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Link between Friesinger Index and Lipid Profile in Patients Undergoing Diagnostic Coronary Angiography

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Abstract

Background: A strong association between abnormal lipid variables and development of atherosclerosis is widely established. However, few data exist on the association between lipid levels and the extent or severity of coronary lesions in patients with coronary artery disease. Objective: We aimed to determine the link between lipid levels and the extent or severity of coronary lesions in patients with suspected coronary artery disease using Friesinger index (FR). Methodology: In this prospective and singe-center study, consecutive patients who underwent coronary angiography for diagnostic purposes were analyzed. Each participant was evaluated for lipid levels *i.e.* total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, very-low-density lipoprotein (VLDL) cholesterol, non-HDL cholesterol, triglycerides/HDL cholesterol, and triglycerides/non-HDL cholesterol. The extent of coronary disease was evaluated using FR index. Results: A total of 566 patients (mean age: 56.17 ± 9.99 years) were included in the study. The mean FR index was 5.40 ± 3.78. A significantly positive correlation was observed between FR index and total cholesterol ($P = 0.002$), triglycerides ($P < 0.001$), VLDL cholesterol ($P < 0.001$), non-HDL cholesterol ($P = 0.006$), triglycerides/HDL cholesterol ratio ($P = 0.008$), and triglycerides/non-HDL cholesterol ratio ($P = 0.002$). On the contrary, an inverse correlation was observed between FR index and HDL cholesterol ($P < 0.001$). Age or gender played no role in governing the FR index severity, while body-mass index, hypertension, diabetes, and smoking showed significant association with FR index ($P < 0.001$ for all). Conclusion: The present study demonstrates a significant link between the extent of coronary artery disease and levels of certain lipid variables.

Keywords

Cholesterol, Coronary Angiography, Coronary Artery Disease, Friesinger Index,

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Lipid Profile, Triglyceride

1. Introduction

Lipid abnormality is a well-established risk factor for the development of coronary artery disease [1]. Several clinical and epidemiological studies have indicated a strong association between dyslipidemia and atherosclerosis [2]-[7]. Nevertheless, data on the association between lipid levels and extent or severity of coronary lesions in patients with coronary artery disease are limited [8]. Friesinger (FR) index [9] is an important tool to assess the extent and severity of coronary artery lesions. A significant association between the FR index and lipid levels has been observed in the past years [8]. However, such investigations are very scarce in literature. In this regard, we conducted a study to determine the correlation between lipid variables and the extent or severity of coronary lesions in patients with suspected coronary artery disease.

2. Methodology

2.1. Study Design and Patient Population

In this prospective, singe-center study, consecutive patients who underwent coronary angiography for diagnostic purposes at our center between February 2013 and March 2014 were enrolled. Patients with congenital heart disease, coronary artery anomaly, cancer, obstructive pulmonary illness, or renal insufficiency and those already on hypolipidemic drugs were excluded from the study. A signed form indicating informed consent was obtained from each participating patient. The protocol of the study was approved by the Ethics Committee of our institution and the study was conducted in accordance with the ethical standards of Good Clinical Practice and the Helsinki Declaration.

2.2. Data Collection

All patients were asked to report their age and gender. Body-mass index (BMI) was estimated based on the height and weight measurements. Patients were defined as having hypertension if they displayed a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or self-report of physician diagnosis of hypertension and/or current use of antihypertensive medications. Diabetes mellitus was considered present if the patient presented with fasting glucose levels > 126 mg/dL, glycated hemoglobin (HbA1c) levels > 6.5%, or self-report of physician diagnosis of diabetes and/or use of antidiabetic medications. Patients were categorized as smokers if they reported smoking within last one year.

Each participating patient was evaluated for total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, very-low-density lipoprotein (VLDL) cholesterol, and non-HDL cholesterol levels using standard techniques. In addition, lipid ratios of triglycerides to HDL cholesterol and triglycerides to non-HDL cholesterol were calculated. Patients with abnormal lipid levels were identified by cutoff points of: >200 mg/dL for total cholesterol, >150 mg/dL for triglycerides, >130 mg/dL for LDL cholesterol, ≤40 mg/dL for HDL cholesterol, >4 for triglycerides/HDL cholesterol ratio, and >0.9 for triglycerides/non-HDL cholesterol ratio.

All patients underwent coronary angiography through transfemoral/transradial route using standard percutaneous techniques in the typical orthogonal projections. The FR index was used to assess the extent of coronary disease. The scores in this index range from 0 to 15. Each of the three main coronary arteries was scored separately from zero to five. The scores were: 0 for no arteriographic abnormalities, 1 for trivial luminal narrowing of <29%, 2 for localized luminal narrowing of 30% - 68%, 3 for multiple luminal narrowings of 30% - 68%, 4 for luminal narrowing of 69% - 100% without 100% occlusion of proximal segments; and 5 for total obstruction of a proximal segment. [9] Based on these, patients were classified in to four groups: patients with 0 FR index score, patients with 1 - 4 FR index score, patients with 5 - 10 FR index score, and patients with 11 - 15 FR index score.

2.3. Analysis of Study Outcomes

Based on the collected data, we evaluated the differences in mean lipid levels (e.g. total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol, non-HDL cholesterol, triglycerides/HDL cholesterol, and triglycerides/non-HDL cholesterol) across the groups of patients classified according to their FR index scores. We also determined the correlation between FR index and lipid levels. Subsequently, we assessed the association between severity of FR index and frequencies of patients classified according to the cut-off levels for each lipid variable as well as the association between FR index and demographic variables such as age, gender, BMI, hypertension, diabetes, and smoking.

2.4. Statistical Analysis

The collected data were analyzed using the Statistical Package for Social Sciences (SPSS for Windows version 20.0; Chicago, IL, USA). Continuous variables were described by mean and standard deviation. Categorical variables were presented as frequency and percentage. Non-parametric ANOVA (Kruskal-Wallis) test was used to assess the significant differences in mean lipid levels across FR index groups (e.g. difference in mean total cholesterol levels across FR index groups). Non-parametric spearman's rho correlation test was used to assess the correlation between two continuous variables (e.g. triglycerides and FR index). Non-parametric Pearson Chi-square test was used to assess the association between categorical variables (e.g. gender and FR index groups). In addition, a binary logistic regression analysis was conducted to predict the extent and severity of cornary artery lesions, in terms of FR index, using lipid variables and demographic characteristics as predictors. The P value < 0.05 was considered to indicate statistical significance.

3. Results

3.1. Baseline Demographics

A total of 566 patients were included in the study. The mean age of study participants was 56.17 ± 9.99 years. Of them, 435 (76.9%) were males, 214 (37.8%) had diabetes, 370 (63.4%) had hypertension, and 359 (63.4%) were current smokers. Mean total cholesterol was 182.72 ± 52.47 mg/dL, triglyceride was 152.57 ± 78.21 mg/dL, HDL cholesterol was 35.37 ± 10.25 mg/dL, LDL cholesterol was 116.00 ± 45.11 mg/dL, TG/HDL cholesterol ratio was 4.68 ± 4.66, and TG/non-HDL cholesterol ratio was 1.09 ± 0.60. The mean FR index was 5.40 ± 3.78. **Table 1** describes the demographics of patient sample, as well as their distribution according to the FR index.

3.2. Lipid Levels across FR Index Groups

The mean lipid levels across patients classified according to their FR index have been depicted in **Figure 1**. Corresponding mean lipid ratios of triglycerides/HDL cholesterol and triglycerides/non-HDL cholesterol across FR index groups are depicted in **Figure 2**. Analysis of various lipid variables indicated that there were significant differences between total cholesterol, triglycerides, HDL cholesterol, VLDL cholesterol, and triglycerides/non-HDL cholesterol across the groups of patients according to their FR index (**Table 2**). In addition, a significantly positive correlation was observed between FR index and total cholesterol, triglycerides, VLDL cholesterol, non-HDL cholesterol, triglycerides/HDL cholesterol ratio, and triglycerides/non-HDL cholesterol ratio. On the contrary, an inverse correlation was observed between FR index and HDL cholesterol levels (**Table 3**).

3.3. Frequency of Patients with Abnormal Lipid Levels across FR Index Groups

Analysis of the lipid profile showed that 189 (33.4%) patients had hypercholesterolemia, 194 (34.3%) had high LDL-cholesterolemia, 437 (77.21%) had low HDL-cholesterolemia, 232 (40.1%) had hypertriglyceridemia, 178 (31.5%) had elevated triglycerides/HDL cholesterol ratio, and 317 (56.0%) had elevated triglycerides/non-HDL cholesterol ratio (**Table 4**). A further analysis of frequency of patients classified according to the cut-off lipid levels revealed that variables like HDL cholesterol levels, triglycerides levels, and triglycerides/non-HDL cholesterol ratio had a significant association with severity of FR index (**Table 4**).

3.4. Association between FR Index and Demographic Variables

The association between FR index and demographic variables such as age, gender, BMI, hypertension, diabetes,

Table 1. Demographic details of patients included in the study[a].

Variable	566 patients
Age, years	56.17 ± 9.99
Males, n (%)	435 (76.9)
BMI, kg/m^2	22.21±2.52
Diabetes mellitus, n (%)	214 (37.8)
Hypertension, n (%)	370 (65.4)
Smoking, n (%)	359 (63.4)
Total cholesterol, mg/dL	182.72 ± 52.47
Triglycerides, mg/dL	152.57 ± 78.21
HDL cholesterol, mg/dL	35.37 ± 10.25
LDL cholesterol, mg/dL	116.00 ± 45.11
VLDL cholesterol, mg/dL	30.44 ± 16.72
Non-HDL cholesterol, mg/dL	147.35 ± 49.02
TG/HDL cholesterol	4.68 ± 4.66
TG/non-HDL cholesterol	1.09 ± 0.60
Friesinger index	5.40 ± 3.78
0, n (%)	96 (17.0)
1 - 4, n (%)	150 (26.5)
5 - 10, n (%)	259 (45.7)
11 - 15, n (%)	61 (10.8)

[a]Continuous variables are described by mean and standard deviation; categorical variables are presented as frequency and percentage.

Table 2. Analysis of lipid levels in patients distributed according to FR index classes.

Variable	FR index[a]				P value for group difference[b]
	0 (n = 96)	1 - 4 (n = 150)	5 - 10 (n = 259)	11 - 15 (n = 61)	
Total cholesterol, mg/dL	169.61 ± 51.39	180.36 ± 47.50	185.95 ± 51.97	195.54 ± 63.80	**0.022**
Triglycerides, mg/dL	136.51 ± 79.48	137.53 ± 59.28	157.43 ± 72.72	194.36 ± 115.60	**<0.001**
HDL cholesterol, mg/dL	37.18 ± 8.46	36.28 ± 8.71	34.45 ± 13.15	33.18 ± 9.61	**<0.001**
LDL cholesterol, mg/dL	108.03 ± 40.45	116.48 ± 42.56	117.34 ± 45.54	121.70 ± 54.94	0.301
VLDL cholesterol, mg/dL	27.91 ± 16.67	27.77 ± 14.13	31.55 ± 17.24	36.28 ± 18.89	**<0.001**
Non-HDL cholesterol, mg/dL	136.44 ± 47.71	145.91 ± 44.36	149.67 ± 48.59	158.36 ± 60.69	0.061
Triglycerides/HDL cholesterol	4.20 ± 2.13	4.47 ± 3.00	4.69 ± 4.85	5.95 ± 8.47	0.140
Triglycerides/non-HDL cholesterol	1.05 ± 0.59	0.99 ± 0.44	1.12 ± 0.60	1.28 ± 0.88	**0.010**

[a]Data are presented as mean ± standard deviation; [b]Kruskal-Wallis Test.

and smoking is described in **Table 5**. We found that age or gender played no role in governing the FR index severity. However, characteristics such as BMI, hypertension, diabetes, and smoking showed significant association with FR index.

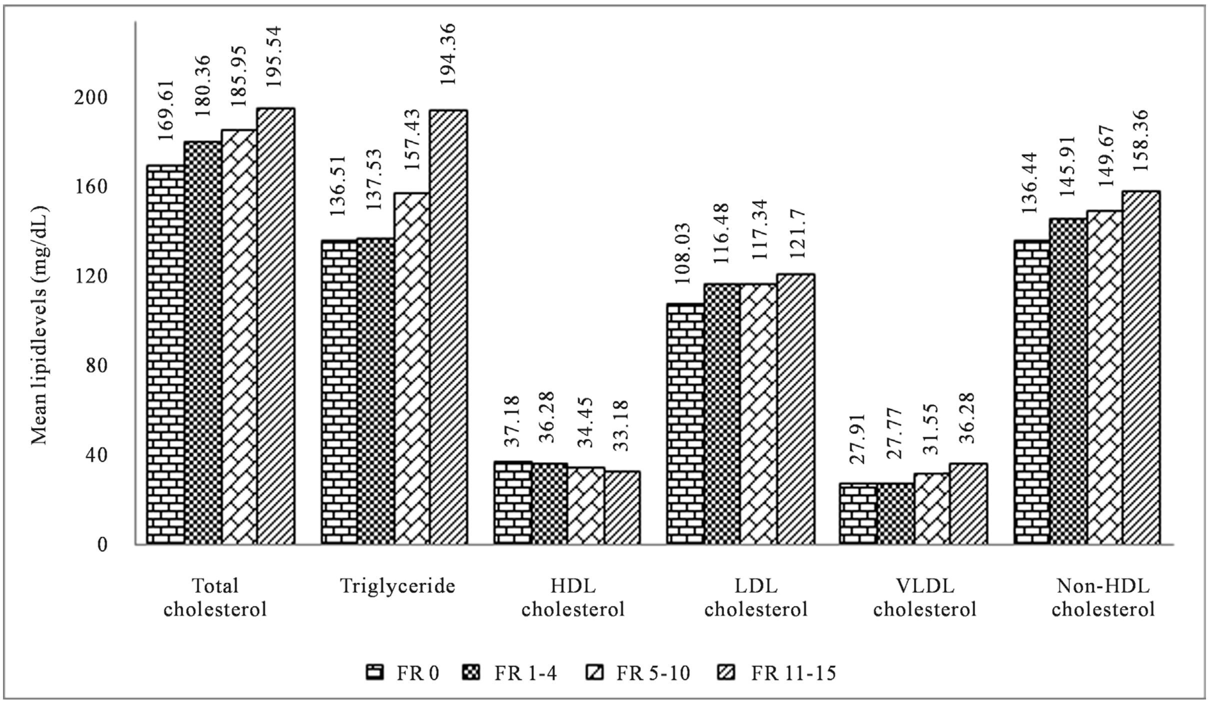

Figure 1. Mean lipid levels across FR index groups.

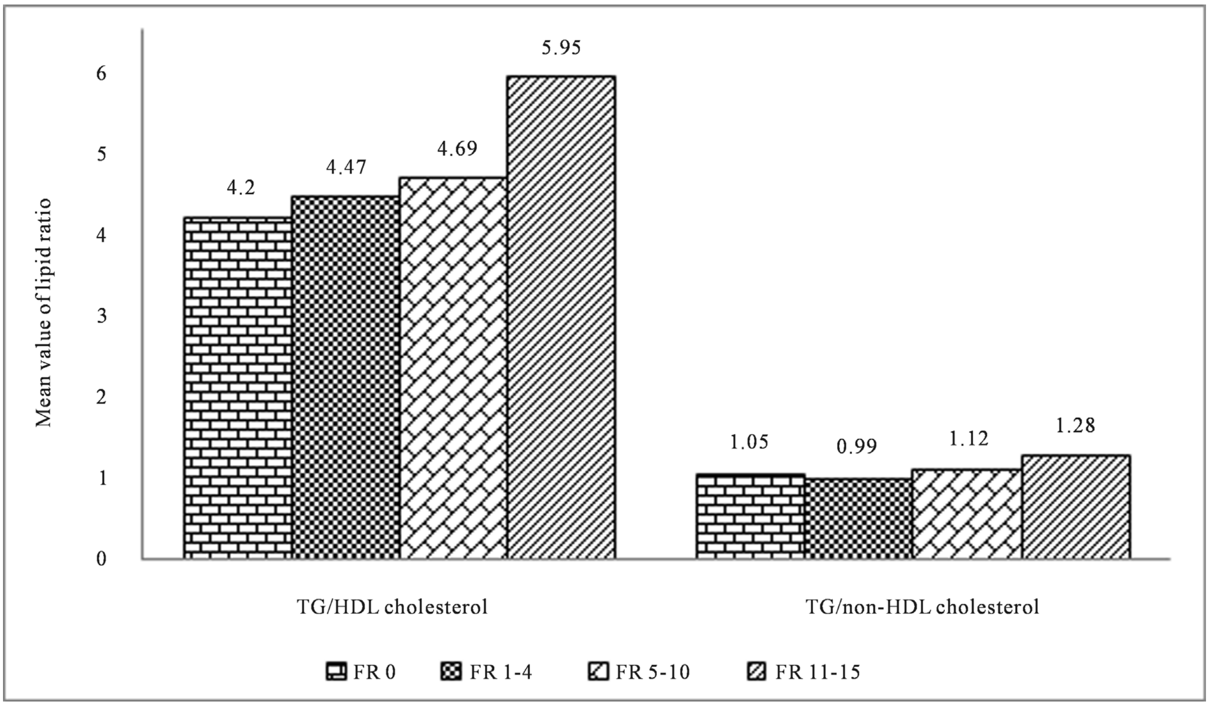

Figure 2. Mean lipid ratios across FR index groups.

3.5. Logistic Regression Analysis

Table 6 represents the major findings of the binary logistic regression analysis conducted in the study**.** Among the variables analyzed, presence of diabetes displayed the strongest correlation with FR index (odds ratio: 7.710, $P < 0.001$). Other variables showing significant correlation with FR index were BMI (odds ratio: 1.106, P =

Table 3. Analysis of correlation between FR index and lipid variables.

Variable	Correlation with FR index[a]	
	Correlation coefficient	P value for correlation
Total cholesterol, mg/dL	0.131	**0.002**
Triglycerides, mg/dL	0.217	**<0.001**
HDL cholesterol, mg/dL	−0.185	**<0.001**
LDL cholesterol, mg/dL	0.060	0.153
VLDL cholesterol, mg/dL	0.191	**<0.001**
Non-HDL cholesterol, mg/dL	0.116	**0.006**
Triglycerides/HDL cholesterol	0.112	**0.008**
Triglycerides/non-HDL cholesterol	0.130	**0.002**

[a]Spearman's rho correlation test.

Table 4. Analysis of frequency of patients according to the cut-off lipid levels across FR index groups.

Variables	Cut-off subgroups	FR index[a]				P value for association[b]
		0	1 - 4	5 - 10	11 - 15	
Total cholesterol	≤200 mg/dL (n = 377)	73 (19.4)	100 (26.5)	165 (43.8)	39 (10.3)	0.159
	>200 mg/dL (n = 189)	23 (12.2)	50 (26.5)	95 (49.7)	22 (11.6)	
HDL cholesterol	>40 mg/dL (n = 129)	16 (12.4)	24 (18.6)	67 (51.9)	22 (17.1)	**0.004**
	≤40 mg/dL (n = 437)	80 (18.3)	126 (28.8)	192 (43.9)	39 (8.9)	
LDL cholesterol	≤130 mg/dL (n = 371)	69 (18.6)	97 (26.1)	165 (44.5)	40 (10.8)	0.563
	>130 mg/dL (n = 194)	27 (13.9)	53 (27.3)	93 (47.9)	21 (10.8)	
Triglycerides	≤150 mg/dL (n = 334)	66 (19.8)	98 (29.3)	143 (42.8)	27 (8.1)	**0.004**
	>150 mg/dL (n = 232)	30 (12.9)	52 (22.2)	116 (50.0)	34 (14.7)	
Triglycerides/HDL cholesterol	≤4 (n = 388)	68 (17.5)	107 (27.6)	175 (45.1)	38 (9.8)	0.574
	>4 (n = 178)	28 (15.7)	43 (24.2)	84 (47.2)	23 (12.9)	
Triglycerides/non-HDL cholesterol	≤0.9 (n = 249)	48 (19.3)	76 (30.5)	108 (43.3)	17 (6.8)	**0.011**
	>0.9 (n = 317)	48 (15.1)	74 (23.3)	151 (47.6)	44 (13.9)	

[a]Data are presented as number of patients (percentage of patients); [b]Pearson Chi-square test for association.

0.032), status of hypertension (odds ratio: 3.713, P < 0.001), and smoking (odds ratio: 5.784, P < 0.001). On the other hand, age and gender showed a weak insignificant correlation with FR index. Of note, the relationship between FR index and all lipid variables was found to be statistically insignificant.

4. Discussion

In this study, we demonstrate a significant association between the extent of coronary artery disease and certain lipid variables in patients with suspected coronary artery disease. Identification of this strong association between lipid levels and the extent of coronary artery disease may help in deciding the potential management strategy for patients with acute coronary syndromes.

High levels of LDL cholesterol are directly correlated with coronary artery disease [10] [11], while low levels of HDL cholesterol have been considered as one of the strongest independent risk factors for the development of coronary artery disease [12] [13]. It has also been established that mild increases in triglyceride levels lead to

Table 5. Analysis of association between FR index and demographic variables.

Variable	FR index[a]				P value for association[b]
	0	1 - 4	5 - 10	11 - 15	
Age					
≤50 years (n = 152)	25 (16.4)	44 (28.9)	66 (43.4)	17 (11.2)	
51 - 60 years (n = 257)	49 (19.1)	63 (24.5)	118 (45.9)	27 (10.5)	0.853
>60 years (n = 157)	22 (14.0)	43 (27.4)	75 (47.8)	17 (10.8)	
Gender					
Female (n = 131)	30 (22.9)	27 (20.6)	61 (46.6)	13 (9.9)	0.116
Male (n = 435)	66 (15.2)	123 (28.3)	198 (45.5)	48 (11.0)	
BMI					
≤25 kg/m^2 (n = 464)	84 (18.1)	134 (28.9)	208 (44.8)	38 (8.2)	**<0.001**
>25 kg/m^2 (n = 102)	12 (11.8)	16 (15.7)	51 (50.0)	23 (22.5)	
Hypertension					
Hypertensive (n = 370)	31 (8.4)	79 (21.3)	205 (55.4)	55 (14.9)	**<0.001**
Nonhypertensive (n = 196)	65 (33.2)	71 (36.2)	54 (27.5)	6 (3.1)	
Diabetes					
Diabetic (n = 214)	15 (7.0)	16 (7.5)	126 (58.9)	57 (26.6)	**<0.001**
Nondiabetic (n = 352)	81 (23.0)	134 (38.1)	133 (37.8)	4 (1.1)	
Smoking					
Smoker (n = 359)	29 (8.1)	65 (18.1)	208 (57.9)	57 (15.9)	**<0.001**
Nonsmoker (n = 207)	67 (32.4)	85 (41.1)	51 (24.6)	4 (1.9)	

[a]Data are presented as number of patients (percentage of patients); [b]Pearson Chi-square test for association.

Table 6. Logistic regression analysis for demographic and lipid variables vs. Freisinger index[a].

Variable	Regression coefficient	Odds ratio	95% confidence interval	P value for regression
Demographic variables				
Age	0.004	1.004	0.982 - 1.026	0.729
Male gender	0.008	1.008	0.603 - 1.682	0.977
BMI	0.101	1.106	1.009 - 1.212	**0.032**
Diabetes mellitus	2.043	7.710	4.598 - 12.929	**<0.001**
Hypertension	1.312	3.713	2.342 - 5.886	**<0.001**
Smoking	1.755	5.784	3.637 - 9.197	**<0.001**
Lipid variables				
Total cholesterol	0.004	1.004	0.982 - 1.026	0.727
HDL cholesterol	−0.022	0.978	0.918 - 1.042	0.497
Triglycerides	0.000	1.000	0.990 - 1.010	0.983
Triglycerides/HDL cholesterol	0.014	1.014	0.984 - 1.046	0.360
Triglycerides/non-HDL cholesterol	0.153	1.165	0.374 - 3.626	0.792

[a]Binary logistic regression analysis.

rapid progression of coronary artery disease and increased risk of formation of new coronary artery lesions [14]-[16]. Further, the ratio of triglycerides to HDL cholesterol has shown promising findings as an attractive surrogate index of the atherogenicity of the plasma lipid profile [17]. Although such associations between lipid profile and obstructive coronary artery disease are well known [18], few data exist regarding the association between lipid levels and extent or severity of coronary lesions in patients with coronary artery disease.

In our study, total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol, and non-HDL cholesterol showed an increasing trend with an increase in FR index. On the other hand, HDL cholesterol levels showed decreasing trend with an increase in the FR index. Corresponding lipid ratios of triglycerides/HDL cholesterol and triglycerides/non-HDL cholesterol were increasing with an increase in FR index. Overall, these findings were in agreement with other study of similar nature [8]. These findings validate the high risk profile for obstructive coronary artery disease in patients with abnormal lipid levels, which makes this population appropriate for the analysis of the correlation between lipid profile and extent of impairment of the coronary arteries.

Earlier, Da Luz *et al*. [8] investigated the association among lipid levels, specifically triglycerides/HDL cholesterol, and the extent of coronary disease in 374 high-risk patients who underwent coronary angiography. They found that the relationship between the extent of coronary disease (dichotomized by a FR index of 5) and lipid levels (normal vs. abnormal) was statistically significant for triglycerides, HDL cholesterol, and triglycerides/HDL cholesterol. However, the relationship was not significant between extent of coronary disease and total cholesterol or LDL cholesterol [8]. In contrary to this study, we had divided the patients in the present study in to four groups based on FR index scores of 0, 1 - 4, 5 - 10, and 11 - 15 respectively. We observed that HDL cholesterol levels, triglycerides levels, and triglycerides/non-HDL cholesterol ratio had a significant association with severity of FR index in our patients. However, it should be noted that logistic regression analysis indicated an insignificant link between FR index and lipid variables.

Overall, we suggest that emphasis should be given on diagnosis and management of dyslipidemia, which is a major modifiable risk factor for the development of coronary artery disease. We are of opinion that identification and control of potential lipid variables are very crucial in the primary and secondary prevention of coronary artery disease and subsequent cardiovascular events. It is also noteworthy that other modifiable risk factors such as BMI, hypertension, diabetes, and smoking are proved to be associated with extent of coronary artery disease in our study. Of significance, the role of hypertension, diabetes, smoking, and obesity was much stronger than the role of lipid variables in predicting the FR index, as demonstrated by logistic regression analysis in the current study.

Our study has several limitations. We compared only lipid variables, and did not take the current use of medication into account. The use of angiotensin enzyme inhibitors or angiotensin II receptor blockers may weaken the relationship between lipid variables and the FR index, effect of which remains unknown in our study. In addition, the patients enrolled in our study present with clinically indicated angiography for diagnostic purposes; hence, it remains unknown whether our findings extend to general population without a history of cardiovascular events. In conclusion, the present study indicates that lipid levels, particularly HDL cholesterol, triglycerides, and triglycerides/non-HDL are useful indicators of development of coronary heart disease, and are significantly associated with the FR index score indicating the extent and severity of coronary artery lesions. Other factors such as hypertension, diabetes, smoking, and obesity also play a significant role. Further studies with large sample size may establish lipid variables as easy and non-invasive tools of predicting the presence and extent of coronary atherosclerosis.

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