JOURNAL OF CLINICAL MEDICINE OF KAZAKHSTAN (E-ISSN 2313-1519)
Original Article DOI: https://doi.org/10.23950/jcmk/12523

The association between non-HDL cholesterol and SYNTAX score in premature heart disease

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Received: 2022-08-10.
Accepted: 2022-10-09

J Clin Med Kaz 2022; 19(5):34-37

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Abstract

Aim: This study aimed to estimate the association of coronary artery disease complexity with non-HDL-C levels in premature CAD.

Background: Primary prevention has utmost importance in terms of minimizing the number of patients who had premature coronary artery disease (CAD). Non-high density lipoprotein cholesterol (non-HDL-C) contains potentially atherogenic lipoprotein fractions.

Material and methods: Coronary angiographic recordings of two hundred acute coronary syndrome patients were evaluated by two cardiologists. Clinical, demographic and lipid parameters of the patients were compared with SYNTAX score.

Results: Median age of the study group was 41 (18-45) years. One hundred eighty five (90.5%) of them were male, nineteen (9.5%) of them were female. Median SYNTAX score and ejection fraction of the patients were 17 (4.5-39) and 50 (33-68), respectively. SYNTAX score of the male patients was significantly higher compared to females [17 (4.5-39) vs 12 (8-26), p=0.048), similarly, diabetic patients had higher values of syntax score compared to non-diabetic patients [19 (10-39) vs 16 (4.5-37), p=0.005), There were no differences of SYNTAX score with respect to presence of hypertension, smoking status and family history of CAD. There were very strong positive correlation between SYNTAX score and non-HDL-C, TC and LDL-C levels (r=0.958, r=0.946 and r=0.921, respectively, p<0.001 for all). HgA1c levels showed positive correlation, whereas HDL-C showed negative correlation with SYNTAX score (r=0.793 and r=-0.620, respectively, p<0.001 for both).

Conclusion: non-HDL-C was a valuable tool in assessing the complexity of atherosclerotic cardiovascular disease in young patients.

Key words: coronary artery disease, young adult, HDL-C

Introduction

Despite advancements in medical therapy and device industry, cardiovascular diseases have been increasing in young population. In our country, cardiovascular mortality rates of men and women between 45-75 years of age were reported as 0.73% and 0.38%, respectively [1]. Atherosclerosis, which has a complex pathophysiology characterized by dysfunctional immune apparatus, oxidative stress and endothelial dysfunction, is the main cause of coronary artery disease (CAD) [2]. Classical risk factors for CAD plays crucial role in each stage of this process. Several studies have shown that CAD incidence has a positive correlation with total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) and a negative correlation with high density lipoprotein cholesterol (HDL-C). In the past decade, studies about value of lipid fractions for predicting atherosclerosis and coronary events have gained momentum. Lipid measurements such as TC to HDL-C ratio, non-HDL-C, and apolipoprotein-B100 have provided additional prognostic information to measured LDL-C levels [3].

CAD, the incidence of which increases with increasing age, has important genetic and environmental underpinnings [4]. Moreover, the prevalence of premature CAD has steadily risen over the past decades [5]. However, in the literature, there is no consensus about the description of premature CAD. Studies have used the cut-off values of 40 years, 45 years, 50 years and 60 years as the description of premature CAD. Family history of early-onset CAD has been denoted as having a first-degree male relative under the age of 55 years and female relative under the age of 65 years.

SYNTAX (Synergy between PCI with TAXUS and Cardiac Surgery) score, angiographic grading score based on lesion number, localization, complexity and functional significance, offers guidance to physicians on identification of the most appropriate revascularization strategy [6].

Moreover, it has been shown to have prognostic value in patients who underwent percutaneous coronary intervention [7]. Our aim was to investigate the relation between SYNTAX score and non-HDL-C concentration values and to test whether it has a better predictive value compared to traditional lipid parameters.

Material and methods

For the conduction of this study, data files of patients less than 45 years old who underwent coronary angiography between April 2015 and April 2017 were screened. Patients with prior PCI and/or coronary artery bypass graft surgery, malignancy, creatinine level more than 1.5 mg/dl, thyroid function disorders, statin use, incomplete data were excluded. A total of 200 patients who underwent coronary angiography because of non-ST myocardial infarction (NSTMI), ST-elevation myocardial infarction (STEMI) and unstable angina pectoris (UAP) were enrolled. Demographic and clinical variables including age, gender, hypertension (HT), diabetes mellitus (DM), smoking status, familial history of CAD were recorded. HT was defined as systolic and/or diastolic blood pressure greater than 140/90 mmHg or use of antihypertensive drugs. DM was defined as fasting blood glucose level more than 126 mg/dl or use of antidiabetic medication. All biochemical analysis results were obtained from hospital data system. Biochemical and complete blood count results of the patients during hospital admission were recorded. Venous blood samples were taken for the analysis of fasting LDL-C, HDL-C, triglyceride (TG), TC, HbA1c during first 24 hours of hospitalization. Non-HDL-C were calculated by subtracting HDL-C from TC. If the patients had TG levels more than 400 mg/dl, direct LDL-C measurements were recorded.

All patients underwent echocardiographic examinations with the use of Vivid 9 device which had a sector transducer of 3.2 MHz (Horten, Norway). Echocardiographic assessments were in compliance with current guidelines [8]. Coronary angiographic recordings of the patients were evaluated by two invasive cardiologists. SYNTAX score of each patient was calculated by using Syntax Score version 2.28 from the website www.syntaxscore.com [5]. Since the prognostic value of SYNTAX score in STEMI patients was demonstrated, those patients were not excluded from the study [9]. During evaluation of patients with STEMI, infarct-related artery was considered to be occluded less than 3 months and scored as such.

Statistical analysis

Normality of the data was assessed by Kolmogorov-Smirnov test. Since all the data showed non-normal distribution, they were expressed as median (minimum-maximum). For the comparison of two groups Mann-Whitney U test was used. Comparison of categorical variables was done by Chi-square test. Correlation analysis was done by Spearman correlation analysis. P value of less than 0.05 was considered as significant. All of the analyses were done by SPSS (Statistical Packagefor Social Science for Windows) 22.0 program.

Results

Median age of the study group was 41 (18-45) years. One hundred eighty five (90.5%) of them were male, nineteen (9.5%) of them were female. Clinical characteristics of the study population are given in Table 1. Median SYNTAX score and ejection fraction of the patients were 17 (4.5-39) and 50 (33-68), respectively. SYNTAX score and biochemical variables of the patients are given in Table 2. SYNTAX score of the male patients was significantly higher compared to females [17 (4.5-39) vs 12 (8-26), p=0.048), similarly, diabetic patients had higher values of syntax score compared to non-diabetic patients [19 (10-39) vs 16 (4.5-37), p=0.005), There were no differences of SYNTAX score with respect to presence of hypertension, smoking status and family history of CAD.

Table 1 Clinical characteristics of the study population

Age (years) (median, min-max)		41 (18-45)	
Gender (n, %)	Male	181	90,5%
	Female	19	9,5%
Smoking (n, %)		126	63,0%
Hypertension (n, %)		30	15,0%
Diabetes mellitus (n, %)		51	25,5%
Family history of CAD (n, %)		36	18,0%

CAD: Coronary artery disease.

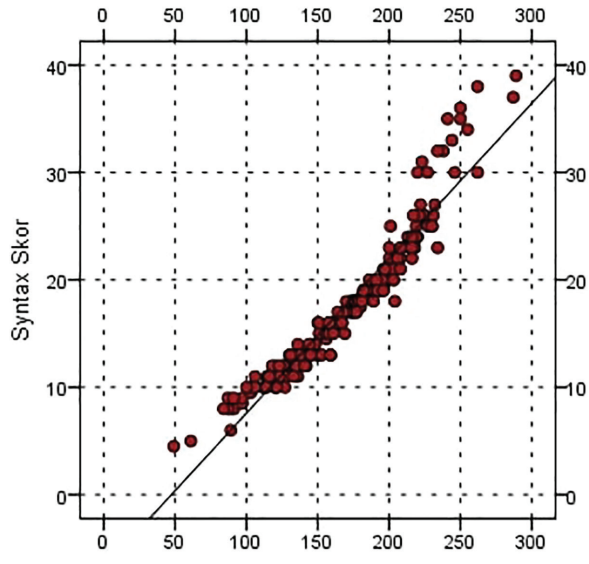
Table 2 SYNTAX score, EF and biochemical variables of the study population

	Min	Max	
Median			
SYNTAX score	4.5	39.0	17.0
Ejection Fraction (%)	33.0	68.0	50.0
HgA1c	4.1	12.6	6.7
Non-HDL-C (mg/dl)	49.0	289.0	169.5
Total Cholesterol (mg/dl)	123.0	326.0	212,0
HDL-C (mg/dl)	23.0	76.0	42.0
LDL-C (mg/dl)	38.0	273.0	152.0
Triglyceride (mg/dl)	35.0	1024.0	138.0

HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol.

There were very strong positive correlation between SYNTAX score and non-HDL-C, TC and LDL-C levels (r=0.958, r=0.946 and r=0.921, respectively, p<0.001 for all). HgA1c levels showed strong positive correlation, whereas HDL-C showed strong negative correlation with SYNTAX score (r=0.793 and r=-0.620, respectively, p<0.001 for both). We found weak positive correlation between TG levels and SYNTAX score (r=0.354, p<0.001). Correlation between SYNTAX score and non-HDL-C is shown in Figure 1.

Figure 1 - Correlation of SYNTAX score with non-HDL-C



Discussion

Premature CAD imposes great burden to patients, families and society. Since the patients are younger, longer sequelae of CAD could hamper quality of life. Hence, primary prevention with risk factor modification has important role in reducing the incidence and prevalence of premature CAD.

Hoit et al. stated that premature CAD is more frequent in males [10]. According to Joshi et al. females had first acute coronary syndrome episode 5.6 years later than their male counterparts [11]. Frequency of premature CAD in males has been reported to be ranged from 79% to 95% [10, 12-14]. One study showed that gender did not have any effect on long term prognosis of acute coronary syndrome [15]. Whereas another study suggested that male patients had more complex CAD in contrast to females. Our study population mainly composed of male patients and they have significantly higher SYNTAX score compared to females.

Prevalence of hypertension in patients with CAD less than 55 years of age has been found as 38.1% [16]. Another study found that 30.8% of acute coronary syndrome patients had hypertension [17]. An Indian study showed that prevalence of hypertension in male CAD patients under the age of 55 years and female CAD patients under the age of 65 years was 49% [18]. The prevalence of HT in our study was less than the aforementioned studies. Moreover, we did not find any difference in SYNTAX scores of patients with or without hypertension. Previous studies reported diabetes mellitus frequency between 14.7% to 44% in premature CAD patients [16-18]. In our study the frequency of DM was 25.1%. Diabetic patients had higher SYNTAX scores indicating more complex atherosclerotic disease.

The incidence of premature CAD has been increasing in developing countries. In INTERHEART study from 52 countries, median age of first myocardial infarction in South Asian countries was significantly lower than the others [19]. In that study, smoking, apolipoproteinB100 to apolipoprotein A-1 ratio, diabetes mellitus, hypertension, abdominal obesity, diet, physical activity and alcohol consumption were the predictive factors of acute coronary syndrome. Smoking was found to be one of the modifiable risk factor for premature CAD. In the literature, prevalence of smoking in premature CAD patients ranges from 51% to 89% [12, 19]. Our results were in concordance with the previous reports with a percentage of 63%. Xiong et al. found that smoking ratio was significantly higher in patients with high SYNTAX score [20]. However, we did not find any difference in SYNTAX score with respect to smoking status.

Family history of CAD is another risk factor for atherosclerotic cardiovascular disease. Several studies reported different values ranging from 41% to 71% for the frequency of family history of CAD [21, 22, 17]. According to Hoit et al.'s study, premature CAD patients had positive family history twice as high as compared to older CAD patients [10]. Our results were lower than the previous reports with a frequency of 18%.

Hyperlipidemia frequency in premature CAD patients differs in the literature. Aggarwal et al. found that frequency of dyslipidemia and low HDL-C concentration levels in premature CAD patients were 91% and 68.9%, respectively [23]. Similarly, Chia et al. revealed that younger CAD patients had higher frequency of hyperlipidemia compared to older ones [17]. On the contrary, Matsis et al. showed that patients with premature CAD had lower risk factors in contrast to older patients. According to their results young patients had at most one risk factor for CAD and they were considered as low risk subjects until the index event [24]. Frequency of dyslipidemia was 73% in our patients. Since we did not include the patients who were under lipid lowering therapy, the frequency of dyslipidemia was expected to be higher than our findings.

Studies about the association of premature CAD with lipid subfractions revealed conflicting results. Goliasch et al. compared the different lipid subfractions using a sample of 302 premature CAD patients [25]. In that study, association between premature CAD and non-HDL-C was found to be stronger compared to very low density lipoprotein cholesterol (VLDL-C), LDL-C, large intermediate density lipoprotein cholesterol (IDL-C), large LDL-C, and intermediate LDL-C. They did not find any correlation between premature myocardial infarction and small-dense LDL-C. 94 Shahid et al. found a positive correlation between low HDL-C concentration levels and premature myocardial infarction [26]. In Quebec Cardiovascular Study, small-dense LDL-C had a predictive value for premature atherosclerotic cardiovascular disease [27]. Rallidis et al. compared 100 premature CAD patients with 100 controls and found that among other lipid subfractions including TC, LDL-C, TG, apoB, lipoprotein(a), apoA; non-HDL-C had the highest predictive value for the premature CAD [28]. In our study, non-HDL-C showed very strong correlation with the extent of CAD in young acute coronary syndrome patients.

In conclusion, in premature CAD patients complexity of the atherosclerotic disease had very strong correlation with non-HDL-C concentration levels. Non-HDL-C might predict atherosclerotic cardiovascular disease better than other lipid parameters. It could be used as a treatment target in young patients.

Limitations of our study are: (1) It was a single center study, (2) sample size was relatively low, (3) Body mass index and waist circumference could not measured because of lack of data, (4) Incidence of familial hyperlipidemia could not determined.

Disclosures: There is no conflict of interest for all authors.

Acknowledgements: None.

Funding: None.

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