ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

Comparison of Martin and Friedewald equation for estimated LDL-C in adults

Erişkinlerde LDL-C hesaplamasında Friedewald ve Martin formüllerinin karşılaştırılması

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ABSTRACT

Objective: In this study, we aimed to compare the directly measured low-density lipoprotein cholesterol (LDL-C), Friedewald, and a new Martin LDL-C formula in the Turkish adult population.

Methods: A total of 1,558 patients between the ages of 18 and 65 years with a triglyceride level of <400 mg/dL were included in this study. Serum lipid profiles of all the patients were measured with Cobas 6000 c501 (Roche Diagnostic), and LDL-C concentrations were measured by a homogeneous direct method using reagents. [TC- (HDL-C+(TG/5)] and Martin [TC- (HDL-C+TG / new adjustable factor)] formulas were used to estimate LDL-C.

Results: The average age of the patients was 52.7±12.3 years. Of the 1,558 patients, 56% were women and 44% were men. The d-LDL-C, F-LDL-C, and M-LDL-C concentrations in all the patients were 148.6±39.8 mg/dL, 123.9±38.7 mg/dL, and 133.4±35.9 mg/dL, respectively. The mean difference between F-LDL-C and M-LDL-C concentrations according to d-LDL-C was 24.6±10.7 and 15.10±10.3, respectively. For comparing the scatter blot plot [estimated LDL-C(x) and d-LDL-C(y)] were calculated by the equations y=1.1665x+0 for Friedewald and y=1.1667x+0 for Martin. When compared to the d-LDL-C concentration, both the Friedewald and Martin formulas showed a strong correlation (r=0.963, r=0.968, respectively). The new adjustable factor mean of the Martin formula was 6.1±0.9.

Conclusion: In our study, the Martin formula showed a relatively better separation. Although there was a strong correlation between the formulas and d-LDL-C, there was a negative bias for the two formulas. These formulas show a lower risk in the determination of the risk of coronary heart disease and in the planning of treatment strategies.

ÖZET

Amaç: Bu çalışmanın amacı, doğrudan ölçülen LDL-C, Friedewald ve yeni Martin LDL-C hesaplama formüllerini, Türk popülasyonunda karşılaştırmaktır.

Yöntemler: Bu çalışmaya trigliserid düzeyi <400 mg/dL olan 18 ve 65 yaşları arası toplam 1.558 hasta dahil edildi. Hastaların serum lipid paneli konsantrasyonları Cobas 6000 c501 (Roche Diagnostic) ile ölçüldü. d-LDL-C düzeyi homojen bir direk yöntem ile ölçüldü. LDL-C'yi hesaplamak için Friedewald [TC- (HDL-C+(TG/5)] ve Martin [TC-(HDL-C+ (TG/değişken faktör)] formülleri kullanıldı.

Bulgular: Hastaların yaş ortalaması 52.7±12.3 olarak kaydedildi. 1.558 hastanın %56'sı kadın, %44'ü erkekti. Tüm hasta grubunda d-LDL-C, F-LDL-C ve M-LDL-C konsantrasyonları sırasıyla, 148.6±39.8 mg/dL, 123.9±38.7 mg/dL ve 133.4±35.9 mg/dL idi. Tüm hastalar da d-LDL-C'e göre F-LDL-C ve M-LDL-C konsantrasyonları arasındaki ortalama fark sırasıyla 24.6±10.7 ve 15.10±10.3'tü. Hastalarda Scatter blot grafiği [tahmini LDL-C (x) ve d-LDL-C (y)] karşılaştırmasında, Friedewald için, y=1.1665x + 0, Martin için y=1.1667x+ 0 denklemleri hesaplandı. d-LDL-C konsantrasyonu ile kıyaslandığında, formüller arasında güçlü bir korelasyon gösterdi (sırasıyla, r=0.960, r=0.966). Martin formülünün ayarlanabilir faktör ortalaması 6.08±0.95 olarak bulundu.

Sonuç: Çalışmamızda Martin formülü nispeten daha iyi bir ayırım ortaya koydu. Formüller ile d-LDL-C arasında güçlü bir korelasyon olmasına rağmen, iki formül için var olan negatif bir bias, koroner kalp hastalığı riskinin belirlenmesinde ve tedavi stratejilerinin planlanmasında daha düşük risk göstermektedir.

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One of the most important variables used for cardiovascular disease (CVD) risk evaluation is increased serum concentrations of low-density lipoprotein cholesterol (LDL-C).[1,2] The American National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) advised that accurate measurement of LDL-C concentrations should be the major goal in dyslipidemia because of a strong positive association between LDL-C levels and CVD.

There are different methods for the measurement of LDL-C concentrations. The reference standard method is ultracentrifugation-polyanion/beta quantification.[3] This method has several disadvantages in a routine laboratory. It is an expensive and time-consuming method that requires special equipment and expertise, and thus is not a popular practice for routine clinical laboratories. Recently, direct homogeneous methods have been developed for LDL-C concentration versus beta quantification. However, clinical laboratories usually use various equations such as Friedewald, Cordova, and Anandaraja for economic reasons.[4,5] Generally, Friedewald's formula is commonly used for estimating LDL-C. A fasting sample is required for estimated LDL-C with the Friedewald equation, and there is a lot of variance in this ratio across the range of TG and non-high-density lipoprotein cholesterol (non-HDL-C) levels. The use of this formula is not suggested for patients with renal failure, diabetes mellitus, and chronic alcoholism. The Friedewald formula features a fixed triglyceride (TG), which has an very low-density lipoprotein cholesterol (VLDL-C) ratio of 5:1. Accordingly, it cannot show the substantial inter-individual variability in TG:VLDL-C ratios. Friedewald is the oldest formula, and when using the Friedewald equation, the inaccuracies were accepted because the VLDL-C estimate was a relatively small amount of the equation. Recently, with an increase in obesity and diabetes resulting in hypertriglyceridemic states and with novel therapeutics achieving historically low LDL-C concentrations, underestimation of LDL-C concentrations with Friedewald equation may result in postponing or discontinuing lipid-lowering therapies in treated high-risk patients for CVD. Therefore, Martin et al.[6] recently developed and validated a different method for estimating LDL-C, using a modifiable factor that varies depending on the levels of TGs and non–HDL-C. This adjustable factor is personalized according to other estimated LDL-C equations and provides accurate risk classification without additional measurements. Two years ago, the American College of Cardiology and American Heart Association guidelines on CVD risk biomarkers recommended the Martin equation as the estimation method for low LDL-C levels, particularly in patients using potent new lipid-reducing drugs, which are of clinical importance in the management of LDL-C.[7] Recent studies in other countries show the performance of estimated LDL-C for Martin equations.[8-11] However, according to our investigation, there are no studies on the performance and validation of estimated LDL-C for Martin equations in Turkey.

Abbreviations:

CVD	*Cardiovascular disease*
d-LDL-C	*Low-density lipoprotein cholesterol measured by the direct method*
F-LDL-C	*Estimated LDL-C for Friedewald*
Glu	*Glucose*
HbA1C	*Hemoglobin A1c*
HDL-C	*High-density cholesterol*
LDL-C	*Low-density lipoprotein cholesterol*
M-LDL-C	*Estimated LDL-C for Martin*
NCEP-ATP III	*American National Cholesterol Education Program Adult Treatment Panel III*
non-HDL-C	*Non-high-density lipoprotein cholesterol*
SD	*Standard deviation*
TC	*Total cholesterol*
TG	*Triglyceride*
VLDL-C	*Very low-density lipoprotein cholesterol*

A large of studies have shown that the Friedewald formula heads to either overestimate or underestimate LDL-C in patients compared with direct LDL measurement. These inexact estimates can be problematic because overestimated LDL-C leads to unnecessary treatment, and underestimated LDL-C can cause delays in getting the proper medication. Thus, accurately determining the LDL-C value is important in clinical laboratories as it is used to manage patients who are at risk of coronary heart disease. In this study, we aimed to compare the application of these two formulas in estimating the LDL-C of Friedewald (F-LDL-C) and Martin (M-LDL-C) in the Turkish population.

METHODS

Study population

In this study, all the laboratory parameters were prospectively obtained from a re-identified dataset of 1,558 patients who were evaluated with TG <400 mg/dL. Our study included individuals aged between 18 and 65 years. The study was conducted at the clinical biochemistry laboratory of Balıkesir State Hospital (Turkey). It was approved by the Clinical Research-

es Ethics Committee of Balıkesir University School of Medicine (Approval Date: March 20, 2019; Approval Number: 2019/83). The dataset of serum lipid concentrations was carried out in patients admitted to hospitals between 2019 and 2020. We excluded participants with a medical history of lipoprotein disorders, such as primary hypolipoproteinemia and hyperlipoproteinemia, any chronic disease (diabetes mellitus, renal and liver diseases), malignancy, and current pregnancy. Furthermore, if the patients had serum with hemolysis or icterus, the samples were rejected. LDL-C is measured directly in patients with TG >400 mg/dL routinely in our and other clinical laboratories. Using this equation is not recommended for estimating LDL-C; therefore, we excluded patients with TG > 400 mg/dL. The data was identified from the medical records of the patients who underwent a general health checkup from the outpatient population. Blood samples were taken after 8 h of fasting. Glucose (Glu), total cholesterol (TC), TG, high-density cholesterol (HDL-C), LDL-C, and hemoglobin A1c (HbA1C) concentrations were immediately tested after a maximum of 2 h of collection. The population were divided into subgroups according to TG (<100 mg/dL, 100-199 mg/dL, 200-299 mg/dL, and 300-399 mg/dL) and HDL concentrations (<40 mg/dL, 40-49 mg/dL, and >50 mg/dL).

Laboratory measurements

The all-biochemical parameters were analyzed using Roche diagnostics reagents base with manufacturer specifications (Roche Cobas 6000 c501 analyzer, Roche Diagnostic, Mannheim, Germany). All tests are presented with the analytical performance in Table 1. The d-LDL-C was directly analyzed with a homogeneous LDL-cholesterol 2nd generation reagent without any centrifugation or pre-procedure, on the 6000 c501 analyzer. In our study d-LDL-C measurement were accepted as the reference method.

Estimated LDL formulation

The formulation used to estimate LDL-C in units of mg/dL is as follows. The TG/VLDL-C ratio used for the Friedewald formula is 5. The Martin formula used a novel (adjustable) factor that was described as the median TG: VLDL-C ratio in strata (180-cell) classified by levels of TG and non-HDLC as a TG/VLDL-C ratio. This adjustable factor changes between 3 and 12.

Table 1. Analytical performances of all the tests

Analytics	CV1	CV2	Bias (%)	TAE
TC, mg/dL	1.9	1.8	3.9	0.73
TG, mg/dL	1.9	1.3	2	0.92
HDL-C, mg/dL	1.9	1.4	1.6	5.1
d-LDL-C, mg/dL	1	1.4	2.01	6.2

CVs: coefficient of variation; TAE: total analytical error; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; d-LDL-C: low-density lipoprotein cholesterol measured by the direct method.

F-LDL-C= TC- HDL-TG/5[4]

M-LDL-C= TC- HDL-TG/ Adjustable factor[6] (http://ldlcalculator.com/).

Statistical analysis

Statistical analyses were performed using the SPSS version 22 for Windows (IBM Corp., Armonk, NY, USA). Results were expressed as mean (X)±standard deviation (SD) or percentages. All variables were tested for abnormalities using the Kolmogorov-Smirnov test. We evaluated correlations using the Pearson's correlation test. The paired-sample t test was also used to compare the differences between the groups d-LDL and two LDL-C formulas. Bland-Altman plots were used to determine the degree of concordance and absolute difference between the two formulas and the directly measured LDL-C. Linear regression analyses were performed to generate linear models for the estimations of LDL-C. p values <0.05 were considered statistically significant.

RESULTS

The mean age of the patients included in the study was 52.7±12.3 years. Of the 1,558 patients, 56% were women, and 44% were men. The d-LDL-C, F-LDL-C, and M-LDL-C concentrations in the entire patient group were 148.6±39.8 mg/dL, 123.9±38.7 mg/dL, and 133.4±35.9 mg/dL, respectively. The adjustable factor mean of the Martin formula was 6.1±0.97. The other demographic characteristics of the patients are summarized in Table 2. As shown in Table 3, we compared the concordance of the d-LDL-C with the estimated LDL-C formulas. All the patients had a negative bias (underestimated) between d-LDL-C and the concentrations of F-LDL-C and M-LDL-C, and the means of the differences were 24.1±10.7 and 15.10±10.3, respectively. There was a statistically significant difference between the

d-LDL-C and estimated LDL-C formulas (p<0.001). In our comparison of F-LDL-C and M-LDL-C among themselves, there was no significant difference between the groups up to a TG level of 200 mg/dL.

Table 2. Baseline patient characteristics

Parameter	Subjects (n=1,558)
Age (years)	52.7±12.3
Sex (female/male)	56%/44%
HbA1c, %	5.02±1.3
Total cholesterol, mg/dL	219±44
TG, mg/dL	233±95
HDL-C, mg/dL	48.2±15.2
Non-HDL C, mg/dL	171±43
d-LDL-C, mg/dL	148.6±39.8
F-LDL-C, mg/dL	123.9±38.7
M-LDL-C, mg/dL	133.4±35.9
Adjustable factor (for Martin)	6.10±0.97
F-LDL-C, mean diff	25.6±11.4
M-LDL-C, mean diff	15.7±10.6

Data are shown as mean±SD or n (%).
TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; d-LDL-C: low-density lipoprotein cholesterol measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; HbA1C hemoglobin A1c; M-LDL-C: estimated LDL-C by the Martin formula; Mean diff: LDL-C measured by the direct method-estimated LDL-C by the formulas.

There was a good positive correlation between Friedewald and Martin with the d-LDL-C measurement (r=0.960, r=0.966, p<0.001, respectively). In addition, there was a good positive correlation between Friedewald and Martin (r=0.979, p<0.001). The correlation coefficient according to TG groups is presented in Table 4.

When we evaluated mean differences and performances of estimated LDL to d-LDL-C for all HDL-C concentrations, there were no significant differences for non-HDL-C and F-LDL-C means among the HDL-C groups. There were significant differences between the estimated F-LDL-C and M-LDL results. For the Martin formula, the adjustable factor decreased with increased HDL-C concentration (Table 5).

Linear regression analysis revealed a good correlation between both formulas and a d-LDL-C measurement (Figure 1). For comparing the scatter blot plot [estimated LDL-C (x) and d-LDL-C (y)] in patients, the equations y=0.97x + 28.78 for Friedewald and y=1.06x + 8.19 for Martin were calculated (Figure 1). Figure

Table 3. Estimated LDL results, performances of mean differences of estimated LDL to d-LDL for all formulas at TG concentrations

TG groups mg/dL	n	TG	d-LDL-C	F-LDL-C	F-LDL-C, Mean diff*	M-LDL-C	M-LDL-C, Mean diff	Adjustable factor
<100	385	79.0±14.5	125.8±39.0	108.8±37.4[a]	16.9±9	107.4±36.9[b]	18.3±10.8	4.5±0.4
100-199	395	141.5±28.3	150.9±36.9	131.14±36.0[a]	19.7±9.0	133.3±34.6[b]	17.6±9.01	5.3±0.4
200-299	410	242.0±29.2	157.1±40.0	130.5±38.7*	26.5±8.3	140.4±35.3[b, c]	16.67±9.3	6.3±0.6
300-399	378	343.2±31.9	145.9±38.6	115.2±39.9*	30.7±12.7	130.4±34.9[b, c]	12.3±12.2	6.9±0.8
<400	1558	233±95	148.6±39.8	123.9±38.7[a]	25.6±11.4	133.4±35.9[b,c]	15.7±10.6	6.10±0.97

[a]There was a statistically significant difference between the d-LDL-C and F-LDL-C formulas in all TG groups (p<0.001).
[b]There was a statistically significant difference between the d-LDL-C and M- LDL-C formulas among all TG groups (p<0.001).
[c]There was a statistically significant difference between the F-LDL-C and M- LDL-C formulas (p<0.001).
*p value <0.05 is statistically significant.
TG: triglyceride; d-LDL-C: LDL-C measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; M-LDL-C: estimated LDL-C by the Martin formula; Mean diff: LDL-C measured by the direct method-estimated LDL-C by the formulas.

Table 4. Performances of correlation of estimated LDL to d-LDL for all formulas at TG concentrations

	TG: <100 mg/dL	100-199 mg/dL	200-299 mg/dL	300-399 mg/dL	0-400 mg/dL
	r (95% CI)	r (95% CI)	r (95% CI)	r (95% CI)	r (95% CI)
F-LDL-C	0.958 (0.910-0.985)	0.970 (0.952-0.983)	0.977 (0.969-0.982)	0.946 (0.924-0.962)	0.960 (0.950-0.966)
M-LDL-C	0.959 (0.910-0.985)	0.998 (0.998-0.999)	0.976 (0.968-0.982)	0.945 (0.923-0.961)	0.966 (0.958-0.972)

There was a good correlation between the F-LDL and M-LDL-C with d-LDL-C in all TG groups (p<0.001). p value <0.05 is statistically significant.
r: coefficients of correlation; CI: confidence interval; TG: triglyceride; d-LDL-C: LDL-C measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; M-LDL-C: estimated LDL-C by the Martin formula.

Table 5. Estimated LDL results, means differences, and performances of estimated LDL to d-LDL for all formulas at HDL-C concentrations

	HDL-C, mg/dL		
	<40 mg/dL (N: 448)	40-49 mg/dL (N: 493)	>50 mg/dL (N: 589)
TG	290.7±75.1	235.8±85.8	177.8±85.9
Non-HDL	171.2±38.1	169.7±43.9	166.7±44.5
HDL-C	33.9±4.7	44.2±2.7	63.2±13.6
d-LDL-C	138.8±36.4	148.4±39.1	157.4±39.14
F-LDL-C	112.9±35.7[a]	125.7±39.1[a]	136.8±39.5
F-LDL-C, mean diff	25.9±10.5	25.6±10.5	24.6±12.1
M-LDL-C	127.6±32.7[a]	135.5±36.9[a]	135.7±38.2
M-LDL-C, mean diff	11.4±10.6[b]	15.6±8.6[b]	19.6±10.3[b]
Adjustable factor	6.6±0.8	6.1±0.8	5.5±0.9

p value <0.05 is statistically significant.
[a]There was a statistically significant difference between F-LDL-C and M-LDL-C (p<0.001).
[b]M-LDL-C, mean diff statistically significant difference among all the groups (p<0.001).
TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; d-LDL-C: LDL-C measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; M-LDL-C: estimated LDL-C by the Martin formula; Mean diff: LDL-C measured by the direct method-estimated LDL-C by the formulas.

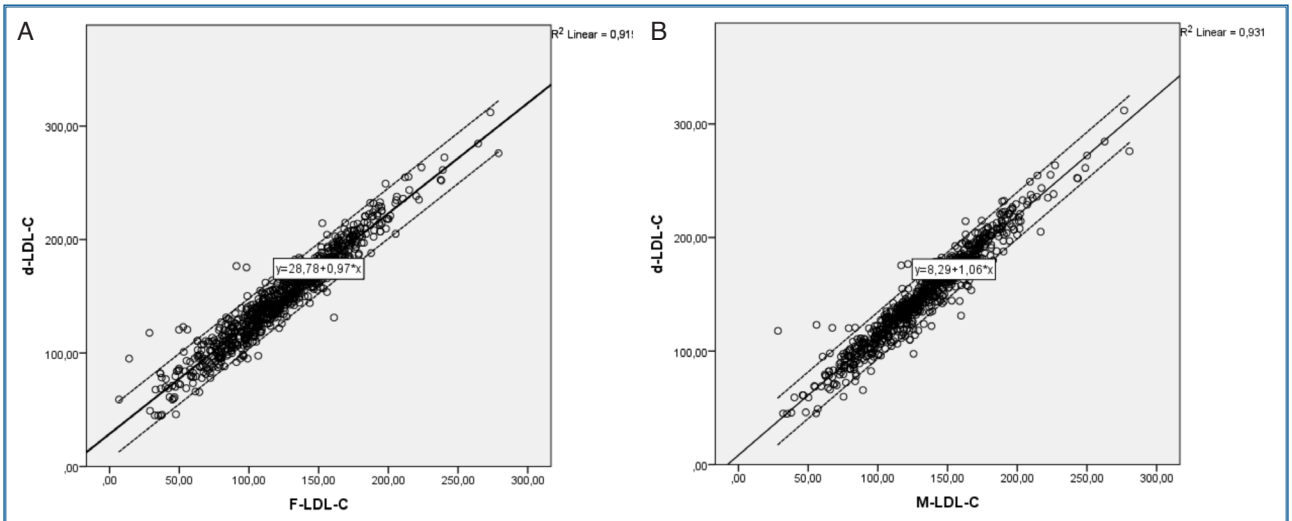

Figure 1. Scatter plots are indicated with the Bland-Altman plot for d-LDL-C and estimated LDL-C by all formulas; **(A)** Friedewald, **(B)** Martin.
d-LDL-C: LDL-C measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; M-LDL-C: estimated LDL-C by the Martin formula.

2 presents Bland-Altman plots for d-LDL-C measurement against Friedewald and Martin formulas.

When we used the cutoff LDL-C >100 mg/dL, which is the minimum risk level for the NCEP ATP III guideline, it was 92% according to the risk classification based on d-LDL-C measurement. It was found to be 73% for F-LDL-C and 82% for M-LDL-C. An underestimated risk in two formulas was detected versus the d-LDL-C measurement.

DISCUSSION

This study evaluated the performance of estimated LDL-C using Friedewald and Martin formulas with a homogeneous d-LDL measurement method in Turkish adults with mild hypertriglyceridemia (<400 mg/dL). The LDL-C results of the Martin formula showed a good accordance with direct LDL-C measurement than the Friedewald formula. However, there was a negative estimation for both formulas in

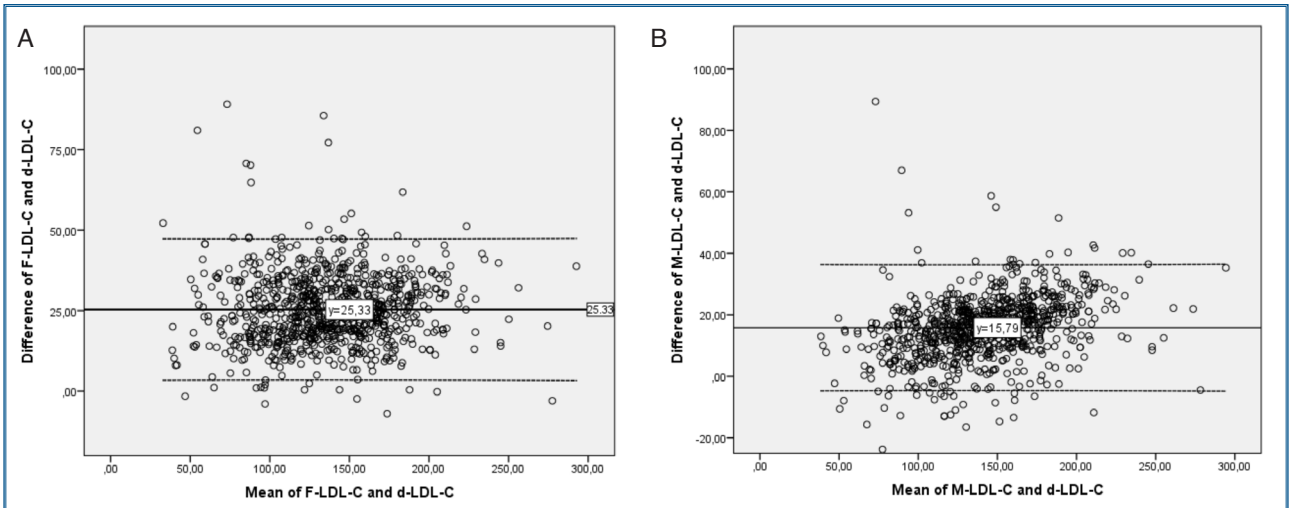

Figure 2. Bland-atman plot (mean±1.96*SD) for d-LDL-C and estimated LDL-C by all formulas; **(A)** Friedewald, **(B)** Martin. d-LDL-C: LDL-C measured by the direct method; F-LDL-C: estimated LDL-C by the Friedewald formula; M-LDL-C: estimated LDL-C by the Martin formula.

the LDL-C prediction in the study population. When the concordance between the two formulas was evaluated, there was a similar agreement at TG levels <200 mg/dL for the two formulas; when TG was 200-399 mg/dL, the Martin formula had a higher accuracy than the Friedewald formula. A study among Korean adults with a much larger participant group found that the Martin formula had the best accordance with d-LDL-C measurement in coronary atherosclerosis.[12] Egbaria et al.[13] compared the Friedewald LDL-C estimation with the Martin formula in patients treated with PCSK9i achieving low LDL-C. They presented discordance between the Friedewald equation and the Martin formula, particularly in those with elevated TG. The American College of Cardiology and American Heart Association guidelines on CVD risk biomarkers recommended the Martin equation as the preferred estimation method for low LDL-C samples in 2018.

In recent years, both the Friedewald and Martin formulas for the estimated LDL-C in the literature were compared in different adult populations. In Kang et al.'s[8] study with Korean adult population, the Martin formula results had a better agreement with direct LDL measurement. In their study, the mean differences were 5.5±4.2 mg/dL for Martin, and 8.2±7.4 for Friedewald. Our study had relatively similar results when compared with results relating to the mean difference; however, the overall results of mean difference were higher than reported in this study. The Bland-Altman graphs exhibited a clear bias between both estimated formulas and the d-LDL-C measurement. The Friedewald formula had a higher negative bias than the Martin formula, and the bias value increased as the TG concentration increased. There were similar results in the studies performed.[6,14] For example, Esawy et al.[14] determined that the Friedewald formula was higher than the existing negative bias in the Martin formula for the individuals with type 2 diabetes in their study.

The difference in the Martin formula according to Friedewald is that an adjustable factor is used for the TG/VLDL ratio. This factor is calculated by making a stratification (180-cell) according to the non-HDL and TG concentrations of the patient. According to the results of this patient, thanks to the factor varying between 3 and 11.9, the Martin formula owing to changes in TG and HDL-C concentration, provides a much more dynamic structure in LDL estimation. In the study, the mean TG/VLDL-C ratio was significantly different in TG groups. The adjustable factor increased in the Martin formula parallel to the TG concentration and in contrast to the HDL concentration. This factor, adjustable for Martin's formula, changed between 3.5 and 11.9 in our study (X±SD: 6.10±0.97). As a result of the TG/VLDL factor change in the Martin formula, a constant negative bias was observed independent of the TG concentration increase.

In this study, there was a strong and similar correlation between Friedewald and Martin with d-LDL-C levels. The correlation was relatively higher in the Martin formula. The Bland-Altman plot demonstrated a better agreement between Martin and the measured LDL-C. However, Martin's formula was not affected by TG levels and had less negative bias, providing an advantage to the formula. Parallel results have been found in studies conducted in various clinical situations and in different populations in the literature.[8,11,13,15-17] The last clinical study in our country found a perfect consistency between the Friedewald and Martin formulas in patients aged >40 years with cardiology. However, the study by Dinç Asarcıklı et al.[18] did not compare the performance of the formulas with a reference method. Similar to our study, there was a strong correlation between the Friedewald and Martin formulas. In our first study, we evaluated the performance of the old 10 formulas (Friedewald, Cordova and Cordova, Ahmadi, Anandaraja, Teerakanchana, Chen, Hattori, Vujovic, Puavillai, and Hatta) in patients with TG 0–<400 mg/dL (n=1112).[19] In this study, the Teerakanchana formula showed a relatively better correlation than the Friedewald formula. Furthermore, all formulas generally showed a high negative bias in the LDL-C estimation in proportion to increasing TG levels. In this our second study that have large number of participants (n:1558) have showed a good concordance the new Martin formula than the Friedewald formula according to direct LDL-C measurement.

In this study, when the LDL-C cutoff of >100 mg/dL was considered according to the minimal risk classification in the NCEP ATP III Guide, 92.0% of patients were classified in the risk group for d-LDL-C. F-LDL-C and M-LDL-C were classified as 73% and 82%, respectively. Although the two formulas showed a lower CAD risk than d-LDL-C, the risk prediction is better in the Martin formula. Similarly, Lee et al.[20] suggested that the Martin equation was associated with a higher agreement in LDL-C risk classification. However, misclassification of risk may lead to the delay of drug and nutritional therapies and may change the treatment strategies for risk groups, which then has negative consequences.

Limitations

Our study had several limitations. We used d-LDL-C measurement instead of the reference method. However, Roche d-LDL-C has been standardized against the reference method. Nauck et al.[21] and Yamashita et al.[22] showed that the homogeneous Roche LDL-C reagent met the analytical performance targets. In our study, analytical performance for the d-LDL-C test was well below the recommended TAE and percentage bias. Another limitation of our study was the relatively small population size and TG concentration <400 mg/dL compared with studies conducted on a population of over 10,000.[11] Therefore, we recommend further studies using both the Friedewald and Martin formulas with a large number of multicenter participants using different lipid reduction treatments and under various clinical situations in our own population.

Conclusion

In multiple clinical laboratories in our country and globally, generally, LDL cholesterol is estimated according to the Friedewald formula in TG concentrations <400 mg/dL. It is measured by the direct homogeneous LDL method in TG concentrations ≥400 mg/dL in the general population and ≥200 mg/dL in risk groups for CVD. However, this measurement method is not available in rural laboratories owing to cost. The detection of individuals with high cardiovascular risk should be the priority of early CVD prevention in the population. Therefore, it is important to get an accurate estimation of LDL-C as an alternative method to the direct homogeneous LDL-C measurement.

We evaluated the performance of the formulas in adults with TG <400 mg/dL. The Martin formula had good diagnostic compatibility with the d-LDL-C measurement. In addition, our study is valuable in that it is the preliminary study conducted in concordance with the Martin and Friedewald formulas according to d-LDL-C measurement in Turkey. This study should not be considered as a definitive work because of its limitations in certain situations; therefore, prospective and well-designed studies are required to evaluate the usefulness of the novel formula.

Ethics Committee Approval: Ethics committee approval was received for this study from the Clinical Researches Ethics Committee of Balıkesir University School of Medicine (Approval Date: March 20, 2019; Approval Number: 2019/83).

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Keywords: Friedewald formula; Martin formula; LDL cholesterol; direct LDL measurement; LDL cholesterol estimation

Anahtar Kelimeler: Friedewald formülü; Martin formülü; LDL kolesterol; direkt LDL ölçümü; LDL kolesterol hesaplama