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Association Between Pre-Radiofrequency Catheter Ablation Serum Lipid Levels and Recurrence of Atrial Fibrillation in 412 Patients in Beijing, China: A Single-Center Study

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Background: This study from a single center in Beijing, China, included 412 patients with atrial fibrillation (AF) who underwent radiofrequency catheter ablation. We aimed to determine whether pre-ablation serum lipid levels were related to recurrence of atrial fibrillation (RAF).

Material/Methods: A total of 412 patients with AF who underwent radiofrequency catheter ablation were enrolled in the study. Fasting levels of triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC), were measured at baseline before ablation, and patients were classified according to lipid level quartiles (Q1-Q4). RAF was affirmed via 24-h electrocardiography or 12-lead electrocardiography.

Results: A total of 82 (19.90%) patients experienced RAF. After adjusting for other relevant factors and sex, univariate logistic regression analysis revealed LDL-C (hazard ratio [HR], 1.17; 95% confidence interval [CI], 0.93-1.47) and TC (HR, 1.17; 95% CI, 0.96-1.42) levels were not significantly related to RAF. Multivariate logistic regression analysis revealed that, compared with the highest quartile (Q4), female patients with lower quartiles of TC had higher RAF, especially Q3 (HR, 16.24; 95% CI, 1.14-231.56). LDL-C levels were higher in Q1 than in Q4 but lower in Q2 and Q3 than in Q4 (Q1: HR, 1.34; 95% CI, 0.08-18.89; Q2: HR, 0.09, 95% CI, 0.06-1.52; Q3: HR, 0.02, 95% CI, 0.14-0.57).

Conclusions: This study showed RAF in almost 20% of treated patients and RAF was significantly related to pre-ablation serum levels of LDL-C and TC in women.

Keywords: **Atrial Fibrillation • Catheter Ablation • Lipids • Neoplasm Recurrence, Local**

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Background

One of independent risk factors for cardiovascular disease is dyslipidemia; however, its relationship with the occurrence of atrial fibrillation (AF) is still controversial. In a recent review [1], 84 studies reporting on the effects of cardiovascular risk factors on the incidence of AF in 32 independent cohorts were systematically analyzed, and serum cholesterol levels were found to be negatively correlated with the incidence of AF. Previous studies [2-4] have demonstrated a negative correlation between cholesterol and AF, indicating that low cholesterol levels lead to a high risk of AF. Previous prospective cohort studies have shown that low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) levels are negatively correlated with the incidence of AF [5,6]. In a case-control study, we found that blood lipid levels were lower in patients with AF than in healthy individuals, especially LDL-C and high-density lipoprotein cholesterol (HDL-C) levels, indicating that LDL-C may increase the susceptibility of patients to AF [7]. Risk factors for the occurrence and recurrence of AF may be similar. The technique of radiofrequency catheter ablation has made significant progress in the treatment of AF; however, the high recurrence rate of AF after catheter ablation remains a major concern, and prognostic factors associated with RAF remain unknown [8]. Moreover, whether lipid levels affect RAF after catheter ablation remains unknown. Therefore, this study from a single center in Beijing, China, included 412 patients with AF who underwent catheter ablation and aimed to determine whether pre-ablation serum lipid levels were associated with RAF after catheter ablation.

Material and Methods

Study Population

All patients provided written informed consent, and the study was approved by the Ethics Committee of Beijing Anzhen Hospital Capital Medical University. In this case-control study, 412 patients with AF who received circumferential pulmonary vein ablation from January 2017 to December 2017 were included. Paroxysmal AF (PAF) was ablated by the circumferential pulmonary vein, and persistent AF (CAF) was ablated by the circumferential pulmonary vein plus the left top line, mitral isthmus line, and tricuspid isthmus line. After ablation, antiarrhythmic drugs were routinely taken for 3 months. According to the diagnostic criteria of the 2020 Atrial Fibrillation Guidelines [9], clinical AF can be diagnosed via standard 12-lead electrocardiography or single-lead electrocardiography of ≥30 s showing undiscernible repeated P waves and irregular RR intervals (when atrial-ventricular conduction is not impaired). RAF was defined as AF, flutter, and atrial tachycardia events lasting for ≥30 s after 3 months of catheter ablation and confirmed via standard 12-lead electrocardiography or 24-h Holter monitoring. The exclusion criteria were as follows: severe hepatic or renal dysfunction, autoimmune or inflammatory disease, malignancy, New York Heart Association grade III and IV disease, severe mitral stenosis, left atrial thrombosis, hyperthyroid or hypothyroidism, and percutaneous coronary intervention within 6 months before ablation. Clinical, echocardiographic, and laboratory assessments were performed before ablation. The study was performed in accordance with the relevant guidelines and regulations.

Data Collection

Data regarding baseline characteristics were collected at admission and included smoking status, sex, age, alcohol use, AF type, body mass index (BMI), hypertension, diabetes, history of coronary heart disease, and medication use (eg, lipid-lowering drugs [LLDs]). Both persistent and long-term persistent AF were referred to as non-paroxysmal AF.

Determination of Blood Lipid Levels

Fasting blood samples were collected on the first morning of admission to evaluate several biochemical indicators, including blood lipids, triglyceride (TG), HDL-C, LDL-C, and TC levels, which were determined via enzymatic colorimetric methods (Zhongsheng Company). According to the quartile grouping of lipid levels, quartiles of TG were determined as follows: Q1, <0.91 mmol/L; Q2, 0.91-1.24 mmol/L; Q3, 1.24-1.67 mmol/L; and Q4, >1.67 mmol/L. Quartiles of HDL-C were determined as follows: Q1, <1.03 mmol/L; Q2, 1.03-1.19 mmol/L; Q3, 1.19-1.38 mmol/L; and Q4, >1.38 mmol/L. Quartiles of LDL-C were determined as follows: Q1, <2.07 mmol/L; Q2, 2.07-2.72 mmol/L; Q3, 2.72-3.36 mmol/L; and Q4, >3.36 mmol/L. Quartiles of TC were determined as follows: Q1, <2.07 mmol/L; Q2, 2.07-2.72 mmol/L; Q3, 2.72-3.36 mmol/L; and Q4, >3.36 mmol/L.

Statistical Analysis

Data with normal distribution were expressed as mean±standard deviation and compared via one-way ANOVA. Data with skewed distribution were expressed as the median and inter-quartile range and were compared using the Mann-Whitney U test. Categorical variables were expressed as percentages and compared with the chi-square test.

Patients were divided into quartiles based on lipid levels, and differences in RAF among quartiles were assessed via the chi-square test. A logistic risk model was established to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) to examine the relationship between lipid levels and RAF. Two models were used for the correction of logistic regression estimates: model 1 was adjusted for age and sex, whereas model 2 was

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Table 1. Characteristics according to quartiles of total cholesterol level.

	Total	TC level (mmol/L)						
		Q1 (<3.86)	Q2 (3.86-4.54)	*P*	Q3 (4.54-5.21)	*P*	Q4 (>5.21)	*P*
Participants, n	412	102	103		101		106	
Age, (years)	60.9±10.97	62.77±10.21	60.03±12.476	0.199	59.47±10.54	0.675	59.63±10.23	0.895
Female, n (%)	210 (35.7)	42 (20)	51 (24.3)	0.20	54 (25.7)	0.382	63 (30)	0.285
BMI, kg/m²	27.6±10.21	26.33±3.85	28.92±3.14	0.361	26.34±4.21	0.376	29.1±2.96	0.300
Alcohol, n (%)	107 (18.20)	27 (25.23)	31 (28.97)	0.175	28 (26.17)	0.081	21 (19.63)	0.372
Smoking, n (%)	142 (24.15)	35 (24.65)	29 (20.42)	0.441	38 (26.76)	0.97	40 (28.17)	0.52
DM, n (%)	81 (13.78)	28 (34.57)	17 (20.99)	0.381	14 (17.28)	0.391	22 (27.16)	0.557
CAD, n (%)	72 (12.24)	39 (54.17)	9 (12.5)	**0.000**	9 (12.5)	0.306	15 (20.83)	0.813
REDO, n (%)	82 (19.90)	22 (26.3)	12 (14.63)	**0.049**	25 (30.494)	0.005	23 (20.05)	0.423
HBP, n (%)	236 (35.7)	72 (30.51)	52 (22.03)	**0.036**	55 (23.31)	1.0	57 (24.15)	0.901
LLD, n %	84 (40.14)	36 (42.86)	22 (26.19)	**0.008**	12 (14.29)	0.066	14 (16.67)	0.870
LAD (cm)	40.67±5.36	41.99±5.14	40.68±5.49	0.05	39.97±5.36	0.295	40.05±5.295	0.899
LDL-C, mmol/L	2.75±0.89	1.79±0.40	2.41±0.46	**0.000**	2.99±0.37	**0.000**	3.81±0.65	**0.000**
HDL-C, mmol/L	1.23±0.23	1.14±0.41	1.22±0.30	0.061	1.25±0.27	0.317	1.32±0.26	0.022
TG, mmol/L	1.45±0.86	1.10±0.49	1.41±0.81	**0.000**	1.41±0.71	0.985	1.90±1.4	**0.000**
uTSH, mIU/L	2.59±2.98	2.89±3.73	2.15±1.73	**0.034**	2.94±3.45	**0.016**	2.38±2.54	0.119
CRP, mg/L	1.96±3.06	1.79±3.09	2.30±3.96	0.218	1.94±2.53	0.359	1.81±2.43	0.653
SBP, mm Hg	126.2±17.7	125.58±15.71	126.58±17.30	0.607	127.14±18.05	0.789	127.06±19.55	0.973
DBP, mm Hg	78.70±12.0	77.17±14.02	79.37±11.34	0.143	78.46±10.27	0.479	79.73±11.91	0.336
FPG, mmol/L	6.0±1.49	6.04±1.53	6.17±1.88	0.512	5.77±1.15	0.032	6.00±1.27	0.111
WBC 10⁹/L	6.48±2.37	6.26±1.55	6.72±3.22	0.018	6.49±2.67	0.525	6.45±1.66	0.839

* Statistically significant value (*P*<0.05). Data are presented as n (%), mean±standard deviation; *P* value was concluded from the comparisons among the quartiles. BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LLD – lipid-lowering drugs; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; Q – quartile.

adjusted for BMI, diabetes, coronary heart disease, PAF, CAF, hypertension, left atrial diameter (LAD), TG levels, HDL-C levels, LDL-C levels, TC levels, C-reactive protein (CRP) levels, ultrasensitive thyroid stimulating hormone (uTSH) levels, fasting plasma glucose (FPG) levels, systolic blood pressure, diastolic blood pressure, and white blood cell (WBC) count. Data of men and women were analyzed separately. A *P* value of <0.05 was considered statistically significant. All analyses were performed using SPSS Statistics (version 17.00) software.

Results

Baseline Characteristics

Detailed information regarding the baseline characteristics of patients in each TC quartile is provided in **Table 1**. From the lowest to the highest TC quartile, the levels of HDL-C, LDL-C, TG, and uTSH increased gradually. In the second quartile (Q2) of TC, hypertension, CAD, RAF after catheter ablation, and LLD use decreased (*P*<0.05). Other risk factors did not differ significantly among TC quartiles.

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Table 2. Univariable analysis of recurrence of atrial fibrillation.

variables	Univariable		
	OR	95% CI	P
Age (years)	1.01	1.0-1.03	0.45
Female, n (%)	0.86	0.55-1.34	0.10
BMI, kg/m	1.0	0.98-1.01	0.64
Alcohol, n (%)	1.38	0.80-2.37	0.24
Smoking, n (%)	1.14	0.71-1.81	0.60
DM	0.82	0.43-1.54	0.53
CAD	0.93	0.50-1.74	0.82
PAF	0.98	0.03-36.57	0.99
CAF	1.02	0.03-35.19	0.99
LLD	1.09	0.64-1.85	0.76
LAD	1.04	1.00-1.08	0.06
LDL-C	1.17	0.93-1.47	0.19
HDL-C	1.21	0.66-2.22	0.54
TG	1.03	0.84-1.28	0.76
TC	1.17	0.96-1.42	0.11
uTSH	1.05	0.99-1.11	1.13
CRP	0.96	0.89-1.04	0.33
SBP	1.00	0.99-1.01	1.00
DBP	1.0	0.99-1.02	1.0
FPG	1.05	0.92-1.20	0.45
WBC	1.04	0.97-1.13	0.26

Statistically significant value (*P*<0.05). AF redo is the dependent variable. BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LLD – lipid-lowering drugs; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; HR – hazard ratio; CI – confidence interval.

Univariate Logistic Regression Analysis of Recurrence and Risk Factors of AF

Univariate logistic regression analysis (**Table 2**) revealed that levels of TC (HR, 1.17; 95% CI, 0.964-1.423; *P*=0.11), LDL-C (HR, 1.17; 95% CI, 0.93-1.47; *P*=0.19), HDL-C (HR, 1.21; 95% CI, 0.66-2.22; *P*<0.54), and TG (HR, 1.03; 95% CI, 0.837-1.275; *P*<0.76) were not associated with RAF. In addition, BMI, sex, age, alcohol use, smoking status, diabetes, CAD, PAF, CAF, LLD use, LAD, uTSH levels, CRP levels, fasting plasma glucose levels, systolic blood pressure, diastolic blood pressure, and WBC counts were found to have no significant correlation with RAF.

Quartiles of Lipid Levels and RAF

Considering lipid levels as a categorical variable (**Table 3**), univariate logistic regression analysis showed that patients in Q1 and Q3 of TC had an increased risk of RAF compared with patients in the highest quartile (Q4). However, the recurrence rate of AF was not different among LDL-C, HDL-C, and TG quartiles. Analysis based on the multivariate model (model 2) adjusted for BMI, sex, age, alcohol use, smoking status, diabetes, CAD, PAF, CAF, LLD use, LAD, uTSH levels, CRP levels, fasting plasma glucose levels, systolic blood pressure, diastolic blood pressure, and WBC count revealed that the risk of

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Table 3. Quartiles of blood lipids and recurrence of atrial fibrillation (total).

	Quartiles (mmol/L)	Recurrence n (%)	Unadjusted model		Model 1		Model 2	
			HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
TC								
Q1	(<3.86)	22 (26.83)	1.46 (0.39-5.51)	0.58	1.31 (0.34-5.05)	0.69	3.10 (0.53-17.95)	0.207
Q2	(3.86-4.54)	12 (14.63)	0.78 (0.26-2.39)	0.68	0.76 (0.25-2.32)	0.627	1.25 (0.31-5.00)	0.76
Q3	(4.54-5.21)	25 (30.49)	2.10 (0.92-4.80)	0.08	2.03 (0.88-4.65)	0.10	2.60 (1.0-8.41)	**0.045**
Q4	(>5.21)	23 (28.05)	1 Reference		1 Reference		1 Reference	
LDL-C								
Q1	(<2.07)	20 (24.4)	0.69 (0.21-2.35)	0.56	0.75 (0.22-2.58)	0.65	0.28 (0.06-1.45)	0.13
Q2	(2.07-2.72)	16 (19.5)	0.60 (0.22-1.65)	0.32	0.63 (0.23-1.74)	0.37	0.35 (0.10-1.26)	0.11
Q3	(2.72-3.36)	19 (23.17)	0.58 (0.26-1.29)	0.18	0.60 (0.27-1.35)	0.22	0.41 (0.14-1.17)	0.10
Q4	(>3.36)	27 (32.93)	1 Reference		1 Reference		1 Reference	
HDL-C								
Q1	(<1.03)	14 (17.07)	0.74 (0.34-1.60)	0.45	0.70 (0.32-1.53)	0.37	0.45 (0.17-1.21)	0.11
Q2	(1.03-1.19)	19 (23.17)	1.03 (0.52-2.03)	0.94	0.98 (0.49-1.97)	0.96	0.67 (0.29-1.55)	0.35
Q3	(1.19-1.38)	28 (34.15)	1.55 (0.83-2.89)	0.17	1.47 (0.78-2.78)	0.23	1.12 (0.52-2.42)	0.77
Q4	(>1.38)	21 (25.61)	1 Reference		1 Reference		1 Reference	
TG								
Q1	(<0.91)	21 (25.61)	0.94 (0.46-1.92)	0.86	0.83 (0.40-1.73)	0.61	1.10 (0.44-2.74)	0.85
Q2	(0.91-1.24)	22 (26.83)	0.87 (0.45-1.69)	0.69	0.81 (0.42-1.59)	0.54	0.95 (0.42-2.17)	0.90
Q3	(1.24-1.67)	16 (19.5)	0.09 (0.35-1.35)	0.28	0.67 (0.33-1.30)	0.23	0.71 (0.30-1.65)	0.42
Q4	(>1.67)	19 (23.17)	1 Reference		1 Reference		1 Reference	

* Statistically significant value (*P*<0.05). **Model 1** was adjusted for sex and age. **Model 2** was adjusted for BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; HR – hazard ratio; CI – confidence interval; Q – quartile. Q4 is the reference of Q1, Q2, and Q3.

RAF was higher in Q1, Q2, and Q3 than in Q4 of TC (HR, 2.66; 95% CI, 1.0-8.41; *P*=0.045).

Correlation Between Blood Lipid Quartiles and RAF Based on Sex

Given that lipid levels were different between men and women (**Tables 4, 5**), patients were divided based on sex. Multivariate analysis (model 2) revealed that low quartiles of LDL-C and TC were associated with a higher risk of RAF in women (**Table 4**) but not in men (**Table 5**).

In addition, no significant correlation was observed between RAF and the levels of HDL-C and TG in male or female patients. The HRs and 95% CIs of different quartiles of lipid levels among women are shown in **Table 4**. According to the multivariate analysis, HRs and 95% CIs in the quartile with low lipid levels and the highest quartile were as follows: Q1 of TC (HR, 1.36; 95% CI, 0.02-86.16; *P*=-0.99), Q3 of TC (HR, 16.24; 95% CI, 1.14-231.56; *P*=0.04), Q1 of LDL-C (HR, 1.34; 95% CI, 0.08-18.89; *P*=0.83), and Q3 of LDL-C (HR, 0.02; 95% CI, 0.14-0.57; *P*=0.03). The increase of 1.0 mmol/L in Q1 of LDL-C was associated with a 34% reduction in the risk of RAF. TG and HDL-C levels were not associated with RAF.

Table 4. Quartiles of blood lipid levels and recurrence of atrial fibrillation (women).

	Quartiles (mmol/L)	Recurrence n (%)	Unadjusted model HR (95% CI)	Unadjusted model P	Model 1 HR (95% CI)	Model 1 P	Model 2 HR (95% CI)	Model 2 P
TC								
Q1	(<3.86)	6 (24.00)	0.33 (0.04-3.10)	0.33	0.24 (0.03-2.68)	0.22	1.36 (0.02-86.16)	0.99
Q2	(3.86-4.54)	4 (16.00)	0.69 (0.11-4.42)	0.69	0.54 (0.09-4.05)	0.52	7.5 (0.23-250.1)	0.26
Q3	(4.54-5.21)	10 (40)	3.67 (0.89-15.2)	0.07	0.83 (0.28-2.96)	0.75	16.24 (1.14-231.56)	**0.04**
Q4	(>5.21)	5 (20.00)	1 Reference		1 Reference		1 Reference	
LDL-C								
Q1	(<2.07)	9 (36.00)	3.48 (0.50-2.42)	0.21	4.08 (0.52-27.5)	0.16	1.34 (0.08-18.89)	0.83
Q2	(2.07-2.72)	5 (20.00)	0.53 (0.11-2.73)	0.85	0.61 (0.10-3.0)	0.56	0.09 (0.06-1.52)	0.10
Q3	(2.72-3.36)	3 (12.00)	0.33 (0.08-1.37)	0.13	0.30 (0.07-1.34)	0.10	0.02 (0.14-0.57)	**0.03**
Q4	(>3.36)	8 (32.00)	1 Reference		1 Reference		1 Reference	
HDL-C								
Q1	(<1.03)	5 (20.00)	1.52 (0.44-5.26)	0.50	1.95 (0.47-5.78)	0.29	1.0 (0.11-8.76)	0.99
Q2	(1.03-1.19)	4 (16.00)	0.82 (0.25-3.01)	0.87	1.04 (0.24-2.96)	0.95	0.25 (0.03-2.48)	0.24
Q3	(1.19-1.38)	7 (28.0)	0.62 (0.45-3.76)	1.31	1.47 (0.78-2.78)	0.23	0.65 (0.10-4.07)	0.64
Q4	(>1.38)	9 (36.00)	1 Reference		1 Reference		1 Reference	
TG								
Q1	(<0.91)	6 (24.00)	0.77 (0.22-2.73)	0.69	0.66 (0.17-2.31)	0.52	0.32 (0.05-2.01)	0.23
Q2	(0.91-1.24)	8 (32.00)	0.94 (0.28-3.14)	0.91	0.85 (0.24-2.91)	0.80	1.46 (0.32-6.64)	0.62
Q3	(1.24-1.67)	5 (20.00)	0.93 (0.29-3.01)	0.90	0.83 (0.28-2.96)	0.75	0.06 (0.01-0.68)	0.29
Q4	(>1.67)	6 (24.00)	1 Reference		1 Reference		1 Reference	

* Statistically significant value (*P*<0.05). **Model 1** was adjusted for age. **Model 2** was adjusted for BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; HR – hazard ratio; CI – confidence interval; Q – quartile. Q4 is the reference of Q1, Q2, and Q3.

Continuous Lipid Levels and RAF

Multivariate logistic analysis (**Table 6**; models 1 and 2) based on the sex of patients showed that elevated levels of TG, HDL-C, LDL-C, and TC were not significantly associated with the reduced risk of RAF among male and female patients.

Discussion

Important findings of this study include the following: (1) TC levels were negatively correlated with RAF after catheter ablation among women, and lower LDL-C levels were negatively correlated with RAF after catheter ablation, whereas high LDL-C levels were positively correlated with RAF. (2) TG and HDL-C levels were not associated with RAF after catheter ablation among men and women. Furthermore, from the lowest to the highest quartile of TC, the levels of TG, HDL-C, LDL-C, and uTSH increased gradually, whereas the incidence of hypertension and CAD and LLD use decreased in Q2 of TC (*P*<0.05). No significant difference was observed in other risk factors among TC quartiles. These findings suggest that low levels of LDL-C and TC may be independent risk factors for RAF among women.

Clinical trials have demonstrated that hyperlipidemia is an independent risk factor for cardiovascular diseases; however, the

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Table 5. Quartiles of blood lipids and recurrence of atrial fibrillation (men).

	Quartiles (mmol/L)	Recurrence n (%)	Unadjusted model		Model 1		Model 2	
			HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
TC								
Q1	(<3.86)	16 (28.07)	3.82 (0.63-23.1)	0.15	5.87 (0.52-66.6)	0.15	3.75 (0.62-22.6)	0.15
Q2	(3.86-4.54)	8 (14.04)	0.84 (0.19-3.85)	0.83	0.78 (0.11-5.31)	0.80	0.86 (0.19-3.89)	0.84
Q3	(4.54-5.21)	15 (26.32)	1.43 (0.46-4.46)	0.54	1.56 (0.35-6.82)	0.56	1.46 (0.47-4.52)	0.52
Q4	(>5.21)	18 (31.58)	1 Reference		1 Reference		1 Reference	
LDL-C								
Q1	(<2.07)	11 (19.30)	3.48 (0.50-2.42)	0.06	0.07 (0.01-0.73)	0.23	0.19 (0.04-1.08)	0.06
Q2	(2.07-2.72)	11 (19.30)	0.53 (0.11-2.73)	0.30	0.37 (0.05-2.54)	0.31	0.46 (0.11-1.96)	0.29
Q3	(2.72-3.36)	26 (28.07)	0.33 (0.08-1.37)	0.74	0.78 (0.18-3.28)	0.73	0.85 (0.29-2.48)	0.76
Q4	(>3.36)	19 (33.33)	1 Reference		1 Reference		1 Reference	
HDL-C								
Q1	(<1.03)	9 (15.79)	0.50 (0.18-1.39)	0.18	0.26 (0.07-0.97)	0.19	0.50 (0.18-1.40)	0.18
Q2	(1.03-1.19)	15 (26.32)	0.89 (0.36-2.19)	0.79	0.61 (0.20-1.86)	0.39	0.90 (0.36-2.21)	0.81
Q3	(1.19-1.38)	21 (36.84)	1.62 (0.71-3.75)	0.26	1.0 (0.37-2.71)	0.99	1.65 (0.71-3.82)	0.25
Q4	(>1.38)	12 (21.05)	1 Reference		1 Reference		1 Reference	
TG								
Q1	(<0.91)	9 (13.85)	1.11 (0.43-2.85)	0.23	1.43 (0.38-4.51)	0.60	1.04 (0.39-2.73)	0.94
Q2	(0.91-1.24)	9 (13.24)	0.83 (0.15-1.92)	0.66	0.83 (0.28-2.48)	0.74	0.80 (0.34-1.86)	0.60
Q3	(1.24-1.67)	8 (11.94)	0.57 (0.24-1.36)	0.21	0.66 (0.22-2.01)	0.47	0.553 (0.230-1.33)	0.18
Q4	(>1.67)	10 (14.50)	1 Reference		1 Reference		1 Reference	

* Statistically significant value (*P*<0.05). **Model 1** was adjusted for age. **Model 2** was adjusted for BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; HR – hazard ratio; CI – confidence interval; Q – quartile. Q4 is the reference of Q1, Q2, and Q3.

relationship between dyslipidemia and the incidence of AF remains controversial. In 1997, Psaty et al [4] examined risk factors for the incidence of AF in elderly individuals and found that high cholesterol levels reduced the risk of AF, indicating a negative correlation between AF and cholesterol. However, the reason for this inverse relationship remains unknown. Annoura et al [2] found that the levels of TG and TC were lower in patients with PAF. Our previous study [6] also supported this result, indicating that lipid levels, especially HDL-C and LDL-C levels, are lower in patients with AF than in healthy individuals. Low lipoproteinemia may increase the susceptibility of patients to AF. Several recent studies [3,5,10] have shown a significant negative association between cholesterol levels and the incidence of AF. In community-based studies on atherosclerosis risk and prospective studies based on the Swedish Primary Care Cardiovascular Database [5], low levels of TC and LDL-C have been associated with the risk of AF in women. However, a combined analysis of the Multi-Ethnic Study of Atherosclerosis and the Framingham Heart Study (MESA-FHS) cohort [11] showed that TG and HDL-C levels, instead of TC or LDL-C levels, were associated with the risk of AF. Low TC and LDL-C levels are associated with RAF in women, revealing a similar paradox. A multi-center study showed that metabolic syndrome is associated with the high recurrence rate of AF, whereas its components, such as hypertension, diabetes, obesity, and hyperlipidemia, are not independent risk factors for RAF [12]. In a recent meta-analysis [13] including

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Table 6. Blood lipid profile and risk for recurrence of atrial fibrillation.

	All patients				Women				Men			
	BE	SE	HR (95% CI)	*P* value	BE	SE	HR (95% CI)	*P* value	BE	SE	HR (95% CI)	*P* value
Model 1												
TC (per 1 mmol/L increase)	0.21	0.26	1.03 (0.74-2.06)	0.91	-0.19	0.42	0.83 (0.37-1.87)	0.65	0.57	0.34	1.77 (0.91-3.45)	0.10
LDL-C (per 1 mmol/L increase)	-0.01	0.28	1.12 (0.57-1.72)	0.58	0.20	0.48	1.22 (0.48-3.10)	0.68	-0.23	0.35	0.79 (0.40-1.58)	0.51
HDL-C (per 1 mmol/L increase)	0.17	0.39	1.09 (0.55-2.58)	0.40	0.10	0.75	1.09 (0.25-4.73)	0.91	0.22	0.52	1.24 (0.44-3.46)	0.68
TG (per 1 mmol/L increase)	-0.01	0.14	0.97 (0.75-1.31)	0.76	0.29	0.22	1.33 (0.87-2.03)	0.18	-0.27	0.21	0.77 (0.50-1.16)	0.21
Tsh (per 1 miu/L increase)	0.05	0.03	1.05 (0.99-1.12)	0.10	0.04	0.04	1.03 (0.74-2.06)		0.07	0.06	1.03 (0.74-2.06)	0.23
Model 2												
TC (per 1 mmol/L increase)	-0.17	0.27	0.79 (0.40-1.56)	0.50	-2.0	1.25	0.14 (0.01-1.57)	0.11	0.42	0.57	1.51 (0.49-4.64)	0.47
LDL-C (per 1 mmol/L increase)	-0.02	0.49	1.63 (0.80-3.3)	0.18	2.01	1.28	7.46 (0.10-91.7)	0.12	0.13	0.54	1.14 (0.40-3.28)	0.81
HDL-C (per 1 mmol/L increase)	0.64	0.83	3.02 (0.87-15.6)	0.18	1.21	1.68	1.63 (0.42-6.38)	0.48	1.38	0.98	3.97 (0.58-27.1)	0.16
TG (per 1 mmol/L increase)	-0.17	0.27	1.08 (0.73-1.60)	0.08	0.49	0.70	1.63 (0.42-6.38)	0.48	-0.10	0.32	0.91 (0.49-1.70)	0.77
Tsh (per 1 miu/L increase)	0.07	0.05	1.08 (0.73-1.60)	0.70	0.02	0.05	1.02 (0.92-1.12)	0.75	0.03	0.08	1.03 (0.87-1.21)	0.75

* Statistically significant value (*P*<0.05). **Model 1** was adjusted for sex and age. **Model 2** was adjusted for BMI – body mass index; DM – diabetes mellitus; CAD – coronary artery disease; PAF – paroxysmal atrial fibrillation; CAF – persistent atrial fibrillation; RAF – recurrence of atrial fibrillation; HBP – hypertension; LAD – left atrial diameter; TC – total cholesterol; LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein cholesterol; TG – triglycerides; CRP – C-reactive protein; uTSH – ultra-sensitive thyrotropin; SBP – systolic blood pressure; DBP – diastolic blood pressure; FPG – fasting plasma glucose; WBC – white blood cells; HR – hazard ratio; CI – confidence interval.

36 studies, factors associated with RAF after catheter ablation were examined, and higher LDL-C levels were observed in patients with RAF, which is inconsistent with the findings of the present study. The relationship between blood lipid levels and RAF remains as controversial as does the relationship between blood lipid levels and the incidence of AF. Therefore, the correlation between blood lipid levels and RAF should be explored further in large-scale clinical studies.

Clinical and basic studies have shown the potential advantages of lipid-lowering agents in the treatment and prevention of AF. The beneficial effects of these agents are mainly attributed to an increase in the activity of endothelial nitric oxide synthase and a reduction in the production of nicotinamide adenine dinucleotide phosphate oxidase, which improve the mechanical and electrical functions of atrial and myocardial tissues and have a pleiotropic effect on AF [14]. However,

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some prospective studies [10,15,16] have not shown the beneficial effects of these agents in reducing RAF after catheter ablation, which indirectly supports the findings this study. In the present study, the incidence of CAD and use of LLD were decreased in Q2 of TC (P<0.05). However, the risk of RAF in Q2 was not high in male or female patients. Therefore, the role of lipid-lowering agents in the prevention of AF is limited and warrants further investigation. As reported in a study by Mourtzinis et al, patients taking LLDs were not excluded, because excluding them might have reduced the number of factors affecting lipids, such as drug intervention, lifestyle intervention, and dietary structure. The present study was focused on the relationship between baseline lipid levels before catheter ablation and the risk of RAF. In the future, we will examine whether the risk of RAF is different between patients with iatrogenic and intrinsic low cholesterol levels.

The mechanisms underlying the findings of this study remain unknown. Previous studies have showed that several mechanisms may be involved. The first mechanism is related to the thyroid hormone. High levels of serum-free thyroxine (FT4) are associated with RAF, and hyperthyroidism can reduce cholesterol levels [17]. In addition, the shortening of the atrial effective refractory period caused by changes in ion channel protein levels and atrial structure increases the susceptibility of patients to AF, and thyroid replacement therapy can prevent electrical and structural remodeling of the thyroid in hypothyroidism [18]. In this study, differences in uTSH levels among TC quartiles partially explain this hypothesis. Furthermore, blood lipids can affect the cell membrane and the nature of cell electrophysiology [19], which is the main factor determining the excitability of cells. In addition, the balance of membrane lipid content can prevent the formation of arrhythmic potential, and lipoproteins can have anti-inflammatory effects. Kim et al [20] reported that the structure of lipoproteins in patients with AF was severely damaged, leading to increased inflammation and oxidation, and inflammation was identified as a risk factor for RAF [21]. Therefore, low levels of LDL-C and TC may increase the risk of RAF by increasing inflammation. However, whether these mechanisms can explain the relationships observed in this study remains unclear.

AF is a heterogeneous disease with complicated mechanisms, and its onset varies with age and sex. Lipid profile and atrial electrophysiological characteristics are different between men and women [22,23]. Therefore, the correlation between lipid levels and the risk of RAF may differ based on sex. A study [24] showed that LDL-C and TC levels were negatively correlated with RAF in women after radiofrequency ablation, whereas TG and HDL-C levels were not independently correlated with RAF in men or women, which is consistent with the results of the present study. Another study [23] reported that cholesterol levels were negatively correlated with the incidence of AF, and the correlation between blood lipid levels and AF was significant in women but weak in men. The study showed that changes in blood lipid levels after menopause may increase the influence of blood lipid levels on the susceptibility of women to AF. Therefore, large prospective studies on women during premenopause and postmenopause are required to confirm this hypothesis. Because inflammation is associated with LDL-C levels and AF are negatively correlated with CRP levels only in women [25], lower lipid levels may increase the risk of RAF by increasing inflammation in women.

Limitations

This study has some limitations. (1) This was a cross-sectional study of patients with RAF from different centers with different operators. (2) A small number of selected participants included elderly patients and postmenopausal women. (3) Patients receiving lipid-lowering treatment and those not receiving the treatment were not separated. (4) Previous studies have shown that low levels of LDL-C and TC are associated with the risk of AF [10], which is consistent with the results of this study and verifies the study approach. In this study, the lower lipid-lowering treatment group did not have a high RAF, and the effects of lipid-lowering treatment on RAF were minimal. (5) Blood lipid levels should be evaluated at different follow-up time points in the same center and by the same personnel, and patients should be selected at different time points to verify whether statins are suitable for use in AF.

Conclusions

This study showed RAF in almost 20% of treated patients, and RAF was significantly associated with pre-ablation serum levels of LDL-C and TC in women. Identifying risk factors for RAF after catheter ablation allows clinicians to select patients eligible for secondary procedures, increase success rates, and attempt new preventive therapies. Our results suggest that low cholesterol levels increase the risk of RAF, and statins or other LLDs should be carefully used for women undergoing catheter ablation. Prevention of RAF after catheter ablation among patients with low cholesterol levels in clinical practice should be explored further in large-scale studies.

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