Original Article / *Özgün Araştırma*

DOI: 10.4274/haseki.galenos.2021.6788
Med Bull Haseki 2021;59:74-79

Comparisson of Different Cardiovascular Risk Scores in Newly Diagnosed Hyperlipidemia Patients and Their Relations with Metabolic Syndrome

Yeni Tanı Almış Hiperlipidemili Hastalarda Farklı Kardiyovasküler Risk Skorlamalarının Karşılaştırılması ve Bunlarin Metabolik Sendromla İlişkileri

Ayşegül İlhan, Sema Uçak*, Nazan Demir**, Okcan Basat***, Yüksel Altuntaş****

University of Health Sciences Turkey, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Medical Oncology, Ankara, Turkey

** University of Health Sciences Turkey, Ümraniye Training and Research Hospital, Clinic of Internal Medicine, Istanbul, Turkey*

***Eskişehir Osmangazi University Faculty of Medicine, Department of Medical Oncology, Eskisehir, Turkey*

**** University of Health Sciences Turkey, Training and Research Hospital, Clinic of Internal Medicine, Istanbul, Turkey*

*****University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Endocrinology, Istanbul, Turkey*

Abstract

Aim: Today, there are many risk calculation methods. In this study, we aimed to compare SCORE, QRISK2, BNF, ASSIGN and Framingham risk scorings for patients who have been first detected that they have hyperlipidemia and to evaluate the relation between metabolic syndrome criteria and cardiovascular risk scorings for the same group patients.

Methods: We included 216 female, 84 male newly diagnosed hyperlipidemic patients. Lipid levels measured using enzymatic calorimetric methods. We also measured weight, height, waist circumference of patients. We used NCEP ATP III for metabolic syndrome identification. For 10 years cardiovascular risk assessment we performed Framingham, SCORE, QRISK 2, ASSIGN, BNF score systems.

Results: The difference between these four different methods found statistically significant with Friedman test (p<0.001). With post-hoc dual analysis, we found that Framinghan score was different from the other 3 methods, QRISK2 score was different from Framingham and ASSIGN score results, ASSIGN score was different from other 3 score results and BNF score was also different from Framingham and ASSIGN score results. Only between BNF-QRISK2 scores we could not find difference.

Conclusions: This study showed that when four different cardiovascular risk score methods are compared in newly diagnosed hyperlipidemia patients, only BNF and QRISK2 scorings revealed similar results but Framingham and ASSIGN scorings resulted differently either from each other or BNF and QRISK2

Keywords: Metabolic syndrome, hyperlipidemia, cardiovascular risk scores

Öz

Amaç: Günümüzde çok sayıda kardiyovasküler risk hesaplama sistemi bulunmaktadır. Biz bu çalışmada ilk kez hiperlipidemi saptanan hastalarda SCORE, QRISK2, BNF, ASSIGN, Framingham risk skorlamalarını karşılaştırmayı ve aynı grup hastalarda metabolik sendrom kriterlerinin varlığı ile kardiyovasküler risk skorlamaları arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: Yeni hiperlipidemi tanısı almış 216 kadın, 84 erkek hastayı çalışmaya dahil ettik. Kan lipid seviyeleri için enzimatik kalorimetrik yöntemler kullanıldı. Hastaların kilosu, boyu, bel çevresi de ölçüldü. Metabolik sendrom tanımlaması için NCEP ATP III kriterlerini kullandık. 10 yıllık kardiyovasküler risk değerlendirmesi için de Framingham, SCORE, QRISK 2, ASSIGN, BNF skor sistemleri uyguladık.

Bulgular: Bu dört farklı yöntem arasındaki fark, Friedman testi ile istatistiksel olarak anlamlı bulundu (p<0,001). Post-hoc ikili analiz ile Framinghan skor sisteminin diğer 3 skor sisteminden, QRISK2 skor sisteminin Framingham ve ASSIGN skor sistemlerinden farklı olduğunu, ASSIGN skor sisteminin, diğer 3 skor sisteminden farklı olduğunu ve BNF skor sisteminin de Framingham ve ASSIGN'den farklı olduğunu bulduk. Sadece BNF ile QRISK2 skor sistemleri arasında fark bulamadık.

Sonuç: Bu çalışma ile yeni tanı konmuş hiperlipidemili hastalarda dört farklı kardiyovasküler risk skorlama sistemi karşılaştırıldığında; sadece BNF ve QRISK2 skorlarının benzer sonuç verdiği ancak FRAMINGHAM ve ASSIGN skorlarının hem birbirinden hem de BNF ve QRISK2'den farklı sonuçlar verdiği ortaya konuldu.

Anahtar Sözcükler: Metabolik sendrom, hiperlipidemi, kardiyovasküler risk skorları

Address for Correspondence/Yazışma Adresi: Ayşegül İlhan, University of Health Sciences Turkey, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Clinic of Medical Oncology, Ankara, Turkey
E-mail: ayse_ilhan85@hotmail.com ORCID: orcid.org/0000-0002-0333-1388
Received/Geliş Tarihi: 08.12.2020 **Accepted/Kabul Tarihi:** 13.01.2021

Introduction

Atherosclerotic cardiovascular diseases (ASCVD) continue to be the leading cause of morbidity and mortality worldwide, especially in developing countries, despite significant advances in this area in recent years (1). Lifelong coronary heart disease (CHD) risk was determined as 49% for men and 32% for women aged 40 years old in the Framingham Heart Study which included 7733 people between the ages of 40-94 who did not have a history of CHD. Even in persons with no known disease at the age of 70, the lifetime risk has been calculated as 35% for men and 24% for women (2). The situation in our country is not different from the global status. According to the Heart Disease and Risk Factors in Turkish Adults (HDRFTA) study, CHD mortality between the ages of 45-74 was 9.1 per 1000 among men and 2.34 among women. It has been shown that both CHD mortality and the prevalence of new coronary events in Turkish adults have an increasing trend compared to neighboring countries, and the study emphasized the need for preventive measures against coronary disease (3).

Age, gender, high blood pressure, smoking, dyslipidemia and the presence of diabetes mellitus are accepted as the major risk factors for ASCVD (4). Stroke, thromboembolism, heart failure, are the most important results of ASCVD that cause morbidity, mortality and decrease quality of life (5). The combination and interaction of these risk factors has been shown to accelerate the risk of vascular disease (6); therefore, risk prediction algorithms assessing the risk of developing ASCVD have been developed in order to be able to reduce the mortality and morbidity of those with high risk and to maintain low risk by encouraging the maintenance of a healthy lifestyle in those with low risk (7).

In order to prevent cardiovascular diseases, current guidelines recommend the calculation of 10-year atherosclerotic cardiovascular disease (ASCVD) risk of individuals aged 40-75 years and performing risk assessment before starting pharmacological treatments (antihypertensive, lipid lowering, antiplatelet, etc.) (1).

There are many risk calculation systems available today, and the oldest and most well-known of these is the Framingham scoring system. Other well-known systems are SCORE, PROCAM, QRISK, WHO/ISH, and various other national risk calculation systems. Since hyperlipidemia is a condition associated with cardiovascular risk, lipid level is included in all risk calculation systems. In our study, we aimed to compare the SCORE, QRISK2, BNF, ASSIGN, Framingham risk scores in patients with hyperlipidemia for the first time, and to evaluate the relationship between the presence of metabolic syndrome criteria and cardiovascular risk scores in the same group of patients.

Methods

The study was approved by the ethics committee on 23/10/2012. Written and verbal informed consent was obtained from each participant for the study. A total of 216 female and 84 male patients who received their initial diagnosis of hyperlipidemia after applying to the internal diseases outpatient clinic between January and April 2014 (and had not received any treatment for this reason) were included in the study.

Diagnosis of Metabolic Syndrome

Participants were evaluated for metabolic syndrome using the NCEP ATP III criteria:

1. Central obesity (waist circumference; female >88 cm, male >102 cm)
2. Fasting triglyceride ≥150 mg/dL
3. Low HDL cholesterol (men <40 mg/dL, women <50 mg/dL)
4. High blood pressure (≥130/≥85 mm Hg) or medication use for hypertension
5. Fasting blood glucose elevation (≥100 mg/dL)

Metabolic syndrome was diagnosed in patients who met 3 of these criteria.

Calculating Cardiovascular Risk

The Framingham, SCORE, QRISK2, ASSIGN, and BNF risk systems were used to evaluate the 10-year coronary artery disease risk of the participants. Framingham, ASSIGN, and BNF were automatically calculated from the website https://www.bloodpressureclinic.ed.ac.uk/calculating-cardiovascular-risk using Joint National Comittee (JNC)-VIII blood pressure categories, NCEP total cholesterol categories, and LDL cholesterol categories. SCORE was calculated automatically from the website http://www.heartscore.org.

Statistical Analysis

For continuous variables, compliance with normal distribution was examined using the Shapiro-Wilk test. Descriptive statistics used to define continuous variables were mean, standard deviation, minimum, median and maximum. Frequency (n) and percentages (%) were used to describe discrete variables. The Wilcoxon signed-rank test was used to compare dependent variables of 2 groups that did not show normal distribution. The Friedman test was used to compare dependent variables with more than 2 groups that did not show normal distribution. Post-hoc evaluations were performed using the Wilcoxon signed-rank test for significant results. Statistical significance level was set at 0.05. All analyses were conducted by the use of the MedCalc Statistical Software version 12.7.7 (MedCalc Software Bvba, Ostend, Belgium; http://www.medcalc.org).

Results

Patient characteristics are shown in Table 1. A statistically significant difference was found between the risk scores of the patients measured by 4 different methods, as determined by the Friedman test (p<0.001).

As a result of post-hoc pairwise comparisons:

- Framingham score was significantly different from scores calculated by the other 3 methods,
- QRISK2 score was significantly different from scores calculated with the Framingham and ASSIGN methods,
- The ASSIGN score was significantly different from the scores calculated by the other 3 methods,
- BNF score was significantly different from Framingham and ASSIGN,
- It was seen that there was no statistically significant difference between BNF and QRISK2 (Table 2).

A statistically significant and high level of correlation was found between all scoring methods (Table 3).

There was a statistically significant difference between the risk scores measured by different methods in groups formed according to the presence/absence of metabolic syndrome (Friedman test, p<0.001). In the post-hoc evaluation, it was seen that each measurement method had significantly different results from each other (Table 4).

When risk scoring systems were compared among themselves (Table 5):

Table 1. General characteristics of the patients

		Mean ± SD	n	%
Age (year)		54.1±11		
Age (year)	<50		111	37
	≥50		189	63
Gender	Female		216	72
	Male		84	28
BMI (kg/m^2)		29.4±5.1		
BMI (kg/m^2)	<25		57	19
	25-30		121	40.3
	≥30		122	40.7
DiabetesMellitus	Yes		69	23
	No		231	77
Hypertension	Yes		98	32.7
	No		202	67.3
Familyhistory	Yes		88	29.3
	No		212	70.7
Smoking	Yes		94	31.3
	No		206	68.7
Metabolic syndrome	Yes		109	36.4
	Mo		191	63.6

BMI: Body mass index, SD: Standard deviation

- Among subjects who were defined to have high-risk according to the Framingham criteria, the QRISK2, BNF and ASSIGN scores identified that 62.5% (n=35), 46.4% (n=26) and 96.4% (n=54) of these were individuals at high risk, respectively.
- Among subjects who were defined to have high-risk according to the QRISK2 criteria, the Framingham, BNF and ASSIGN scores identified that 71.4% (n=35), 46.9% (n=23) and 91.8% (n=45) of these were individuals at high risk, respectively.
- Among subjects who were defined to have high-risk according to the BNF criteria, the Framingham, QRISK2 and ASSIGN scores identified 86.7% (n=26), 76.7% (n=23) and 100% (n=30) of these were individuals at high risk, respectively.
- Among subjects who were defined to have high-risk according to the ASSIGN criteria, the Framingham, QRISK2 and BNF scores identified that 47.8% (n=54), 39.8% (n=45) and 26.5% (n=30) of these were individuals at high risk, respectively.

While the ASSIGN scoring system tended to assign patients to a higher risk group, the BNF and QRISK2 systems showed a tendency for categorizing patients into lower risk categories.

Discussion

In our study, we evaluated the results of different cardiovascular risk scoring systems in patients with newly diagnosed hyperlipidemia, and the relationships between the presence of metabolic syndrome and cardiovascular risk scores in the same group. Our findings revealed that when all patients with hyperlipidemia are considered (without distinction for metabolic syndrome), only the BNF and QRISK2 scores of these 4 cardiovascular risk scoring system provided similar results, and the Framingham and each on risk score often produced different results as well Ncho IS Different results. It has been shown that patients with hyperlipidemia with metabolic syndrome have higher cardiovascular risk than patients without metabolic syndrome.

As of the year 2000, 9.2 million people aged older than 30 years have been identified to have metabolic

Table 2. Comparison of different cardiovascular risk scores (Post-hoc analysis)

Post-hoc analysis	p
Framingham vs QRISK2	<0.001
Framingham vs ASSIGN	<0.001
Framingham vs BNF	<0.001
BNF vs QRISK2	0.648
BNF vs ASSIGN	<0.001
ASSIGN vs QRISK2	<0.001

Table 3. Correlation between different cardiovascular risk scores

	Framingham	QRISK2	ASSIGN	BNF
	r (p)	r (p)	r (p)	r (p)
Framingham	1.00	0.881 (<0.001)	0.894 (<0.001)	0.891 (<0.001)
QRISK2	0.881 (<0.001)	1.00	0.845 (<0.001)	0.808 (<0.001)
ASSIGN	0.894 (<0.001)	0.845 (<0.001)	1.00	0.882 (<0.001)
BNF	0.891 (<0.001)	0.808 (<0.001)	0.882 (<0.001)	1.00

Table 4. Comparison of differentcardiovascular risk scores in patients with or without metabolic syndrome (Post-Hoc analysis)

	Metabolic syndrome (+)	Metabolic syndrome (-)
Framingham vs QRISK2	<0.001	<0.001
Framingham vs ASSIGN	<0.001	<0.001
Framingham vs BNF	<0.001	<0.001
QRISK2 vs ASSIGN	<0.001	<0.001
QRISK2 vs BNF	0.001	0.019
ASSIGN vs BNF	<0.001	<0.001
*Wilcoxon Signed-rank test		

Table 5. Distribution of patients according to risk status using different scoring methods

	Low Risk	Moderate Risk	High Risk	Total
	n (%)	n (%)	n (%)	N(%)
Framingham	148 (49.5)	95 (31.8)	56 (18.7)	299 (100)
QRISK2	173 (58.1)	76 (25.5)	49 (16.4)	298 (100)
ASSIGN	123 (41.0)	64 (21.3)	113 (37.7)	300 (100)
BNF	179 (59.9)	90 (30.1)	30 (10)	299 (100)

syndrome in Turkey. On the other hand, 53% of individual who developed coronary artery disease wereals patients with metabolic syndrome (8). In the retrospective study, in which they conducted a 10-year cardiovascular risk assessment, Lee et al. (9) revealed that Framingham had a low sensitivity (37%) in patients younger than 40 years. Although young patients were not differentiated in our study, Framingham and other risk models gave similar results in the general patient group, unlike the findings of Lee et al. (9) Furthermore, unlike the findings of Ghandehari et al. (10) showed that Framing ham results were significantly associated with body mass index (BMI) and abdominal obesity. Similar to our results, the aforementioned study demonstrates that the selection of risk assessment models is critical for accurate analysis of patients in terms of cardiovascular risks, since this diseases have been shown to be associated with obesity and metabolic syndrome and the fact that the incidence of cardiovascular diseases can be reduced even with lifestyle changes (11). Marsh et al. (12) stated in their study that the risk of cardiovascular disease increases in direct proportion to thein crease in risk factors, concluding that individuals' future cardiovascular risk can be predicted via such risk factors. Although the results of our study support the argument of Marsh et al. (12), it is evident that choosing a valid model specific to population characteristics in each region is required for better assessment of cardiovascular risk.

A study from Canada aimed at identifying individuals with cardiovascular risk who may need statin therapy, John Mancini et al. (13) compared the Framingham, ATP III, Reynolds, and score risk models in a massive cohort study including one million individuals. As a result of the study (in which individuals with diabetes and familial cardiovascular risk were excluded), they showed that SCORE results were compatible with Framingham, especially in men. All other risk algorithms, except for the high-risk SCORE model, gave similar results to Framingham. In our study, it was determined that the Framingham and ASSIGN models resulted in greater risk estimations compared to the BNF and QRISK2 models in the whole group. In addition, it was revealed that the predicted risk score in the presence and absence of metabolic syndrome differed in all risk models. G B John Mancini, et al. (13) found that a sudden transition from the Framingham model to other risk models, such as the ATP III Reynolds, would put low-risk groups into a higher-risk category, which would significantly alter the treatment protocol to be applied. According to the results of our study, our suggestion is to carry out a gradual transition to a new model after determination of reliability via population-based studies, rather than attempting a rigid change into a pre-determined model. In a study involving 40,000 people conducted in the Netherlands, Scheltens et al. (14) examined the Framingham and SCORE risk models in terms of distinctiveness, ability to measure, and the number of people that would require treatment according to the new treatment guidelines. They found that both models were similar in distinguishing patients, based on the resulting ROC curve analysis. However, the measurement capability of both models was found to be low. According to the treatment guidelines applied in the Netherlands, 0.7% of the participants required treatment according to Framingham, while this value was found to be 0.4% for SCORE. As a result, while they reported the results of the two models to be similar, they also

concluded that attempts to procure newer models should pay attention to providing better measurement capability, since the measurement capabilities of both methods were limited (14). Scheltens et al. (14) evaluated two risk models similar to the work of Mancini and colleagues; whereas we assessed four risk models in a specific patient group. In our study, differently, the distinctiveness and measurement ability of the risk models were compared over the probability values predicted by risk models in the low, medium and high-risk groups. Cardiovascular risk estimates for the hyperlipidemia and metabolic syndrome groups were found to differ in all four risk models.

In the study by Simmonds et al. (15), which included 500,000 individuals, the Framingham 1991, Framingham 2008, Reynolds, ASSIGN, SCORE and QRISK2 cardiovascular risk models were used to ascertain the risk of cardiovascular events in England. Sensitivity and specificity criteria were emphasized in evaluating the performance of the models. The correct measurement values of all six algorithms were found between 72-79% with a 20% margin of error. Simmonds et al. (15) reported that, different from our study results, all tests yielded similar results at the end of the study. In our study, it was found that the QRISK2, BNF and ASSIGN scores respectively estimated high risk among 62.5%, 46.4% and 96.4% of subjects who were defined to have high-risk according to the Framingham criteria. Additionally, among the subjects who were defined to have high-risk according to the QRISK2 criteria, the Framingham, BNF and ASSIGN scores identified that 71.4%, 46.9% and 91.8% of these were individuals at high risk, respectively.

One of the most important limitations of our study is the absence of cardiovascular risk assessment via coronary angiography and the lack of atherosclerosis evaluation or follow-up studies. As such, we can no tinder superiority any of the models. As a consequence, any risk assessment method can be preferred depending on its applicability to the patients, the features of the institution that is utilizing the measures, and possibly, the ease of application. The presence or absence of metabolic syndrome does not appear to have an effect size that could alter the reference of scoring models. However, in our study, we showed that all of the four scoring systems provided significantly different results in both groups with and without metabolic syndrome.While the BNF and QRISK2 scores were similar in the whole group, these risk scores gave different results in the two subgroups formed according to the presence of metabolic syndrome. It was thought that the reason for this might be the different parameters evaluated in these two risk scores and the homogenous absence of these parameters in the groups with and without metabolic syndrome. In order to understand which of these risk scores has a higher diagnostic and prognostic predictive value in both the whole group and the group with metabolic syndrome, it is necessary to perform follow up for cardiovascular events and to investigate cardiovascular disease with a highly reliable method (such as coronary angiography, or carotid intima media thickness measurement) in prospective studies.

Conclusion

When four different risk scores were compared in newly diagnosed hyperlipidemia patients without differentiation of metabolic syndrome, it was revealed that only BNF and QRISK2 scores gave similar results, while the Framingham and ASSIGN scores provided different results from each other, as well as from BNF and QRISK2. In the literature, a cardiovascular risk probability model for the metabolic syndrome and hyperlipidemia patient group has not been determined yet; therefore, we believe that the results of our study will contribute to literature in this regard. However, our data should be supported by further objective evaluations and prospective studies.

Authorship Contributions

Concept: S.U., Design: S.U., Data Collection or Processing: A.İ., Analysis or Interpretation: O.B., S.U., Literature Search: N.D., Y.A., Writing: A.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Referances

1. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2019;74:1376-414.
2. Lloyd-Jones DM, Larson MG, Beiser A, Levy D. Lifetime risk of developing coronary heart disease. Lancet 1999;353:89-92.
3. Onat A, Albayrak S, Karabulut A. TEKHARF 2006. Available from: https://file.tkd.org.tr/PDFs/TEKHARF-2017.pdf Türk Kardiyoloji Dern Arş 2007;35:149-153.
4. Cupples LA, D'Agostino RB, Kiely D; The Framingham Study . An Epidemiological Investigation of Cardiovascular Disease, Section 34. Some Risk Factors Related to the Annual Incidence of Cardiovascular Disease and Death Using Pooled Repeated Biennial Measurements Framingham Heart Study, 30-Year Follow-Up. Bethesda, MD: National Heart, Lung, and Blood Institute; 1987.
5. Demir N, Yucelen SY, Cetin EG, et al. Determining INR Awareness of the Patients who Use Warfarin and Rates

of Achieving the Target Dosage. Sisli Etfal Hastan Tip Bul 2020;54:357-63.

6. Jackson R, Lawes CM, Bennett DA, Milne RJ, Rodgers A. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. Lancet 2005;365:434-41.
7. Calim A, Turkoz FP, Ozturkmen YA, et al. The Relation between Homocysteine Levels in Patients with Acute Coronary Syndrome and Grace Score. Sisli Etfal Hastan Tip Bul 2020;54:346-50.
8. Şendur MAN, Güven GS. Metabolik Sendroma Güncel Bakış. Available from: http://ichastaliklaridergisi.org/managete/fu_folder/2011-03/html/2011-18-3-125-131.htm. İç Hastalıkları Dergisi 2011;18:125-131.
9. Lee GK, Lee LC, Liu CW, et al. Framingham risk score inadequately predicts cardiac risk in young patients presenting with a first myocardial infarction. Ann Acad Med Singap 2010;39:163-7.
10. Ghandehari H, Le V, Kamal-Bahl S, Bassin SL, Wong ND. Abdominal obesity and the spectrum of global cardiometabolic risks in US adults. Int J Obes (Lond) 2009;33:239-48.
11. Aronson D, Edelman ER. Coronary artery disease and diabetes mellitus. Cardiol Clin 2014;32:439-55.
12. Marsh RW. Predicting cardiovascular events using three stage Discriminant Function is much more accurate than Framingham or QRISK. Eur J Epidemiol 2011;26:915-8.
13. G B John Mancini, Arnold Ryomoto , Comparison of cardiovascular risk assessment algorithms to determine eligibility for statin therapy: implications for practice in Canada. Can J Cardiol. 2014 Jun;30(6):661-6.
14. Scheltens T, Verschuren WM, Boshuizen HC, et al. Estimation of cardiovascular risk: a comparison between the Framingham and the SCORE model in people under 60 years of age. Eur J Cardiovasc Prev Rehabil 2008;15:562-6.
15. Simmonds MC, Wald NJ. Risk estimation versus screening performance: a comparison of six risk algorithms for cardiovascular disease. J Med Screen 2012;19:201-5.