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Original Article

Association between dyslipidemia and breast cancer risk: a retrospective case-control study stratified by menopausal status

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Abstract: Objective: To investigate the association between dyslipidemia and breast cancer risk in women, aiming to provide insights for prevention and clinical practice. Methods: A retrospective case-control study was conducted on 840 women who underwent breast cancer evaluation from December 2019 to April 2024. Baseline characteristics, lipid profiles (total cholesterol [TC], triglycerides [TG], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]), and tumor markers were compared between patients with confirmed breast cancer and non-cancer controls. Multivariate logistic regression was used to identify independent risk factors, and receiver operating characteristic (ROC) analysis assessed the diagnostic performance of lipid indicators. Results: Patients with breast cancer exhibited significantly higher TC and LDL-C levels than the controls ($P<0.05$). Elevated TC, TG, and LDL-C showed positive correlation with carcinoembryonic antigen (CEA), carbohydrate antigen 153 (CA153), and carbohydrate antigen 125 (CA125) ($P<0.05$). HDL-C was negatively correlated with these tumor markers ($P<0.05$). Independent predictors of breast cancer included age ≥55, nulliparity, premenopausal status, and elevated TC, TG, and LDL-C ($P<0.05$). ROC curves yielded area under the curve (AUC) values of 0.621 for TC and 0.600 for LDL-C. Subgroup analysis revealed that, in premenopausal women, only elevated TC was associated with breast cancer risk, whereas in postmenopausal women, elevated TC, TG, and LDL-C were significantly associated with the risk. Conclusion: Elevated blood lipid levels, particularly increased TC and LDL-C, are associated with the occurrence of breast cancer and may serve as auxiliary markers for assessing the risk in high-risk subgroups such as nulliparous and premenopausal women.

Keywords: Lipids, breast cancer, incidence risk, case-control study

Introduction

Breast cancer remains a major global health concern for women, with rising incidence and imposing significant emotional and economic burdens on patients and families [1]. Epidemiological data consistently identifies it as the most common female malignancy in many developed countries and a leading cause of cancer-related mortality worldwide [2]. According to WHO statistics, approximately 2.3 million new breast cancer cases and 685,000 related deaths were reported in 2020, emphasizing the urgent need for effective prevention and control measures [3, 4].

Established risk factors include genetic predisposition, lifestyle factors (diet, physical inactivity, smoking, alcohol consumption), reproductive/hormonal factors, and obesity [5]. Among these, obesity has garnered growing attention for its strong association with heightened breast cancer risk [6]. An increasing body of evidence links metabolic disturbances with obesity and breast cancer development [7]. In particular, dyslipidemia, a hallmark of metabolic dysfunction in obesity, has emerged as an important research focus [8].

Dyslipidemia is characterized by an atherogenic lipid profile, typically involving elevated total

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cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), combined with reduced high-density lipoprotein cholesterol (HDL-C) concentrations [9]. While its contribution to cardiovascular diseases such as atherosclerosis is well established, recent studies suggest that dyslipidemia may also be implicated in carcinogenesis [10]. In breast cancer, abnormal lipid metabolism might influence disease risk through several biological mechanisms, including altered estrogen production regulating breast cell growth and apoptosis, as well as inflammatory responses and oxidative stress triggered by lipid imbalance, all of which may promote tumorigenesis [11].

Nevertheless, the association between dyslipidemia and breast cancer remains controversial, with studies reporting inconclusive or conflicting findings. Given the substantial public health burden of breast cancer, clarifying their relationship is essential to inform preventive strategies and clinical practice.

Methods

Study subjects

This retrospective case-control analysis included 840 women aged 18-85 years who underwent evaluation for suspected breast cancer at Ankang People's Hospital and Xi'an International Medical Center Hospital between December 2019 and April 2024. "Suspected breast cancer" was defined as referral for further diagnosis due to abnormal breast ultrasound or mammography findings, clinically palpable masses, or nipple discharge. Data were obtained from electronic health records, and only participants with complete medical records were included. Exclusion criteria: prior diagnoses of breast cancer or other major malignancies; use of medications affecting lipid metabolism within the preceding 3 months; and absence of lipid profile data. The study protocol was approved by the Medical Ethics Committee of Xi'an International Medical Center Hospital.

Data collection

Baseline characteristics and fasting lipid profiles were obtained for all participants. The collected variables were as follows: (1) Demographics and medical history: Age, body mass index (BMI), parity (nulliparous vs. parous), menopausal status (premenopausal vs. postmenopausal), family history of malignancy in first-degree relatives, smoking and alcohol consumption history, marital status (married vs. unmarried/divorced), and comorbidities (hypertension, diabetes). (2) Lipid profiles: Fasting venous blood samples were analyzed enzymatically to determine serum levels of TC, TG, HDL-C, and LDL-C. Dyslipidemia was defined according to established diagnostic criteria [12] as follows: TC ≥5.2 mmol/L, TG ≥1.7 mmol/L, HDL-C <1.0 mmol/L, and LDL-C ≥3.4 mmol/L. (3) Tumor Markers (Breast Cancer Group Only): Serum levels of carcinoembryonic antigen (CEA), carbohydrate antigen 153 (CA153), and carbohydrate antigen 125 (CA125).

Statistical analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. All continuous variables were normally distributed and were expressed as mean ± standard deviation. Categorical variables were presented as number (percentage). Intergroup comparisons were performed using the chi-square test for categorical variables and the independent-samples t-test for continuous variables.

Variables with statistically significant differences ($P<0.05$) in univariate analysis were entered into a multivariate logistic regression model to identify independent risk predictors. Adjusted odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) were calculated. The diagnostic performance of TC, TG, and LDL-C was evaluated using receiver operating characteristic (ROC) curve analysis, and the area under the curve (AUC) was used to quantify discriminative ability. Pearson correlation coefficients were calculated to evaluate associations between lipid parameters and tumor markers. All statistical analyses were performed using SPSS 26.0 and GraphPad Prism 9.0 software, with a two-tailed *P*-value <0.05 considered statistically significant.

Results

Baseline characteristics of included participants

A total of 840 women were included, comprising 149 (17.7%) patients with breast cancer and 691 (82.3%) cancer-free controls (**Table 1**).

Table 1. Comparison of baseline data between the breast cancer group and non-cancer group

	Breast Cancer Group (n=149)	Non - Breast Cancer Group (n=691)	χ^2/t	P
Age			9.433	0.002
<55 years	72 (48.32)	428 (61.94)		
≥55 years	77 (51.68)	263 (38.06)		
BMI			2.645	0.104
<30 kg/m^2	42 (28.19)	152 (22.00)		
≥30 kg/m^2	107 (71.81)	539 (78.00)		
Reproductive History			6.180	0.013
Yes	109 (73.15)	567 (82.05)		
No	40 (26.85)	124 (17.95)		
Family History of Cancer			0.521	0.470
Yes	46 (30.87)	193 (27.93)		
No	103 (69.13)	498 (72.07)		
Smoking			0.794	0.373
Yes	33 (22.15)	131 (18.96)		
No	116 (77.85)	560 (81.04)		
Alcohol Consumption			1.607	0.205
Yes	30 (20.13)	173 (25.04)		
No	119 (79.87)	518 (74.96)		
Marital Status			1.624	0.203
Married	115 (77.18)	498 (72.07)		
Unmarried or Divorced	34 (22.82)	193 (27.93)		
Menopausal Status			9.466	0.002
Post-menopause	95 (63.76)	525 (75.98)		
Pre-menopause	54 (36.24)	166 (24.02)		
Hypertension			0.358	0.550
Yes	33 (22.15)	138 (19.97)		
No	116 (77.85)	553 (80.03)		
Diabetes			0.359	0.549
Yes	21 (14.09)	111 (16.06)		
No	128 (85.91)	580 (83.94)		

BMI: Body Mass Index.

The control group consisted of women who presented with symptoms or abnormal screening findings but were subsequently diagnosed with benign breast conditions (e.g., fibroadenoma, cystic disease) after comprehensive clinical, imaging, and/or pathological evaluation.

Significant demographic differences were observed between the groups. Participants aged ≥55 accounted for 51.68% of the cancer group versus 38.06% of the control group (P=0.002). Conversely, postmenopausal status was less prevalent among breast cancer patients (63.76%) than that among non-cancer subjects (75.98%) (P=0.002). No significant intergroup differences were found between the groups for BMI, parity, familial malignancy history, smoking or alcohol consumption status, hypertension, or diabetes mellitus (all P>0.05).

Lipid profiles in breast cancer and control groups

The levels of TC and LDL-C were significantly higher in the breast cancer group than those in the control group (both P<0.001). The mean TC concentration in breast cancer group was 5.12±0.79 mmol/L, compared with 4.81±0.61 mmol/L in the control group. The mean LDL-C

Table 2. Comparison of lipid profile between breast cancer and non-breast cancer groups

	Breast Cancer Group (n=149)	Non - Breast Cancer Group (n=691)	t	P
TC (mmol/L)	5.12±0.79	4.81±0.61	4.499	<0.001
TG (mmol/L)	1.17±0.52	1.11±0.41	1.477	0.141
HDL-C (mmol/L)	1.51±0.33	1.48±0.27	0.923	0.357
LDL-C (mmol/L)	2.91±0.73	2.67±0.64	3.708	<0.001

TC: Total Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

Table 3. Prevalence of breast cancer in dyslipidemic populations

		Breast Cancer Group (n=149)	Non - Breast Cancer Group (n=691)	χ^2	P
TC	Normal (n=592)	83 (14.02)	509 (85.98)	18.994	<0.001
	Abnormal (n=248)	66 (26.61)	182 (73.39)		
TG	Normal (n=768)	126 (16.41)	642 (83.59)	10.892	<0.001
	Abnormal (n=72)	23 (31.94)	49 (68.06)		
HDL-C	Normal (n=803)	139 (17.31)	664 (82.69)	2.289	0.130
	Abnormal (n=37)	10 (27.03)	27 (72.97)		
LDL-C	Normal (n=673)	101 (15.01)	572 (84.99)	17.299	<0.001
	Abnormal (n=167)	48 (28.74)	119 (71.26)		

TC: Total Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

level was 2.91±0.73 mmol/L in the breast cancer group, compared with 2.67±0.64 mmol/L in the control group. However, there were no significant differences in TG (1.17±0.52 mmol/L vs. 1.11±0.41 mmol/L) or HDL-C (1.51±0.33 mmol/L vs. 1.48±0.27 mmol/L) levels between the two groups (both P>0.05) (**Table 2**).

Association between dyslipidemia and breast cancer incidence

Analysis of the association between dyslipidemia and breast cancer revealed significantly higher detection rates of breast cancer in the participants with abnormal TC, TG, and LDL-C compared with those with normal levels. Specifically, the proportion of breast cancer cases among individuals with abnormal TC was 26.61%, significantly higher than 14.02% in those with normal TC (P<0.001). Similarly, breast cancer prevalence was 31.94% in participants with abnormal TG, higher than 16.41% in the normal TG group (P<0.001). Similarly, the proportion of breast cancer cases in the LDL-C abnormal group was 28.74%, also significantly higher than the 15.01% in the LDL-C normal group (P<0.001). In contrast, although the proportion of breast cancer cases in the HDL-C abnormal group (27.03%) was higher than that in the normal group (17.31%), the difference was not statistically significant (P=0.130) (**Table 3**).

Tumor marker levels in dyslipidemic populations

Among breast cancer patients, serum tumor marker levels were generally higher in those with dyslipidemia compared with those with normal lipid profiles. The CEA, CA153, and CA125 levels in patients with abnormal TC were significantly higher than those with normal TC (18.20±2.61 vs. 14.97±2.73 ng/mL; 33.52±4.76 vs. 28.80±5.26 U/mL; 52.96±4.77 vs. 46.38±5.96 U/mL; all P<0.001). Similarly, the CEA, CA153, and CA125 levels in patients with abnormal TG were significantly elevated (20.50±2.30 vs. 15.65±2.62 ng/mL; 37.74±3.62 vs. 29.64±4.90 U/mL; 57.34±3.88 vs. 47.82±5.58 U/mL; all P<0.001). Regarding HDL-C levels, the abnormal group showed significantly higher CEA, CA153, and CA125 levels (21.88±2.67, 40.00±3.18, and 57.36±5.62, respectively) compared to the normal group (16.00±2.75, 30.24±5.10, and 48.71±6.02, respectively) (all P<0.001). Likewise, the three tumor marker levels in the abnormal LDL-C group (CEA: 19.07±2.40 ng/mL; CA153:

Table 4. Comparison of tumor marker levels between patients with and without dyslipidemia

	TC Normal (n=83)	TC Abnormal (n=66)	t	P
CEA (ng/mL)	14.97±2.73	18.20±2.61	7.351	<0.001
CA153 (U/mL)	28.80±5.26	33.52±4.76	5.741	<0.001
CA125 (U/mL)	46.38±5.96	52.96±4.77	7.483	<0.001
	TG Normal (n=126)	TG Abnormal (n=23)	t	P
CEA (ng/mL)	15.65±2.62	20.50±2.30	9.074	<0.001
CA153 (U/mL)	29.64±4.90	37.74±3.62	9.286	<0.001
CA125 (U/mL)	47.82±5.58	57.34±3.88	10.023	<0.001
	HDL - C Normal (n=139)	HDL - C Abnormal (n=10)	t	P
CEA (ng/mL)	16.00±2.75	21.88±2.67	6.701	<0.001
CA153 (U/mL)	30.24±5.10	40.00±3.18	8.909	<0.001
CA125 (U/mL)	48.71±6.02	57.36±5.62	4.681	<0.001
	LDL - C Normal (n=101)	LDL - C Abnormal (n=48)	t	P
CEA (ng/mL)	15.13±2.57	19.07±2.40	9.144	<0.001
CA153 (U/mL)	28.88±4.57	35.12±5.07	7.242	<0.001
CA125 (U/mL)	46.69±5.44	54.76±4.40	9.670	<0.001

TC: Total Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; CEA: Carcinoembryonic Antigen; CA153: Carbohydrate Antigen 153; CA125: Carbohydrate Antigen.

35.12±5.07 U/mL; CA125: 54.76±4.40 U/mL) were significantly higher than those in the LDL-C normal group (CEA: 15.13±2.57 ng/mL; CA153: 28.88±4.57 U/mL; CA125: 46.69± 5.44 U/mL; all P<0.001) (**Table 4**).

Correlations of lipids with tumor markers in breast cancer patients

Pearson correlation analysis showed that TC was positively correlated with CEA, CA153, and CA125 (r=0.709, r=0.645, r=0.677, all P<0.001); TG were positively correlated with CEA, CA153, and CA125 (r=0.725, r=0.636, r=0.784, all P<0.001); HDL-C was negatively correlated with CEA, CA153, and CA125 (r=-0.671, r=-0.679, r=-0.606, all P<0.001); and LDL-C was positively correlated with CEA, CA153, and CA125 (r=0.683, r=0.653, r= 0.716, all P<0.001) (**Figure 1**).

Multivariate logistic regression analysis of breast cancer risk

Multivariable logistic regression, incorporating predictors significant in univariate analysis (**Tables 1** and **3**; **Figure 2**), identified six independent determinants of breast cancer risk (P<0.05): Age ≥55 years was associated with a 1.78-fold increased risk (adjusted OR[aOR]= 1.787, 95% CI 1.233-2.590; P=0.002), nulliparity 1.72-fold (aOR=1.722, 1.117-2.653; P= 0.014), and premenopausal status 1.67-fold (aOR=1.673, 1.126-2.486; P=0.011). Lipid abnormalities demonstrated particularly strong associations: hypercholesterolemia (TC ≥5.2 mmol/L) nearly tripled the risk (aOR=2.247, 1.539-3.281; P<0.001), hypertriglyceridemia (TG ≥1.7 mmol/L) 2.16-fold (aOR=2.156, 1.234-3.776; P=0.007), and elevated LDL-C (≥3.4 mmol/L) 2.24-fold (aOR=2.242, 1.482-3.392; P<0.001).

Evaluation of lipid indicators in breast cancer diagnosis

ROC curve analysis was conducted to assess the diagnostic performance of TC, TG, and LDL-C as independent predictors of breast cancer. The AUC values were 0.621 for TC, 0.535 for TG, and 0.600 for LDL-C, respectively, as depicted in **Figure 3**.

The incidence of dyslipidemia in populations with various risk factors

The prevalence of dyslipidemia in populations with various risk factors was analyzed (**Figure 4**). TC abnormalities were more frequent in women aged ≥55 years (30.59%), in nulliparous women (30.49%), and in premenopausal women (27.27%). However, the incidences of TG and LDL-C abnormalities were relatively low.

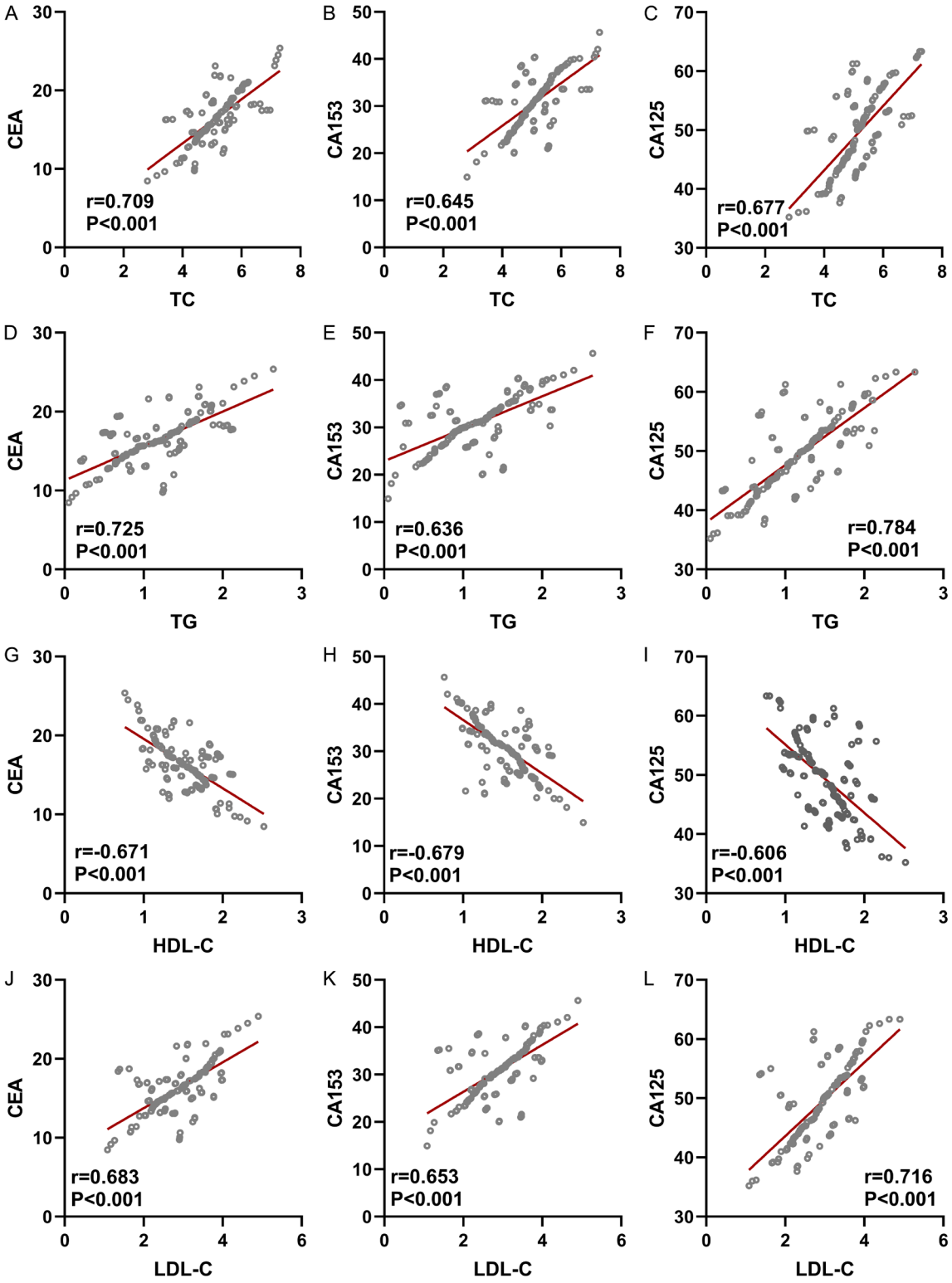

Figure 1. Correlation between lipid levels and tumor markers in the breast cancer population. A-C. Correlations between CEA, CA153, CA125 and TC in the breast cancer population. D-F. Correlations between CEA, CA153, CA125 and TG in the breast cancer population. G-I. Correlations between CEA, CA153, CA125 and HDL-C in the breast cancer population. J-L. Correlations between CEA, CA153, CA125 and LDL-C in the breast cancer population. TC: Total Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; CEA: Carcinoembryonic Antigen; CA153: Carbohydrate Antigen 153; CA125: Carbohydrate Antigen.

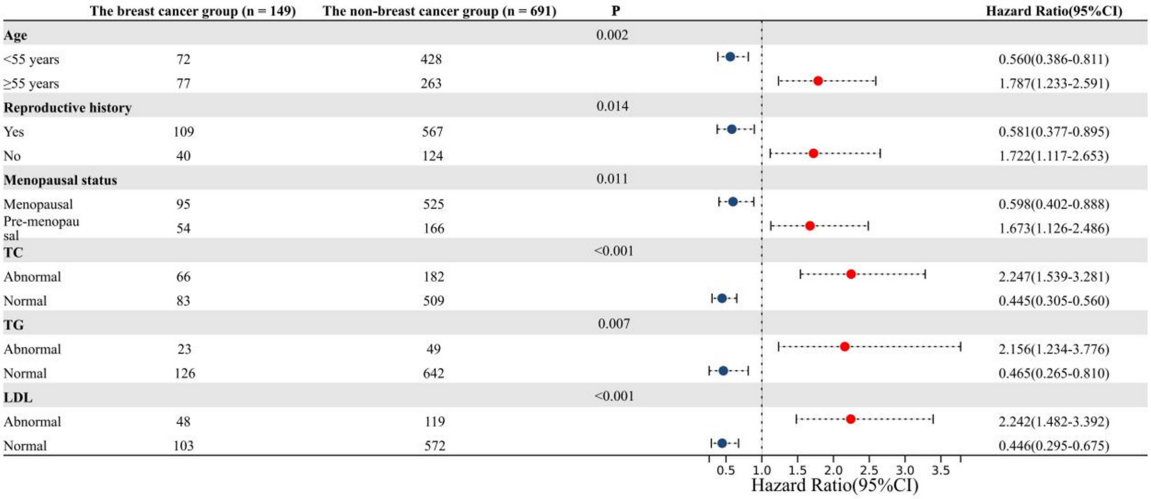

Figure 2. Multivariate analysis of breast cancer incidence. TC: Total Cholesterol; TG: Triglyceride; LDL-C: Low-Density Lipoprotein Cholesterol.

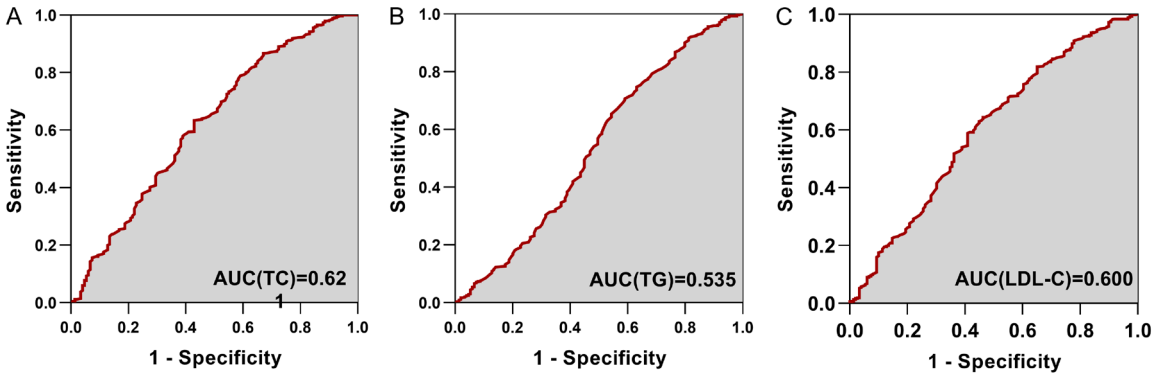

Figure 3. Diagnostic value of lipid levels for breast cancer. A. ROC curve for TC in diagnosing breast cancer (AUC=0.621). B. ROC curve for TG in diagnosing breast cancer (AUC=0.535). C. ROC curve for LDL-C in diagnosing breast cancer (AUC=0.600). TC: Total Cholesterol; TG: Triglyceride; LDL-C: Low-Density Lipoprotein Cholesterol; ROC: Receiver Operating Characteristic; AUC: Area Under the Curve.

Diagnostic value of blood lipid levels in high-risk populations

The AUC values of TC, TG, and LDL-C for breast cancer diagnosis in populations aged ≥55 years were 0.658, 0.643, and 0.579 respectively; in nulliparous women, the AUCs were 0.758, 0.700, and 0.696, respectively; while in premenopausal women, they were 0.667, 0.628, and 0.731, respectively, indicating that all three lipid parameters possess certain diagnostic values in these populations, as shown in **Figure 5**.

Menopausal status-specific association of dyslipidemia with breast cancer risk

Stratified analysis by menopausal status revealed distinct risk patterns (P<0.05, **Table 5**). Among 220 premenopausal women, dyslipidemia involving TC and HDL-C was correlated with elevated incidence of breast cancer, whereas TG and LDL-C abnormalities showed no significant association. Conversely, among 620 postmenopausal women, elevated TC, TG, and LDL-C were significantly associated with increased breast cancer risk, while HDL-C abnormalities demonstrated no significant correlation.

Multivariate logistic regression confirmed menopause-specific predictors (**Figure 6**). In premenopausal women, independent risk factors included age ≥55 years (aOR=2.120, 95% CI: 1.118-4.085; P=0.022) and elevated TC (aOR=2.771, 95% CI: 1.413-5.437; P=0.003). Although abnormal HDL-C showed a positive trend (aOR=2.908, 95% CI: 0.801-10.526;

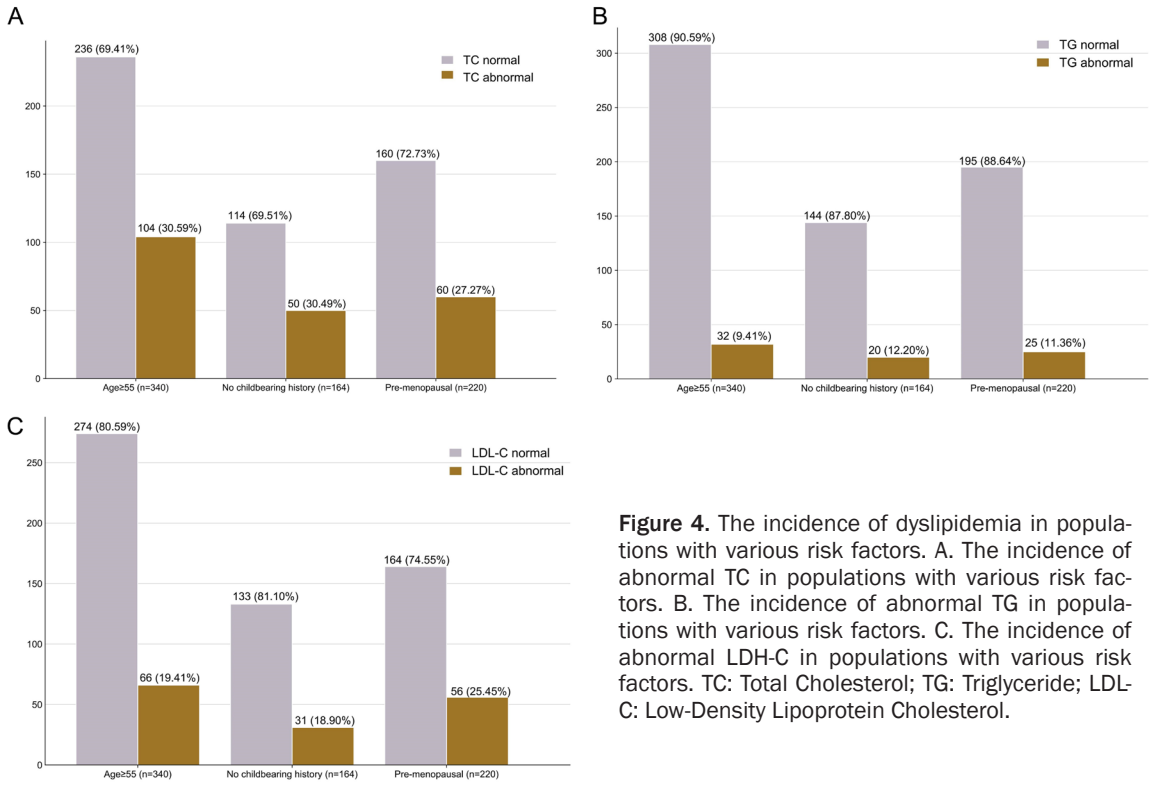

Figure 4. The incidence of dyslipidemia in populations with various risk factors. A. The incidence of abnormal TC in populations with various risk factors. B. The incidence of abnormal TG in populations with various risk factors. C. The incidence of abnormal LDH-C in populations with various risk factors. TC: Total Cholesterol; TG: Triglyceride; LDL-C: Low-Density Lipoprotein Cholesterol.

P=0.098), it didn't reach statistical significance. Among postmenopausal women, significant predictors included age ≥55 years (aOR=1.609, 95% CI: 1.016-2.550; P=0.042), BMI <30 kg/m^2 (aOR=1.718, 95% CI: 1.035-2.812; P=0.033), nulliparity (aOR=1.995, 95% CI: 1.168-3.349; P=0.010), dyslipidemia of TC (aOR=1.946, 95% CI: 1.219-3.092; P=0.005), TG (aOR=2.795, 95% CI: 1.370-5.501; P=0.004), and LDL-C (aOR=2.711, 95% CI: 1.599-4.544; P<0.001).

Discussion

This case-control study elucidates significant associations between dyslipidemia and breast cancer risk, offering potential implications for prevention and clinical management.

Our baseline analyses revealed distinct demographic differences in age distribution, parity, and menopausal status between cancer patients and controls. Consistent with previous reports [13, 14], multivariate analysis identified age ≥55 years, nulliparity, and premenopausal status as independent risk factors. These findings support the established concept that aging alters hormonal regulation, while nulliparity and premenopause prolong the duration of breast tissue exposure to endogenous hormonal fluctuations and other potential carcinogenic stimuli [15, 16]. Further stratification by menopausal status revealed distinct risk profiles. Among premenopausal women, age ≥55 years and elevated TC were key risk factors, whereas in postmenopausal women, additional risk factors included BMI <30 kg/m^2 and abnormal TG/LDL-C levels. This divergence aligns with findings by Ribas et al. [17], who reported that lipid metabolism may influence breast cancer development differently depending on hormone status and disease stage, highlighting the need for subtype-specific interventions.

The breast cancer cohort demonstrated significantly higher serum TC and LDL-C levels, alongside higher disease incidence among individuals with dyslipidemia of TC, TG, or LDL-C compared to normolipidemic controls, collectively establishing dyslipidemia - particularly hypercholesterolemia - as a significant determinant of breast cancer risk. Mechanistically, lipid metabolism disorders may promote tumorigenesis through dysregulation of estrogen biosynthesis, thereby altering breast cell proliferation, differentiation, and apoptosis [18], while chronic inflammation and oxidative stress foster a procarcinogenic microenvironment [19, 20].

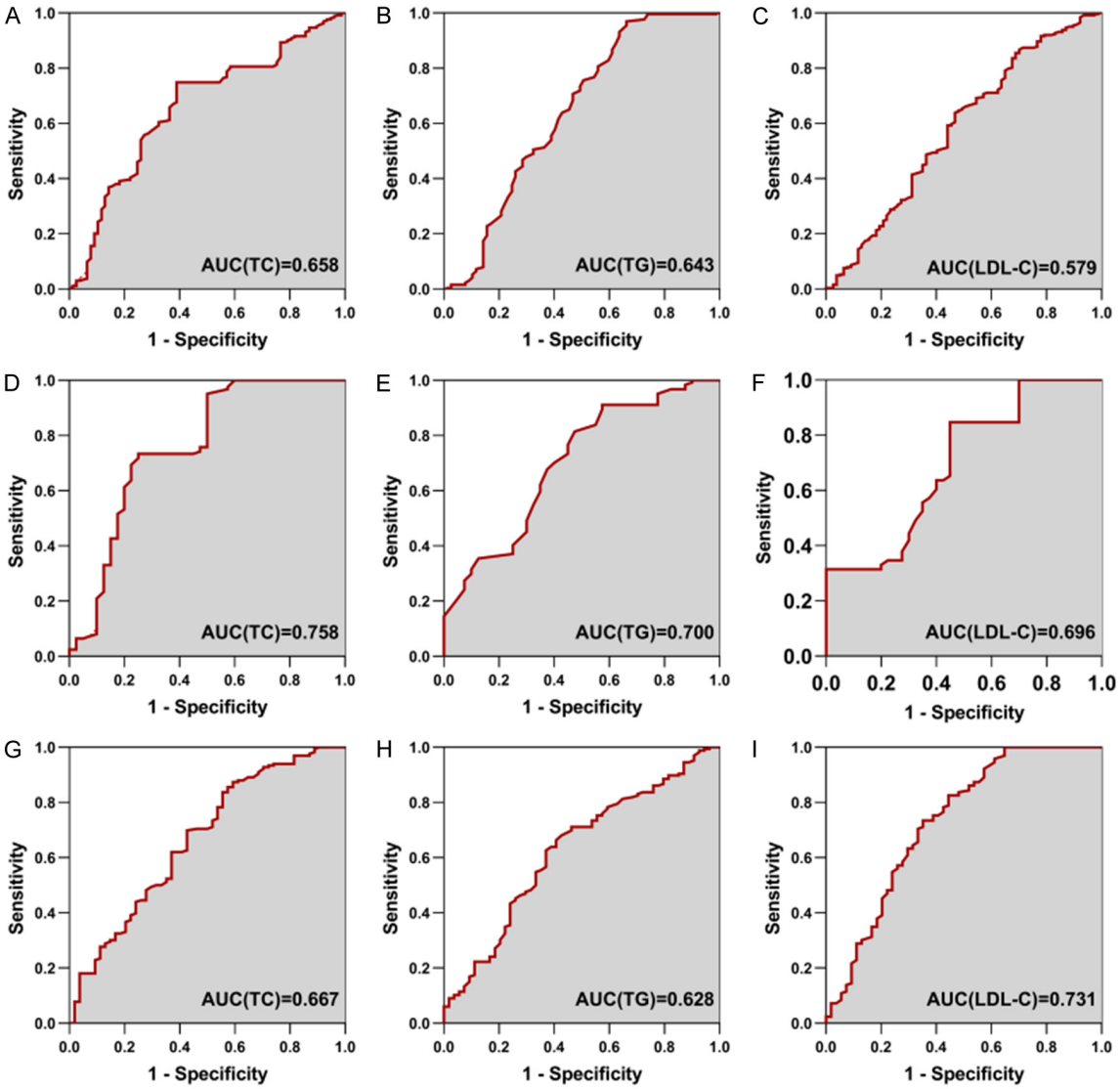

Figure 5. Diagnostic value of blood lipid levels for breast cancer in high-risk populations. A-C. ROC curves of TC, TG, and LDL-C for diagnosing breast cancer in the population aged ≥55 years. D-F. ROC curves of TC, TG, and LDL-C for diagnosing breast cancer in the nulliparous population. G-I. ROC curves of TC, TG, and LDL-C for diagnosing breast cancer in the premenopausal population. TC: Total Cholesterol; TG: Triglyceride; LDL-C: Low-Density Lipoprotein Cholesterol; ROC: Receiver Operating Characteristic; AUC: Area Under the Curve.

Substantiating this pathophysiological link, Sun et al. [21] identified associations between specific dyslipidemia patterns (elevated TC/LDL-C with reduced HDL-C) and aggressive molecular subtypes, including triple-negative and HER2-positive breast cancers, potentially mediated by upregulated proliferative markers such as Ki-67. Wan et al. [22] further emphasized that lipid metabolic reprogramming in breast cancer supports tumor progression by fueling energy production and signaling.

Multivariate analysis further confirmed that age ≥55 years, nulliparity, pre-menopause, abnormal TC, TG, and LDL-C were all independent risk factors for breast cancer. These findings underscore the value of these variables for the risk assessment and preventive strategies. Clinicians can conduct closer monitoring and targeted intervention in high-risk populations. For instance, Goto et al. [23] demonstrated that effective lipid control in postmenopausal HR-positive/HER2-negative patients improved

Table 5. Prevalence of dyslipidemia in patients with and without breast cancer, stratified by menopausal status

The Menopausal Population (n=620)	The Breast Cancer Group (n=95)	The Non-Breast Cancer Group (n=525)	χ^2	P
TC Normal (n=432)	53 (55.79)	379 (72.19)	10.241	0.001
TC Abnormal (n=188)	42 (44.21)	146 (27.81)		
TG Normal (n=573)	80 (84.21	493 (93.90)	10.791	0.001
TG Abnormal (n=47)	15 (15.79)	32 (6.10)		
HDL-C Normal (n=432)	90 (94.74)	505 (96.19)	0.439	0.508
HDL-C Abnormal (n=188)	5 (5.56)	20 (3.81)		
LDL-C Normal (n=573)	66 (69.47)	440 (84.29)	11.951	<0.001
LDL-C Abnormal (n=47)	29 (30.53)	82 (15.71)		
The premenopausal population (n=220)	The breast cancer group (n=54)	The non-breast cancer group (n=166)	χ^2	P
TC Normal (n=160)	30 (18.75)	130 (81.25)	10.639	0.001
TC Abnormal (n=60)	24 (40.00)	36 (60.00)		
TG Normal (n=573)	46 (23.59)	149 (76.41)	0.846	0.358
TG Abnormal (n=47)	8 (32.00)	17 (68.00)		
HDL-C Normal (n=432)	48 (88.89)	160 (96.39)	4.440	0.035
HDL-C Abnormal (n=188)	6 (11.11)	6 (3.61)		
LDL-C Normal (n=573)	35 (64.81)	129 (77.71)	3.571	0.059
LDL-C Abnormal (n=47)	19 (35.19)	37 (22.29)		

TC: Total Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

recurrence-free survival and enhanced antitumor immunity via reduced neutrophil-to-lymphocyte ratios and increased tumor-infiltrating lymphocytes, suggesting that lipid management could modulate the tumor microenvironment to improve clinical outcomes.

In the evaluation of the diagnostic value of lipid levels for breast cancer, the AUCs for TC, TG, and LDL-C were 0.621, 0.535, and 0.600, respectively, indicating modest standalone diagnostic utility, as AUCs between 0.5 and 0.7 generally suggest low discriminative power. However, their clinical relevance increased when stratified by high-risk subgroups: in nulliparous women, TC and LDL-C achieved AUCs of 0.758 and 0.696, respectively, and in premenopausal women, LDL-C reached 0.731. While lipid markers have limited standalone diagnostic value for breast cancer (overall AUCs <0.7), their diagnostic performance improves in high-risk subgroups (e.g., AUC of TC =0.758 in nulliparous women, AUC of LDL-C =0.731 in premenopausal women), supporting their use as auxiliary risk assessment tools in these specific populations. This aligns with Xiao et al. [24], who suggested that lipid metabolism remodeling could inform personalized therapy. Notably, TG consistently showed low AUCs across subgroups (0.535 overall), reflecting its weaker association with breast cancer pathogenesis compared to cholesterol fractions, as also observed by Sun et al., who found no correlation between TG and Ki-67 [21].

Elevated serum levels of CEA, CA153, and CA125 were significantly associated with dyslipidemia across all lipid parameters (TC, TG, HDL-C, LDL-C) compared to normolipidemic controls. Notably, within the breast cancer cohort, TC, TG, and LDL-C demonstrated positive correlations with these tumor markers, while HDL-C exhibited inverse correlations. This consistent pattern underscores a pathophysiological interplay between dyslipidemia and tumor progression, wherein altered tumor marker levels may reflect dyslipidemia-mediated perturbations in tumor cell proliferation and host immune responses [25, 26]. The positive correlations between TC/LDL-C and tumor markers align with Wan et al.'s proposal that lipids drive tumor progression through signaling pathways, while the inverse relationship with HDL-C is consistent with its potential protective role in suppressing carcinogenesis, as noted in lipidomic studies [17, 22].

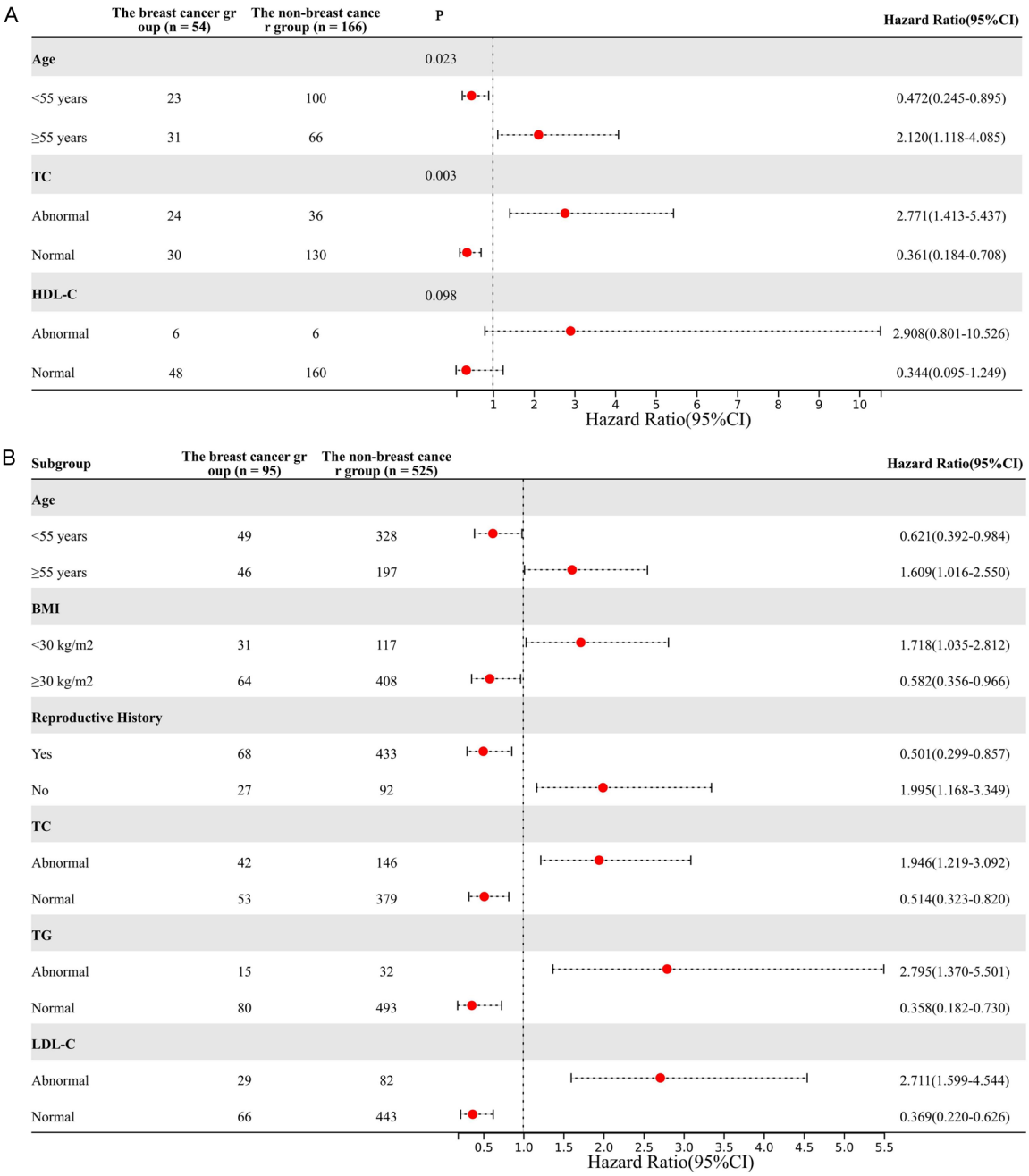

Figure 6. Multivariate analysis for breast cancer in premenopausal (A) and postmenopausal (B) patients. BMI: Body Mass Index; TC: Total Cholesterol TG: Triglyceride; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol.

Moreover, the differential impact of dyslipidemia across menopausal statuses adds nuance to clinical practice. Premenopausal women with abnormal TC had a 2.77-fold higher risk of breast cancer, whereas postmenopausal women faced elevated risks from multiple lipid abnormalities, including TG and LDL-C. This aligns with Ribas et al.'s observation that lipid profiles vary by hormone status, with postmenopausal obesity linked to luminal tumors and premenopausal dyslipidemia linked to BRCA-mutated disease [17]. Such findings underscore the need for tailored lipid monitoring: premenopausal women may benefit from TC screening, while postmenopausal women may benefit from broader lipid panels.

However, this study also has certain limitations. First, although tumor markers (CEA, CA153, CA125) were analyzed, these indicators primarily reflect tumor burden rather than malignancy (e.g., TNM stage, histological grade), which limits the interpretation of the association between dyslipidemia and tumor aggressiveness. Second, the study was conducted at only two hospitals in China, which may introduce regional bias and limit the generalizability of the findings to other populations. Third, the absence of data on lifestyle factors (e.g., dietary habits, physical activity) precluded adjustment for these potential confounders, which may affect the robustness of the observed associations.

In conclusion, elevated blood lipid levels, particularly increased TC and LDL-C, are associated with the occurrence of breast cancer and may serve as an auxiliary tools for assessing breast cancer risk in high-risk subgroups such as nulliparous and premenopausal women.

Disclosure of conflict of interest

None.

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