemia (p=0.031), previous coronary artery disease (p=0.007), and prior CABG (p=0.034). Hemoglobin levels were lower (p=0.038), while urea and creatinine levels were higher p<0.001), and glomerular filtration rate was lower (p<0.001) in the high-complexity group. Angiographically, CTO length >20 mm (p=0.006), presence of calcification (p=0.048), and blunt stump morphology (p=0.012) were more frequent in the high-complexity group. Procedural success was significantly lower in the high-complexity group (p=0.041). Correlation analysis showed no significant association between menopausal age or menopause duration and J-CTO score.

Conclusion: In this cohort of women with CTO, menopausal age and menopause duration were not significant determinants of CTO lesion complexity. Rather, lesion complexity was more closely associated with traditional cardiovascular risk factors, impaired renal function, and adverse angiographic characteristics. Although our study did not demonstrate a statistically significant association between menopause duration and CTO lesion complexity, the observed trend toward longer menopause duration in the high-complexity group may still be clinically relevant.

Keywords: Chronic total occlusion; coronary artery disease; J-CTO score; lesion complexity; menopause.

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Menopoz Süresi ile Kronik Total Oklüzyon Lezyon Kompleksitesi Arasindaki İlişki: J-CTO Skoru Üzerinden Değerlendirme

Özet

Amaç: : Menopoz ile birlikte östrojen düzeylerinde meydana gelen azalma, endotelyal disfonksiyon, inflamasyon ve metabolik değişiklikler yoluyla aterosklerotik süreci hızlandırmaktadır. Bu süreç, postmenopozal dönemde kardiyo-

vasküler riskte artışa ve daha ileri koroner arter lezyonlarının gelişimine katkıda bulunabilir. Kronik total oklüzyon (CTO) lezyon kompleksitesinin değerlendirilmesinde yaygın olarak kullanılan J-CTO skoru, girişimsel başarıyı öngörmede önemli bir parametredir. Bu çalışmada, menopoz süresi ile CTO lezyon kompleksitesi arasındaki ilişkinin J-CTO skoru kullanılarak değerlendirilmesi amaçlanmıştır.

Yöntem: Bu retrospektif gözlemsel çalışmaya, Ocak 2021–Aralık 2025 tarihleri arasında üçüncü basamak bir merkezde CTO nedeniyle perkütan koroner girişim uygulanan hastalar arasından menopozal durumu bilinen 60 postmenopozal kadın hasta dahil edildi. Hastalar, J-CTO skoruna göre düşük kompleksite (J-CTO<2) ve yüksek kompleksite (J-CTO ≥ 2) olmak üzere iki gruba ayrıldı. Demografik, klinik, laboratuvar ve anjiyografik veriler hastane kayıt sisteminden elde edildi. Menopoz yaşı, menopoz süresi ve obstetrik öyküye ilişkin eksik veriler telefon görüşmeleri ile tamamlandı.

Bulgular: Çalışmaya dahil edilen 60 hastanın 32'sinde (%53,3) düşük kompleksiteli, 28'inde (%46,7) yüksek kompleksiteli CTO lezyonu saptandı. Yaş, vücut kitle indeksi, menopoz yaşı, menopoz süresi ve parite açısından gruplar arasında anlamlı fark izlenmedi (p>0,05). Yüksek kompleksite grubunda menopoz süresi daha uzun olma eğiliminde olmakla birlikte, bu fark istatistiksel anlamlılığa ulaşmadı (20,5 vs. 15 yıl; p=0,094). Yüksek kompleksite grubunda diyabetes mellitus (p=0,039), hiperlipidemi (p=0,031), koroner arter hastalığı öyküsü (p=0,007) ve CABG öyküsü (p=0,034) daha sık saptandı. Bu grupta ayrıca hemoglobin düzeyi daha düşük (p=0,038), üre ve kreatinin düzeyleri daha yüksek (p<0,001), glomerüler filtrasyon hızı ise daha düşüktü (p<0,001). Anjiyografik olarak CTO uzunluğu >20 mm (p=0,006), kalsifikasyon varlığı (p=0,048) ve künt stump morfolojisi (p=0,012) yüksek kompleksite grubunda daha sıktı. Prosedürel başarı oranı yüksek kompleksite grubunda anlamlı olarak daha düşüktü (p=0,041). Korelasyon analizinde menopoz yaşı ve menopoz süresi ile J-CTO skoru arasında anlamlı ilişki saptanmadı.

Sonuç: CTO'lu kadın hastalardan oluşan bu kohortta menopoz yaşı ve menopoz süresi, CTO lezyon kompleksitesinin anlamlı belirleyicileri olarak saptanmamıştır. Buna karşılık, lezyon kompleksitesi daha çok geleneksel kardiyovasküler risk faktörleri, bozulmuş renal fonksiyon ve olumsuz anjiyografik özellikler ile ilişkili bulunmuştur. Yüksek kompleksite grubunda menopoz süresinin daha uzun olma eğilimi göstermesi, bu ilişkinin klinik açıdan anlamlı olabileceğini düşündürmektedir.

Anahtar sözcükler: Kronik total oklüzyon; koroner arter hastalığı; J-CTO skoru; lezyon kompleksitesi; menopoz.

Introduction

Cardiovascular diseases continue to represent a major global health burden and remain among the leading causes of death and disability worldwide.[1] Sex-related differences influence the clinical manifestation, diagnosis, and outcomes of coronary artery disease, and women are frequently underdiagnosed or treated later than men in routine clinical practice.[2,3]

Menopause reflects the permanent cessation of ovarian function and is clinically recognized after 12 consecutive months without menstruation. The reduction in endogenous estrogen exposure accompanying menopause has been associated with multiple adverse vascular and metabolic effects. Previous evidence has demonstrated that premature menopause, early menopause, and surgically induced menopause are linked to increased rates of coronary artery disease, cerebrovascular events, heart failure, arrhythmias, and cardiovascular mortality. Several mechanisms have been proposed to explain this association, including endothelial dysfunction, oxidative stress, inflammatory activation, impaired vascular repair mechanisms, and unfavorable alterations in glucose and lipid metabolism.[4–6] Through these pathways, prolonged estrogen deficiency may facilitate progressive atherosclerotic burden and contribute to the formation of more advanced coronary lesions.

Chronic total occlusion (CTO) describes the complete interruption of antegrade coronary blood flow for a duration exceeding 3 months and is encountered in a considerable proportion of patients with established coronary artery disease.[7,8] CTO lesions are generally regarded as one of the most complex manifestations of coronary atherosclerosis because they are associated with increased procedural difficulty and lower interventional success rates.[9] Nevertheless, contemporary developments in guidewire technology, revascularization strategies, and operator experience have substantially improved CTO percutaneous coronary intervention (PCI) outcomes over recent years.[10–12] To estimate anatomical difficulty before intervention, the Japanese CTO (J-CTO) score has become one of the most frequently utilized scoring systems in contemporary practice.[13]

Although the relationship between menopause and cardiovascular risk has been investigated extensively, limited information is available regarding the potential association between menopausal duration and CTO lesion complexity. Moreover, whether prolonged estrogen deprivation contributes to more anatomically challenging CTO lesions remains unclear. Therefore, the present study aimed to examine the relationship between menopausal duration and lesion complexity assessed by the J-CTO scoring system.[14,15]

Materials and Methods

This single-center retrospective study evaluated consecutive patients who underwent PCI for CTO lesions between January 2021 and December 2025 at a tertiary referral institution. Among 300 screened patients, 60 postmenopausal women with available menopausal history and complete clinical datasets were included in the final study population (Fig. 1).

Patients with severe systolic heart failure (left ventricular ejection fraction <30%), advanced hepatic or renal dysfunction, active malignancy, systemic inflammatory disorders, or incomplete medical records were not eligible for inclusion.

Information regarding menopausal age and total menopausal duration was obtained from hospital databases and patient interviews. Menopause was accepted as a permanent cessation of menstruation lasting at least 12 months. To avoid potential hormonal confounding, patients receiving hormone replacement therapy were excluded. According to lesion complexity determined by the J-CTO score, participants were categorized into low-complexity (J-CTO <2) and high-complexity (J-CTO ≥2) groups.

Clinical characteristics, angiographic findings, and laboratory measurements were retrieved from the institutional electronic

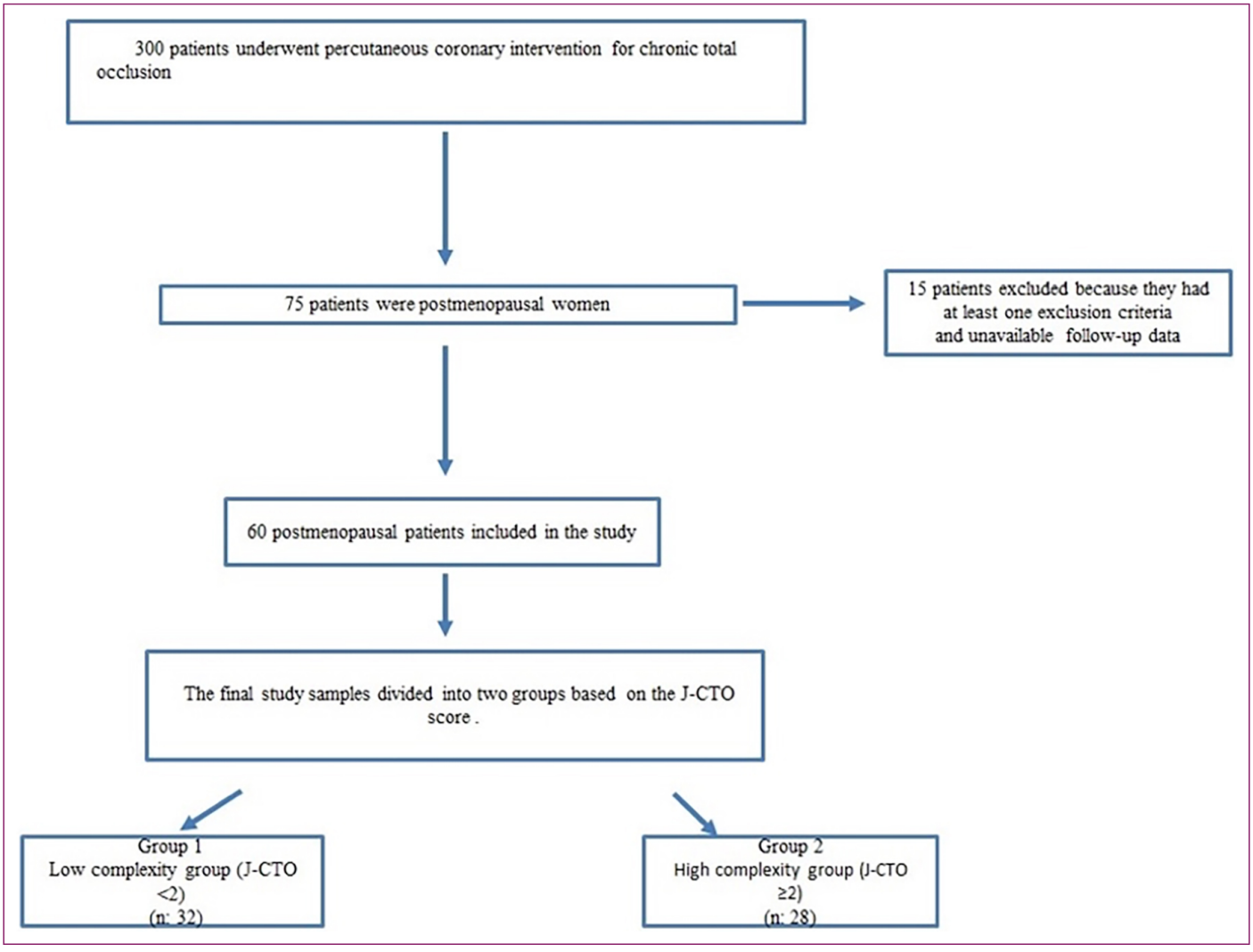

Figure 1. Consort diagram of the study.

J-CTO: Japanese chronic total occlusion score.

medical record system. Venous blood samples were collected after overnight fasting within 24 h before the procedure. Standard laboratory techniques routinely used in our institution were applied for biochemical and hematological analyses. When menopausal variables or reproductive history were missing in hospital records, additional information was obtained through structured telephone interviews.

Coronary Angiography and CTO Definition

Diagnostic coronary angiography was performed using standard femoral or radial techniques according to operator preference. Multiple angiographic views were acquired for a comprehensive assessment of both coronary systems. CTO was defined as a complete interruption of antegrade coronary flow with thrombolysis in myocardial infarction (TIMI) grade 0 perfusion and estimated occlusion duration longer than 3 months. Collateral circulation was graded according to the Rentrop classification, and grades 2–3 were considered indicative of advanced collateral development.

Determination of CTO Complexity

CTO anatomical complexity was evaluated using the J-CTO scoring algorithm. The score was calculated based on five angiographic characteristics: Blunt proximal cap, severe calcification, vessel bending >45°, occlusion length >20 mm, and previous failed CTO intervention. Each parameter contributed one point to the total score, resulting in values ranging from 0 to 5. Higher scores represented increasing procedural complexity. Angiographic analyses were independently reviewed by two experienced interventional cardiologists blinded to patient-related clinical data. Disagreements were resolved by consensus evaluation.

CTO PCI

The interventional strategy, including antegrade or retrograde crossing technique, guidewire escalation, and adjunctive device selection, was left to the operator's discretion. Drug-eluting stents were implanted following successful recanalization. Technical success was defined as restoration of TIMI grade 3 flow with residual stenosis below 30%.

Table 1. Baseline demographic, menopausal, and clinical characteristics according to J-CTO score

Demographic and menopausal characteristics					
Variables	**Low complexity (J-CTO <2) (n=32) Median (5th–95th percentile)**		**High complexity (J-CTO ≥2) (n=28) Median (5th–95th percentile)**		**p**
	n	**%**	**n**	**%**	
Age, years	63 (51–79)		69 (52–78)		0.121
BMI (kg/m²)	26 (21–34)		28 (22–35)		0.268
Menopausal age, years	49 (38–54)		47 (42–55)		0.582
Duration of menopause, years	15 (1–29)		20.5 (0–31)		0.094
Parity	3 (1–6)		3 (1–7)		0.471
Clinical characteristics					
Menopause <50 years	18	56.3	18	64.3	0.526
Hypertension	24	75.0	26	92.9	0.064
Diabetes mellitus	17	53.1	22	78.6	**0.039**
Hyperlipidemia	21	65.6	25	89.3	**0.031**
Smoking history	7	33.3	1	5.9	**0.039**
Coronary artery disease	17	53.1	24	85.7	**0.007**
Previous PCI (stent)	13	40.6	17	60.7	0.121
CABG history	4	12.5	10	35.7	**0.034**
Peripheral artery disease	5	15.6	6	21.4	0.562

Mann–Whitney U test, Chi-square test, p<0.05. BMI: Body mass index; CABG: Coronary artery bypass grafting; J-CTO: Japanese chronic total occlusion score; PCI: Percutaneous coronary intervention.

Statistical Analysis

Statistical evaluation was performed using the Statistical Package for the Social Sciences software (version 26.0; IBM Corporation, Armonk, New York, USA). Distribution patterns of numerical variables were assessed before analysis. Since most variables demonstrated skewed distribution and the study population was limited in size, continuous data were reported using median values together with percentile ranges (5th–95th percentile). Discrete variables were presented as counts and corresponding percentages.

Patients were categorized according to lesion difficulty as low J-CTO (<2) or high J-CTO (≥2). Intergroup comparisons for continuous measurements were carried out with the Mann–Whitney U method. For categorical variables, Pearson Chi-square analysis or Fisher's exact method was preferred depending on cell distribution characteristics.

The relationship of menopausal variables with CTO complexity was additionally explored using Spearman's rho correlation coefficient. Independent determinants associated with higher lesion complexity were examined by binary logistic regression analysis. Because menopausal age and menopause duration were considered potentially interrelated variables, separate multivariable models were generated for each parameter. Diabetes mellitus, hypertension, hyperlipidemia, and glomerular filtration rate were included in the adjustment models. Probability values below 0.05 were interpreted as indicating statistical significance.

Ethics Approval

The study was approved by the Kartal Koşuyolu Training and Research Hospital Local Ethics Committee (Date: 24.04.2026, Decision no: 2026/08/1444) and conducted in accordance with the Declaration of Helsinki.

Results

The final study consisted of 60 postmenopausal women undergoing CTO intervention. Of these, 32 (53.3%) had low-complexity CTO lesions (J-CTO <2), while 28 (46.7%) had high-complexity CTO lesions (J-CTO ≥2). In the overall cohort, the median age was 65 years, the median age at menopause was 49 years, and the median duration of menopause was 17.5 years. Procedural success was achieved in 44 patients (73.3%). There were no significant differences between the low- and high-complexity groups in terms of age, body mass index, age at menopause, duration of menopause, or parity (p>0.05). Although menopause duration tended to be longer in the high-complexity group, this difference did not reach statistical significance (20.5 vs. 15, p=0.094). In terms of clinical characteristics, diabetes mellitus (78.6% vs. 53.1%, p=0.039), hyperlipidemia (89.3% vs. 65.6%, p=0.031), coronary artery disease (85.7% vs. 53.1%, p=0.007), and prior CABG (35.7% vs. 12.5%, p=0.034) were significantly more prevalent in the high-complexity group. No significant differences were observed in hypertension, previous PCI, or peripheral artery disease (all p>0.05) (Table 1).

No significant differences were observed between the groups in white blood cell, neutrophil count, lymphocyte count, platelet count, glucose, uric acid, albumin, alanine aminotransferase, lipid parameters, C-reactive protein, or left ventricular ejection fraction (p>0.05). However, hemoglobin levels were significantly lower in the high-complexity group (11.85 vs.

Table 2. Laboratory and angiographic characteristics according to J-CTO score

Variables	Laboratory findings				p
	Low complexity (J-CTO <2) (n=32) Median (5th–95th percentile)		High complexity (J-CTO ≥2) (n=28) Median (5th–95th percentile)		
	n	%	n	%	
Hemoglobin (g/dL)	12.7 (9.5–14.5)		11.85 (10–14)		**0.038**
WBC (×10³/μL)	8.0 (5.0–12.59)		7.35 (5.1–11.6)		0.335
Platelet (×10³/μL)	254 (151–414)		253.5 (143–382)		0.722
Neutrophil (×10³/μL)	5.23 (2.85–9.54)		4.80 (3.20–7.86)		0.865
Lymphocyte (×10³/μL)	2.15 (1.0–3.1)		1.80 (0.9–2.7)		0.101
Glucose (mg/dL)	126.5 (90–358)		141 (78–374)		0.836
Uric acid (mg/dL)	4.7 (2.8–8.0)		5.3 (3.3–7.1)		0.116
Albumin (g/dL)	42 (38–48)		42 (36–48)		0.957
Urea (mg/dL)	32.5 (21–54.7)		42.9 (27–70)		**<0.001**
Creatinine (mg/dL)	0.75 (0.51–1.33)		0.97 (0.69–1.75)		**<0.001**
GFR (mL/min)	82 (37–111)		62.5 (29–92)		**<0.001**
ALT (U/L)	13.5 (8–66)		13 (5–22)		0.401
LDL-C (mg/dL)	122 (75–196)		99 (30–190)		0.094
HDL-C (mg/dL)	49 (35–66)		45 (34–72)		0.280
Triglycerides (mg/dL)	184 (93–311)		199 (90–446)		0.887
Total cholesterol (mg/dL)	211.5 (144–306)		191 (111–312)		0.115
CRP (mg/L)	4.34 (0.70–24)		6.29 (0.73–45)		0.086
LVEF (%)	65 (35–65)		55 (35–65)		0.225
Angiographic characteristics					
Target vessel (LAD)	12	37.5	13	46.4	0.48
Target vessel (RCA)	14	43.7	14	50.0	0.62
Target vessel (Cx)	6	18.8	4	14.3	0.64
Rentrop grade 2–3 collateral	15	46.9	18	64.3	0.18
CTO length >20 mm	10	31.2	19	67.9	**0.006**
Presence of calcification	7	21.9	13	46.4	**0.048**
Vessel tortuosity >45°	4	12.5	8	28.6	0.11
Blunt stump	6	18.8	14	50.0	**0.012**
Prior failed attempt	3	9.4	7	25.0	0.10
Procedural success	27	84.4	17	60.7	**0.041**

Mann–Whitney U test, Chi-square test, p<0.05. ALT: Alanine aminotransferase; CRP: C-reactive protein; CTO: Chronic total occlusion; Cx: Circumflex artery; GFR: Glomerular filtration rate; HDL-C: High-density lipoprotein cholesterol; J-CTO: Japanese chronic total occlusion score; LAD: Left anterior descending artery; LDL-C: Low-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; RCA: Right coronary artery; WBC: White blood cell count.

12.70, p=0.038). Regarding renal function parameters, urea (42.9 vs. 32.5, p<0.001) and creatinine (0.97 vs. 0.75, p<0.001) levels were significantly higher, whereas glomerular filtration rate (GFR) was significantly lower (62.5 vs. 82.0, p<0.001) in the high-complexity group.

Angiographic assessment showed that lesion complexity-related features were significantly more common in the high J-CTO group. Specifically, CTO length >20 mm (67.9% vs. 31.2%, p=0.006), presence of calcification (46.4% vs. 21.9%, p=0.048), and blunt stump morphology (50.0% vs. 18.8%, p=0.012) were significantly more frequent in the high-complexity group. Vessel tortuosity >45° and prior failed attempt did not differ significantly between the groups (p>0.05). Target vessel distribution and collateral status were also similar between the groups. Procedural success was significantly lower in the high-complexity group (60.7% vs. 84.4%, p=0.041) (Table 2).

Correlation analysis showed no significant association between age at menopause and J-CTO score (rho=−0.072, p=0.584). Similarly, duration of menopause was not significantly correlated with J-CTO score (rho=0.077, p=0.560) (Table 3). Age at menopause was not independently associated with high CTO complexity (odds ratio [OR]: 0.957, 95% confidence interval [CI]: 0.823–1.111, p=0.562) (Table 4). Likewise, duration of menopause was not an independent predictor of high CTO complexity (OR: 1.008, 95% CI: 0.939–1.083, p=0.822) (Table 5). In both models, reduced GFR remained the only independent predictor of high CTO complexity (model 1: OR: 0.963, 95% CI: 0.934–0.993, p=0.015;

Table 3. Correlation analysis of menopausal variables and J-CTO score

Variables	Spearman's rho	p
Age at menopause versus J-CTO score	-0.072	0.584
Duration of menopause versus J-CTO score	0.077	0.560

J-CTO: Japanese chronic total occlusion score.

Table 4. Multivariable logistic regression analysis for predictors of high CTO complexity (model including age at menopause)

Variable	B	SE	Wald	p	OR	95% CI for OR
Age at menopause	-0.044	0.077	0.337	0.562	0.957	0.823–1.111
Diabetes mellitus	0.477	0.735	0.421	0.516	1.611	0.382–6.798
Hypertension	1.161	0.960	1.463	0.226	3.195	0.487–20.975
Hyperlipidemia	0.781	0.855	0.834	0.361	2.183	0.409–11.658
GFR	-0.038	0.015	5.923	0.015	0.963	0.934–0.993

Dependent variable: high CTO complexity (J-CTO ≥2). Model statistics: Omnibus test p=0.006; −2 log likelihood=66.445; Cox and Snell R^2=0.240; Nagelkerke R^2=0.320; overall classification accuracy=71.7%. CTO: Chronic total occlusion; SE: Standard error; OR: Odds ratio; CI: Confidence interval; GFR: Glomerular filtration rate.

Table 5. Multivariable logistic regression analysis for predictors of high CTO complexity (model including duration of menopause)

Variable	B	SE	Wald	p	OR	95% CI for OR
Duration of menopause	0.008	0.036	0.051	0.822	1.008	0.939–1.083
Diabetes mellitus	0.412	0.756	0.297	0.586	1.510	0.343–6.644
Hypertension	1.213	0.965	1.580	0.209	3.362	0.508–22.267
Hyperlipidemia	0.731	0.846	0.746	0.388	2.076	0.396–10.898
GFR	−0.037	0.018	4.187	0.041	0.964	0.930–0.998

Dependent variable: High CTO complexity (J-CTO ≥2). Model statistics: Omnibus test p=0.006; −2 log likelihood=66.735; Cox & Snell R^2=0.236; Nagelkerke R^2=0.316; overall classification accuracy=68.3%. CTO: Chronic total occlusion; GFR: Glomerular filtration rate; OR: Odds ratio; SE: Standard error; CI: Confidence interval.

model 2: OR: 0.964, 95% CI: 0.930–0.998, p=0.041), whereas diabetes mellitus, hypertension, and hyperlipidemia were not independently associated with lesion complexity.

Discussion

The principal finding of the present study was the absence of a statistically significant relationship between menopausal duration and CTO lesion complexity assessed by the J-CTO score. Although women with more complex lesions tended to have a longer menopausal period, this tendency did not reach statistical significance. The relatively limited number of patients included in the analysis may partially explain this observation. While menopause-related hormonal alterations are known to influence cardiovascular biology, evidence specifically evaluating their relationship with CTO anatomical complexity remains limited. Therefore, our findings provide additional insight into the potential interaction between menopausal characteristics and advanced coronary artery disease.

The increased cardiovascular risk observed in menopause is mediated by several pathophysiological mechanisms related to estrogen deficiency. Reduced estrogen levels are associated with endothelial dysfunction, decreased nitric oxide bioavailability, increased oxidative stress, and activation of inflammatory pathways.[4,16] These mechanisms collectively contribute to impaired vascular tone and structural alterations of the vessel wall. In addition, the menopausal transition is characterized by adverse changes in lipid metabolism, including elevated low-density lipoprotein, cholesterol, and triglyceride levels, along with reduced high-density lipoprotein cholesterol.[17] These alterations are more pronounced in women with early menopause or premature ovarian failure who also exhibit a higher prevalence of type 2 diabetes mellitus and hyperlipidemia.[18,19] Consequently, this metabolic profile may promote a more atherogenic milieu and accelerate plaque progression. Consistent with these mechanisms, our findings demonstrated that diabetes mellitus, hyperlipidemia, and a prior history of coronary artery disease were significantly more prevalent in the high-complexity group. This observation supports the concept that an increased metabolic burden and cumulative atherosclerotic load are associated with the development of more complex lesions. Furthermore, patients in the high-complexity group exhibited higher serum urea and creatinine levels and lower glomerular filtration rates, suggesting a potential link between renal dysfunction and CTO lesion complexity.

Menopause is also associated with increased arterial stiffness and accelerated progression of subclinical atherosclerosis, both of which may facilitate the development of advanced atherosclerotic lesions. Large-scale cohort studies and meta-analyses have demonstrated that women with early menopause or

premature ovarian insufficiency have a significantly increased risk of coronary artery disease, myocardial infarction, and stroke.[20–22] Similarly, large epidemiological studies evaluating the relationship between menopausal age and cardiovascular outcomes have shown a strong association between early menopause and both coronary heart disease and cardiovascular mortality, with meta-analyses indicating an approximately 50% increase in coronary artery disease risk.[23,24] In addition, surgical menopause has been associated with a higher cardiovascular risk compared with natural menopause.[25] These findings suggest that prolonged exposure to estrogen deficiency may amplify atherosclerotic processes and predispose to more advanced forms of disease.

Recent studies further indicate that menopause is associated not only with overt cardiovascular events but also with subclinical atherosclerosis and biological aging markers. Leukocyte telomere length has been shown to correlate with age at menopause, with shorter telomeres being linked to coronary artery disease.[26] These findings support the notion that longer menopausal duration may contribute to cumulative vascular damage over time.

Emerging evidence suggests that coronary artery disease severity and lesion complexity are influenced not only by anatomical factors but also by hormonal, metabolic, and inflammatory determinants.[8,9] In postmenopausal women, estrogen deficiency-related metabolic disturbances and heightened inflammatory activity may accelerate atherosclerotic progression and contribute to the development of more severe coronary lesions.[5,27] Moreover, early increases in vascular resistance and endothelial dysfunction have been demonstrated following surgical menopause.[28,29]

From an interventional perspective, CTO lesions remain among the most technically demanding forms of coronary artery disease. Lesion anatomy strongly influences procedural duration, technical difficulty, and likelihood of successful revascularization. The J-CTO scoring system proposed by Morino et al.[13] has been widely adopted to estimate procedural complexity before intervention. Previous reports consistently demonstrated lower procedural success and greater technical difficulty in lesions with higher J-CTO values. In agreement with these observations, procedural success rates were also reduced in patients with more complex lesions in the current study.

Although no statistically significant association was identified between menopausal duration and lesion complexity, this finding should be interpreted with caution, given the known cardiovascular effects of menopause. Considering the limited sample size of the present study, a potential contribution of menopausal duration to CTO lesion complexity cannot be definitively excluded.

From a clinical perspective, menopausal duration is an easily obtainable parameter; however, based on our findings, it should not be considered a standalone predictor of CTO lesion complexity. Nonetheless, the hormonal, metabolic, and vascular alterations associated with menopause may indirectly contribute to atherosclerotic progression. Therefore, evaluating menopausal duration in conjunction with other clinical and angiographic variables may provide a more comprehensive risk assessment. Incorporating menopausal history into cardiovascular risk stratification in women may enhance individualized patient evaluation.

Although our study did not demonstrate a statistically significant association between menopause duration and CTO lesion complexity, the observed trend toward longer menopause duration in the high-complexity group may still be clinically relevant. This may reflect the cumulative vascular effects of prolonged estrogen deficiency over time, even if the present sample size was insufficient to detect a significant difference. In this regard, previous evidence suggesting beneficial cardiometabolic effects of hormone therapy, including improvement in endothelial function, blood pressure, insulin resistance, renal function, and lipid parameters, further supports the concept that hormonal status may influence cardiovascular structure and function. Therefore, while traditional cardiovascular risk factors and adverse lesion characteristics appear to play a more prominent role in determining CTO complexity in our cohort, the contribution of menopausal duration and long-term estrogen deprivation warrants further investigation in larger, prospective studies.

Limitations

Certain methodological issues should be acknowledged when interpreting the present findings. First, its retrospective and single-center design may limit the generalizability of the findings. Second, the small sample size may have reduced the statistical power. Third, because menopausal age and duration were based on patient self-report, recall bias cannot be excluded. In addition, potentially relevant variables such as hormonal profiles were not comprehensively assessed.

Furthermore, coronary lesion complexity was evaluated solely using the J-CTO score, and plaque characterization was not performed using intravascular imaging modalities such as intravascular ultrasound or optical coherence tomography. Finally, the study focused only on anatomical lesion complexity and did not include long-term clinical outcomes.

Conclusion

The present findings suggest that menopausal age and menopause duration were not independent determinants of CTO lesion complexity in female patients with CTO. Instead, lesion complexity appeared to be more strongly associated with conventional cardiovascular risk factors, impaired renal function, and unfavorable angiographic characteristics. Nevertheless, larger prospective studies are needed to further clarify the potential influence of menopause duration on CTO procedural outcomes. Given the vascular protective effects of estrogen through regulation of endothelial function, vasodilation, vascular remodeling, and atherosclerotic progression, the role of estrogen deficiency in CTO lesion complexity and procedural success warrants further investigation.

Disclosures

Ethics Committee Approval: The study was approved by the Kartal Koşuyolu Training and Research Hospital Local Ethics Committee (no: 2026/08/1444, date: 24/04/2026).

Informed Consent: Written informed consent was obtained.

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