ANATOL J FAMILY MED

The Anatolian Journal of Family Medicine

Original Article

DOI: 10.5505/anatoljfm.2021.20053
Anatol J Family Med 2021;4(3):257–262

Determining the Relationship between Non-HDL Cholesterol and Syntax Score in Patients with Acute Coronary Syndrome Under 45 Years of Age

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ABSTRACT

Objectives: This study aimed to evaluate the relationship between non-HDL cholesterol level, which is a risk factor for coronary artery disease (CAD), and Syntax score.

Methods: This retrospective study included patients less than 45 years of age who underwent coronary angiography with a diagnosis of acute coronary syndrome between August 2015 and July 2020. Syntax scores of the patients were evaluated by two experienced cardiologists using the www.syntaxscore.com version on 2.28. Metabolic parameters such as total cholesterol, HDL cholesterol, LDL cholesterol, triglyceride and HbA1c of the patients were obtained from their files. Non-HDL cholesterol levels were calculated by subtracting HDL cholesterol from total cholesterol.

Results: In total, 296 patients were included in this study, 264 (89.1%) of patients were male. The mean Syntax score of the patients was 16.7±6.5. A significant positive correlation was determined between the Syntax score and non-HDL cholesterol, total cholesterol, LDL cholesterol, triglyceride, whereas a negative correlation was noted between the Syntax score and HDL cholesterol value (r=0.360 and p<0.001; r=0.426 and p<0.001; r=0.414 and p<0.001; r=0.388 and p=0.001; r=-0.396 and p<0.001, respectively). Besides, there was a significant correlation between Syntax score and HbA1c (r=0.768 and p<0.001).

Conclusion: The Syntax score which, indicates the severity and complexity of CAD, was noted to have a significant positive correlation with non-HDL cholesterol, HbA1c, total cholesterol, LDL cholesterol, triglyceride, and a negative correlation with HDL cholesterol.

Keywords: Acute coronary syndrome, coronary artery disease, HDL cholesterol, LDL cholesterol, triglyceride

Please cite this article as:
Akkaya H. Determining the Relationship between Non-HDL Cholesterol and Syntax Score in Patients with Acute Coronary Syndrome Under 45 Years of Age. Anatol J Family Med 2021;4(3):257–262.

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Received Date: 03.01.2021
Accepted Date: 09.04.2021
Published online: 29.12.2019

INTRODUCTION

Cardiovascular diseases (CVDs) remains to be the most common cause of death in the world despite the growing medical knowledge, many emerging cardiovascular drugs, and the development of the medical device industry in the 21st century. According to the data of the World Health Organization, 17.9 million deaths were reported in the world due to CVDs in 2019, representing 32% of all global deaths.[1] In the TEKHARF study conducted in our country, coronary mortality in the age range of 45-74 years was found to be 7.3 per 1000 population in men and 3.8 years in women.[2]

Atherosclerosis has been identified as the most common cause of coronary artery disease

(CAD). Atherosclerosis does not only result from a passive lipid accumulation in the vascular endothelium, but it is also a disease in which chronic inflammation with multiple factors and multiple stages plays a role. The classic risk factors of CAD are known toplay a role in every stage of this process. Several studies have shown that the incidence of CAD is positively correlated with plasma concentrations of total cholesterol and low-density lipoprotein (LDL) cholesterol and negatively correlated with high-density lipoprotein (HDL) cholesterol concentrations. Studies on the properties of lipid fractions in predicting atherosclerosis and coronary events have gained momentum in the last 10 years. It has been determined that lipid measurements such as triglyceride/HDL cholesterol, non-HDL cholesterol, and apolipoprotein B 100 can provide additional prognostic information to Friedewald-measured LDL cholesterol.[3]

It is known that genetic and environmental factors can cause CAD, and the incidence of this disease increases with age. However, it has been found that the incidence of CAD at an early age has seen a recent increase.[4] There is no consensus in the literature regarding the age of onset of early age CAD. The definition of family history in CAD risk factors is the presence of CAD in first-degree male relatives under 55 years of age and in first-degree female relatives under 65 years of age.[5] In a number of studies, 40, 45, 50, and 60 years of age were used as the limit for early age CAD.

Syntax (SYNergy between percutaneous coronary intervention (PCI) with TAXus and Cardiac Surgery) scoring system, which is prepared by taking into account the features such as the number of lesions angiographically, the location of the lesion, its functional importance, and intervention complexity, provides substantial data in the evaluation of the coronary artery bed.[6] This scoring system is intended to guide the decision of which patient will be given PCI and which patient will undergo coronary artery bypass grafting while planning revascularization. The Syntax scoring system can show the anatomical severity and complexity of CAD since it is a quantitative and reproducible basic measurement before revascularization; further, this can be used as an independent prognostic variable in patients undergoing PCI.[7] Syntax score is calculated with the help of computer algorithm with 12 basic questions. These questions include coronary dominance, the total number of lesions, and the vessel segment where the lesions are located, and the lesion characteristic. After each lesion is evaluated separately, the algorithm calculates the patient's Syntax score. When the Syntax score is 0-22, it is considered to be low; if the score is 23-32, it is medium; and if it is 33 and above, it is deemed to be high. The Syntax score aims to provide evidence-based data for decision-making in the revascularization of coronary lesions and provides information about lesion complexity.

This study aimed to evaluate the relationship between non-HDL cholesterol level, which is a risk factor for CAD, and Syntax score.

METHOD

This retrospective study included patients under 45 years of age who applied to the Niğde Ömer Halisdemir University Faculty of Medicine Cardiology Clinic and underwent coronary angiography with a diagnosis of acute coronary syndrome (Unstable angina, non-ST elevation myocard infarct, ST-elevation myocard infarct) between August 2015 and July 2020.

Risk factors such as age, gender, hypertension (HT), diabetes mellitus (DM), smoking, family history of heart disease of the patients were recorded from their files. In the file evaluations, a comparison was made for data accuracy from the electronic medical records of the hospital, the patient's outpatient clinic anamnesis form, and the epicrisis reports of other clinics. HT was defined as a resting systolic or diastolic blood pressure value of at least 140/90 mmHg or previous diagnosis with HT by the clinician, and DM was defined as a previous diagnosis, use of diet or antidiabetic medication, or a fasting blood glucose level >126 mg/dl. Routine blood count and biochemical tests of all cases were recorded from the data recording system of Niğde Ömer Halisdemir University Faculty of Medicine Training and Research Hospital. Serum biochemistry and complete blood count results were obtained from all patients included in this study. LDL cholesterol, HDL cholesterol, and triglyceride levels and HbA1c levels in venous blood samples following 12-hour fasting within 24 hours after admission were entered into the data form. Non-HDL cholesterol levels were calculated by subtracting HDL cholesterol from the total cholesterol. LDL cholesterol direct measurement values of patients with triglyceride values above 400 mg/dL were entered into the data form.

Ejection fraction values of the patients were processed from the echocardiography reports performed during admission. Echocardiographic examinations were performed using an echocardiography device (EPIQ 7, Philips Healthcare, Andover, Massachusetts) in the parasternal long and short axis and apical 2,4,5 space sections in the left lateral decubitus position.

Vessels with a Syntax score of at least 1.5 mm in diameter and at least 50% stenosis were included in the scoring. Images were evaluated using the PACS system. Angiographic images of the patients were evaluated by two experienced cardiologists. In intermediate lesions, the decision was

made based on the coronary angiography report of two cardiologists and operators. Syntax scores were calculated using the 2.28 version on www.syntaxscore.com.[6]

Patients with previous PCI or coronary artery bypass grafting operation, malignancies, basal creatinine above 1.5 mg/dl, thyroid dysfunction, on statin use, and patients whose data could not be reached were excluded from the study.

SPSS (Statistical Package for the Social Sciences for Windows) 23.0 program was used in the analyses. Frequency, percentage, mean, standard deviation, median, minimum and maximum values were used in the descriptive statistics of the data. The Kolmogorov–Smirnov test was used to measure the distribution of variables. Independent sample t test was used to compare the mean scores of the two groups. Pearson's correlation test and Spearman correlation test were used for correlation analysis. A p-value of less than 0.05 was considered to be significant.

RESULTS

In total, 296 patients were included in this study, 264 (89.1%) of patients were male. Mean age of patients was 39.8±4.6 years and mean Syntax score was 16.7±6.5. Age, Syntax score and metabolic parameters of the patients are summarized in Table 1.

While the syntax score was 17.1±6.6 for males, it was 14.6±5.8 for females (p=0.044). In addition, the mean of the Syntax score was significantly higher in patients with DM compared to the in patients with non-DM (p=0.002). The Syntax score according to clinical characteristics is summarized in Table 2.

Table 1. Age, Syntax score and metabolic parameters of the patients

	Mean±SD
Age (years)	39.8±4.6
SYNTAX score	16.7±6.5
Ejection fraction (%)	51.6±8.6
Non-HDL cholesterol (mg/dL)	156.1±34.5
Total cholesterol (mg/dL)	209.0±40.3
HDL cholesterol (mg/dL)	42.6±7.6
LDL cholesterol (mg/dL)	141.7±36.9
HbA1c (%)	7.2±2.4
	Median (minimum-maximum)
Triglyceride (mg/dL)	146.0 (39.0–1044.0)

HbA1c: Haemoglobin A1c; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; Non-HDL: Non- high density lipoprotein.

Table 2. The Syntax score according to clinical characteristics

	Syntax score		p
	n (%)	Mean±SD	
Smoking			
Yes	189 (63.8)	16.9±6.5	0.698
No	107 (36.2)	16.4±6.6	
Hypertension			
Yes	72 (24.4)	16.3±6.6	0.449
No	224 (75.6)	16.9±6.8	
Diabetes mellitus			
Yes	73 (24.6)	19.6±7.4	0.002
No	223 (75.4)	15.8±6.3	
Family history of heart disease			
Yes	56 (18.9)	16.8±7.1	0.451
No	240 (81.1)	16.5±6.7	

Independent samples t-test.

When the relationship between Syntax score and metabolic parameters were evaluated, there was a positive correlation was found between Syntax score and HbA1c, non-HDL cholesterol, total cholesterol and LDL cholesterol. The relationship between Syntax score and metabolic parameters is summarized in Table 3.

DISCUSSION

With the occurrence of CAD at an early age, serious consequences arise for the individual, his family, and society. The loss of individuals between the ages of 35 and 65 years who join the workforce poses an important problem in society. Careful management of all risk factors with primary prevention will thus play an important role in addressing

Table 3. The relationship between Syntax score and metabolic parameters

	Syntax Score	
	r	p
HbA1c (%)	0.768	<0.001*
Non-HDL cholesterol (mg/dL)	0.360	<0.001*
Total cholesterol (mg/dL)	0.426	<0.001*
HDL cholesterol (mg/dL)	-0.396	<0.001*
LDL cholesterol (mg/dL)	0.414	<0.001*
Triglyceride (mg/dL)	0.388	0.001†

HbA1c: Haemoglobin A1c; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; Non-HDL: Non- high density lipoprotein.

*Pearson's correlation test; †Spearman correlation test.

this problem. Early age CAD can have a worse prognosis, and patients have a longer life expectancy.[8,9]

The prevalence of early age CAD is increasing in developing countries. In the INTERHEART study, 1.732 acute coronary syndrome patients and 2.204 control patients were compared in terms of risk factors. It was stated that smoking, apolipoprotein B100/apolipoprotein A-1 ratio, DM, HT, abdominal obesity, daily fruit and vegetable intake, physical activity, alcohol use, and psychosocial risk factors predicted the risk of acute coronary syndrome in individuals under the age of 40.[10]

The Syntax study is an algorithm that tries to provide a standard for the treatment of coronary arteries. In the Syntax study, the Syntax score was found to be a strong predictor of long-term adverse cardiovascular events. In this same study, it was shown that both numerical and categorical values of the Syntax score can be used.[11] The Syntax score is used both for prognostic purposes (prevalence of CAD) and to determine treatment options. The relationship between a cardiovascular risk factor and the prevalence of CAD by examining whether there was a non-HDL cholesterol relationship with the Syntax score, which has a prognostic value and shows the prevalence and complexity of CAD in patients with early CAD was investigated in our study.

CAD can be attributed to genetic and environmental factors, and this incidence of the disease is known to increase with age. However, in recent years, it has been determined that the incidence of CAD has increased at an early age.[12] There is no clear age definition for early age CAD in the literature. In our study, patients under the age of 45 were considered to have early age CAD.

It is known that early age CAD is more common among the males. In addition, it was found that females had acute coronary syndrome at 5.6 years older than the males. In the literature, the prevalence of the male gender in early age CAD was found to be 79-95%.[13] In our study, the male gender ratio was found to be 89.1%, which is consistent with the literature. It is known that the Syntax score is higher in men.[14] In our study, the Syntax score was significantly higher among males compared to females.

Smoking leads the changeable risk factors for early age CAD. In the literature, the prevalence of smoking in patients with early age CAD varies between 51% and 89%.[15] The smoking rate was 63.8% in our study, which is consistent with previous literature. In a study conducted on 451 patients, the rate of smoking was found to be statistically significantly higher in the group with a high Syntax score.[14] However, in our study, no significant difference was found between the Syntax score in the smoker and non-smoker groups. It was thought that this result might be related to our use of numerical values, not categorical values, as a method in the evaluation of the Syntax score.

In a 10-year retrospective study of early age CAD patients, the frequency of HT was found to be 30.8% in acute coronary syndrome patients under the age of 45.[16] In our study, the frequency of HT was found to be 24.4%, which is less compared to previous literature. In a retrospective study investigating the effect of DM and HT on the Syntax score in 2.163 stable CAD patients, the absence of HT and DM was determined to be negatively correlated with the Syntax score, while no such relationship was observed in hypertensive patients without DM or DM patients without HT.[17] In our study, no significant difference was observed between the Syntax scores in the groups with and without HT.

The frequency of DM in early age CAD has been observed in the range of 14.7-44%.[18] In our study, the frequency of DM was found to be 24.6%. In other study, they found a positive correlation between DM and the Syntax score in non-ST elevation myocard infarct patients.[19] In our study, the Syntax score in the group with DM was significantly higher than the group without DM. Complex CAD is observed in DM patients, and the high Syntax score in DM patients in our study supports this finding. In light of this information, a positive correlation was found between HbA1c and the Gensini score in early-age CAD patients, and they detected HbA1c as an independent risk factor for coronary artery complexity.[20] In another prospective study, a positive correlation was found between HbA1c levels and the Syntax score in stable CAD patients.[21] In our study, a strong positive correlation was noted between HbA1c and the Syntax score.

Patients with family history of CAD have been determined to be twice more vulnerable to developing early CAD than elderly CAD patients.[13] In our study, family history of CAD was found to be 18.9%, which is at a lower rate compared to previous literature.

The relationship between early age CAD and lipid fractions has been examined in different studies in the literature. In a meta-analysis, a positive correlation was found between the low HDL cholesterol level and early age CAD in patients less than 55 years of age.[22] In the Quebec Cardiovascular Study in which a man was followed for 13 years, it was stated that large LDL cholesterol particles did not predict future cardiovascular events, and small dense LDL cholesterol was predictive for early age CAD.[23] Additionally, in a study

wherein 100 early age acute coronary syndrome patients and 100 control patients were evaluated, it was found that non-HDL cholesterol, among the lipid risk factors, was the highest predictor of acute coronary syndrome.[24] In a study comparing the Gensini score and cholesterol parameters, they reported that non-HDL cholesterol predicted coronary atherosclerosis better than LDL cholesterol.[25] In our study, there was a significant positive correlation between numeric Syntax score and non-HDL cholesterol, total cholesterol, LDL cholesterol, and triglycerides. There was a significant negative correlation between the Syntax score and HDL cholesterol.

Collecting the data on a retrospective file, with some data gone missing, has resulted in a relatively low number of patients. The single-center nature of this study is one of its limitations. Data as regards waist circumference and body mass index were not examined in this study due to insufficient file data. The effect of metabolic syndrome could not be investigated. Since the Dutch Lipid Clinic information of the patients could not be obtained from the file data, the familial hyperlipidemia frequency could not be determined.

CONCLUSION

In this study, a positive correlation was found between non-HDL cholesterol and Syntax score, however a negative correlation was found with HDL cholesterol. Besides, there was a significantly positive correlation was detected between the Syntax score and HbA1c value. In light of the data in our study, more careful treatment for non-HDL cholesterol should be performed in primary and secondary prevention of CAD, especially in patients under the age of 45.

Disclosures

Acknowledgements: Thanks to Dr. Ertuğrul Emre Güntürk for his contribution in the evaluation of Syntax scores.

Peer-review: Externally peer-reviewed.

Ethics Committee Approval: The ethical approval for this study Ethics Committee of Niğde Ömer Halisdemir University was obtained from (Approval date: June 01, 2020, and Approval number: 2020/05-13)

Conflict of interest: The author declares that no conflict of interest exists regarding this article.

Financial support: The author declares that no financial support was received for this article.

REFERENCES

1. WHO. Cardiovascular diseases fact sheet; May 2017. p. 114–5.
2. Onat A, Can G, Yüksel H, Ademoglu E, Erginel-Ünaltuna N, Kaya A, et al. TEKHARF 2017. İstanbul: Logos Yayıncılık; 2017. p. 25.
3. Ridker PM, Rifai N, Cook NR, Bradwin G, Buring JE. Non-HDL cholesterol, apolipoproteins A-I and B100, standard lipid measures, lipid ratios, and CRP as risk factors for cardiovascular disease in women. JAMA 2005;294(3):326–33.
4. Fournier JA , Sánchez A, Quero J, Fernández-Cortacero JA, González-Barrero A. Myocardial infarction in men aged 40 years or less: a prospective clinical-angiographic study. Clin Cardiol 1996;19(8):631–6.
5. BP Griffin, EJ Topol, D Nair, K Ashley. Manual of cardiovascular medicine. 2nd ed. London: Lippincott Williams & Wilkins; 2004. p. 528
6. Sianos G, Morel M, Kappetein AP, Morice M, Colombo A, Dawkins K, et al. The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. Euro Interv 2005;1(2):219–27.
7. Girasis C, Garg S, Raber L, Sarno G, Morel MA, Garcia-Garcia HM, et al. SYNTAX score and Clinical SYNTAX score as predictors of very long-term clinical outcomes in patients undergoing percutaneous coronary interventions: a substudy of SIRolimus-eluting stent compared with pacliTAXel-eluting stent for coronary revascularization (SIRTAX) trial. Eur Heart J 2011;32(24):3115–27.
8. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al: Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364(9438):937–52.
9. Bundhun PK, Sookharee Y, Bholee A, Huang F. Application of the SYNTAX score in interventional cardiology: A systematic review and meta-analysis. Medicine (Baltimore) 2017;96(28):e7410.
10. Kannel WB, Abbott RD. Incidence and prognosis of unrecognized myocardial infarction. N Engl J Med 1984;311(18):1144–7.
11. Hoit BD, Gilpin EA, Henning H, Maisel AA, Dittrich H, Carlisle J, et al. Myocardial infarction in young patients: an analysis by age subsets. Circulation 1986;74(4):712–21.
12. Xiong Z, Zhu C, Qian X, Zhu J, Wu Z, Chen L. Predictors of clinical SYNTAX score in coronary artery disease: serum uric acid, smoking, and Framingham risk stratification. J Invasive Cardiol 2011;23(12):501–4.
13. Larsen GK, Seth M, Gurm HS. The ongoing importance of smoking as a powerful risk factor for ST-segment elevation myocardial infarction in young patients. JAMA Intern Med 2013;173(13):1261–2.
14. Chan CM, Chen WL, Kuo HY, Huang CC, Shen YS, Choy CS, et al. Circadian variation of acute myocardial infarction in young people. Am J Emerg Med 2012;30(8):1461–5.
15. Youn YJ, Lee JH, Lee JW, Ahn MS, Ahn SG, Kim JY, et al. Effect of hypertension and diabetes on high Syntax score in patients with coronary artery disease. JACC 2012;59(13):E99.

16. McManus DD, Piacentine SM, Lessard D, Gore JM, Yarzebski J, Spencer FA, et al. Thirty-year (1975 to 2005) trends in the ıncidence rates, clinical features, treatment practices, and short-term outcomes of patients <55 years of age hospitalized with an ınitial acute myocardial ınfarction. Am J Cardiol 2011;108(4):477–82.
17. Montero-Cabezas JM, Karalis I, Wolterbeek R, Kraaijeveld A, Hoefer I, Pasterkamp G, et al. Classical determinants of coronary artery disease as predictors of complexity of coronary lesions, assessed with the SYNTAX score. Neth Heart J 2017;25(9):490–7.
18. Ayhan SS, Tosun M, Ozturk S, Alcelik A, Ozlu MF, Erdem A, et al. Glycated haemoglobin is correlated with the severity of coronary artery disease independently of traditional risk factors in young patients. Endokrynol Pol 2012;63(5):367–71.
19. Ikeda N, Iijima R, Hara H, Moroi M, Nakamura M, Sugi K. Glycated haemoglobin is associated with the complexity of coronary artery disease, even in non-diabetic adults. J Atheroscler Thromb 2012;19(12):1066–72.
20. Shahid M, Sun RL, Liu Y, Bao JL, Huang CX, Liao Y, et al. Is high high-density lipoprotein cholesterol beneficial for premature coronary heart disease? A meta-analysis. Eur J Prev Cardiol 2016;23(7):704–13.
21. St-Pierre AC, Cantin B, Dagenais GR, Mauriege P, Bernard PM, Despres JP, et al. Low-density lipoprotein subfractions and the long-term risk of ischemic heart disease in men: 13-year follow-up data from the Québec Cardiovascular Study. Arterioscler Thromb Vasc Biol 2005;25(3):553–9.
22. Rallidis LS, Pitsavos C, Panagiotakos DB, Sinos L, Stefanadis C, Kremastinos DT. Non-high density lipoprotein cholesterol is the best discriminator of myocardial infarction in young individuals. Atherosclerosis 2005;179(2):305–9.
23. Zhang Y, Wu NQ, Li S, Zhu CG, Guo YL, Qing P, et al. Non-HDL-C is a better predictor for the severity of coronary atherosclerosis compared with LDL-C. Heart Lung Circ 2016;25(10):975–81.