Published in final edited form as:

Clin Chim Acta. 2013 August 23; 423: 135–140. doi:10.1016/j.cca.2013.04.009.

Evaluation of Four Different Equations for Calculating LDL-C with Eight Different Direct HDL-C Assays

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Abstract

Background—Low-density lipoprotein-cholesterol (LDL-C) is often calculated (cLDL-C) by the Friedewald equation, which requires high-density lipoprotein-cholesterol (HDL-C) and triglycerides (TG). Because there have been considerable changes in the measurement of HDL-C with the introduction of direct assays, several alternative equations have recently been proposed.

Methods—We compared 4 equations (Friedewald, Vujovic, Chen, and Anandaraja) for cLDL-C, using 8 different direct HDL-C (dHDL-C) methods. LDL-C values were calculated by the 4 equations and determined by the quantification reference method procedure in 164 subjects.

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Results—For normotriglyceridemic samples (TG < 200mg/dl), between 6.2 to 24.8% of all results exceeded the total error goal of 12% for LDL-C, depending on the dHDL-C assay and cLDL-C equation used. Friedewald equation was found to be the optimum equation for most but not all dHDL-C assays, typically leading to less than 10% misclassification of cardiovascular risk based on LDL-C. Hypertriglyceridemic samples (>200 mg/dl) showed a large cardiovascular risk misclassification rate (30 - 50%) for all combinations of dHDL-C assays and cLDL-C equations.

Conclusion—Friedewald equation showed the best performance for estimating LDL-C, but its accuracy varied considerably depending on the specific dHDL-C assay used. None of the cLDL-C equations performed adequately for hypertriglyceridemic samples.

Keywords

Cholesterol; Cardiovascular Disease; Low Density Lipoproteins; Friedewald equation

1. Introduction

In fasting human plasma, cholesterol is primarily associated with three major lipoprotein classes, namely VLDL, LDL and HDL [1,2]. Because LDL is a proatherogenic lipoprotein, whereas HDL is anti-atherogenic, the measurement of cholesterol on these 2 different types of lipoproteins is routinely performed for cardiovascular disease (CVD) risk assessment and for monitoring patients on lipid-lowering therapy [3-6]. The “gold standard” or reference method for LDL-C is called the “beta quantification” procedure, which requires the use of ultra-centrifugation to first remove chylomicrons and VLDL, followed by measurement of cholesterol in the LDL and HDL containing “bottom” fraction, selective precipitation of LDL, and measurement of the HDL cholesterol (HDL-C) in the supernatant[7]. The beta quantification procedure is labor intensive and time consuming, thus making it impractical for routine clinical laboratories. With the advent of dLDL-C assays, many laboratories now use a procedure in which cholesterol in non-LDL fractions is either masked or consumed, thus allowing the direct measurement of LDL-C without the physical separation and removal of LDL from the sample. dLDL-C assays offer many advantages, such as good precision, complete automation, and they do not require a fasting sample [6].

The other common procedure for LDL-C determination involves its estimation from fasting samples, using other lipid and lipoprotein parameters. The most widely used equation for estimating LDL-C is the Friedewald equation ($LDL-C = TC - (HDL-C) - (TG/5)$), which requires the measurement of serum TC, HDL-C, and TG [8]. The basis for this equation is that in a fasting sample most cholesterol is either in LDL, HDL or VLDL; therefore, one can calculate LDL-C by subtracting HDL-C and VLDL-C from TC. When concentration units are in mg/dl, the term $TG/5$ provides an estimate of VLDL-C [8, 9]. Although it is only an approximation, the Friedewald equation is still commonly used for estimating LDL-C, because of the extra cost involved in performing dLDL-C assays and because of the lack of specificity of some dLDL-C assays, particularly in patients with dyslipidemias [10, 11].

The Friedewald equation for estimating LDL-C is also known to have many limitations. It is inaccurate in patients with hypertriglyceridemia, particularly when TG > 400 mg/dl [6]. It does not perform well for patients with Type III hyperlipidemia, because the $TG/5$ term for

estimating VLDL-C is inaccurate when there is enrichment of lipoproteins with triglycerides [8]. Furthermore, the Friedewald equation can only be used on fasting samples, because it does not account for cholesterol in chylomicrons that form in the post-prandial state [6]. The Friedewald formula also does not take into account cholesterol in intermediate-density lipoproteins or on Lipoprotein (a); therefore, cholesterol in these lipoprotein fractions are incorporated into the LDL-C value, although these same lipoprotein fractions are also frequently measured as LDL-C by the beta quantification procedure [2].

Another important limitation of the Friedewald equation is that it depends on accurate measurement of HDL-C. In the past 10 y most clinical laboratories have switched from precipitation-based methods for measuring HDL-C to fully automated dHDL-C assays [10]. Like the direct assays for LDL-C, dHDL-C assays can be affected by various disease conditions and in some cases can have substantial biases compared to rHDL-C [10, 11]. In an effort to overcome Friedewald formula limitations, several alternative equations for estimating LDL-C, which utilize the newer dHDL-C assays, have been proposed [12-14]. There has been no systematic study, however, on the performance of these alternative cLDL-C equations with all the current dHDL-C assays. In addition, many of the original studies first describing these alternative equations for cLDL-C did not compare the results to the quantification reference procedure for LDL-C [12-14].

2. Materials and methods

2.1. Study design and patient samples

Participants for the study were recruited from the National Institutes of Health (Bethesda, MD) or the Virginia Commonwealth University Medical Center (Richmond, VA), with approval of their respective institutional review boards. Data from a previous study [10] on 145 participants with TG levels < 200 mg/dl, and 19 subjects with TG levels > 200 and < 400 mg/dl were used in the analysis. The study population contains 37 healthy control subjects, with the majority of the remaining subjects recruited from specialty clinics for dyslipidemia and cardiovascular disease and thus are representative of the population of patients for which accurate lipid testing is important for making clinical decisions on the use of lipid lowering drug. Approximately, one quarter of the subjects were not fasting for at least at 10 h. Details of the lipid profile, diagnosis and use of lipid-lowering medication of each participant in the study has been previously described [10].

2.2. Lipid and Lipoprotein Analysis

Ultracentrifugation reference method procedures for LDL-C and HDL-C were performed at the CDC (Atlanta, GA), as previously described [10]. Direct HDL-C methods [Denka Seiken, Niigata, Japan; Kyowa Medex, Tokyo, Japan; Sekisui Medical (formerly Daiichi), Tokyo, Japan; Serotec, Hokkaido, Japan; Sysmex International Reagents, Hyogo, Japan; UMA, Shizuoka, Japan; Wako Pure Chemical Industries, Osaka, Japan; and Roche Diagnostics, Indianapolis, IN (distributor of Kyowa Medex reagents with Roche calibrator and controls)] were done on a Hitachi 917 analyzer (Roche Diagnostics, Indianapolis, IN), using manufacturer specific parameters. TC was measured with Roche reagent on a Siemens Advia 1650 analyzer (Roche Diagnostics, Indianapolis, IN). Triglycerides were measured

without glycerol blanking, using Siemens Advia reagents on an Advia 1650 analyzer (Siemens Diagnostics, Tarrytown, NY). All analyses were done on fresh (<48 h) serum samples stored at 4°C. The calibration traceability of the TC and TG methods to their respective reference methods was certified by the Centers for Disease Control and Prevention (CDC) Lipid Standardization Program.

2.3. Data analysis

Total error for cLDL-C was calculated, according to the following equation: Total Error (%) = $[(cLDL-C - rLDL-C) / rLDL-C] \times 100$. Misclassifications for CVD risk were determined by the difference in risk classification based on rLDL-C versus cLDL-C for the following NCEP risk categories based on LDL-C values: optimal for secondary prevention (<70 mg/dl), optimal (71 to 100 mg/dl), near optimal (101 to 130 mg/dl), borderline high (131 to 160 mg/dl), high (161 to 190 mg/dl) and very high (> 190 mg/dl) [4,15]. The comparison of the results for cLDL-C versus rLDL-C was done by the Pearson correlation method. All values are reported in mg/dl units and multiplication of the following conversion factors can be used to convert to SI units (mmol/l): total cholesterol, HDL-C, LDL-C: 0.0259; and triglycerides: 0.0113. Chi-Square analysis was used to determine the optimum equation for cLDL-C for each of the dHDL-C methods based on the total number of subjects misclassified into an incorrect CVD risk category based on LDL-C. JMP Software (SAS Institute, Cary, NC) was used for statistical analysis. A $P < .05$ were considered statistically significant. Because the Anandaraja equation unlike the other 4 equations does not use HDL-C as a variable [8,12-14], only one cLDL-C value was calculated for each patient, whereas 8 different values of cLDL-C were calculated with the other three equations; one for each of the 8 different dHDL-C assays evaluated in this study.

3. Results

3.1. Equations for calculating LDL-C

Inspection of the 4 original equations for cLDL-C [8,12-14], after some minor algebraic manipulations, showed that the different formulas have significant similarities (Table 2). With the exception of the Anandaraja equation, they all use TC, TG and HDL-C as variables for predicting LDL-C. The Friedewald and Vujovic equation are the most similar and only differ in the coefficient for the TG term. The Chen equation contains a coefficient less than one in front of the TC and HDL-C terms and has a smaller coefficient for the TG variable compared to the other equations. The Anandaraja equation does not contain HDL-C as a variable and, therefore, would not be affected by errors related to the measurement of HDL-C. The Anandaraja equation, however, does contain a relatively large fixed negative term of -28 and a different set of coefficients for the TC and TG variables than the Friedewald equation. The large fixed term that is subtracted from total cholesterol in the Anandaraja equation will act like HDL-C, so we also included it in our analysis to determine the accuracy of the equation in estimating LDL-C.

3.2. Comparison of cLDL-C equations for normotriglyceridemic subjects

The mean and range of lipid and lipoprotein values, as determined by reference method procedures, for the study participants are shown in Table 1. The performance of the 4

different cLDL-C formulas on this population was evaluated, using 8 different methods for dHDL-C for samples with TG < 200 mg/dl (Tables 3 and 4). Samples with TG > 200 mg/dl have previously been shown to lead to inaccuracies in HDL-C measurement [10, 11] and hence a separate analysis was done for samples below and above this cutpoint for triglycerides.

When compared to rLDL-C, the Friedewald equation for cLDL-C had correlation coefficients close to unity ($R^2=0.98$), with the UMA ($R^2=0.96$) and Wako ($R^2=0.97$) assays having slightly lower R^2 values. All dHDL-C assays showed a small negative proportional bias (slope= 0.94 to 0.98), but 7 out of 8 assays had a relatively large positive fixed bias (intercept= 5.52 to 11.59 mg/dl). The percent of results that exceeded the NCEP 12% total error goal for LDL-C [2] was relatively small (7.6 to 14.5%) when the Friedewald equation was used to calculate LDL-C, except for the Wako dHDL-C assay in which 24.8% of the results exceeded the total error goal.

When cLDL-C was calculated by the Chen equation, values of R^2 similar to the Friedewald equation were observed, but a slight positive proportional bias instead of a negative bias was present, and overall a smaller fixed bias was observed for most dHDL-C assays (intercept= -2.76 to 5.01 mg/dl). Most of the direct assays used for estimating cLDL-C by the Chen equation showed similar % of results (6.2-16.6%) exceeding the total error goal compared to the Friedewald equation, except for the UMA and Wako assays in which 22.8% and 24.8% results, respectively, exceeded the total error goal.

In the case of the Vujovic equation, values of R^2 and slopes were also very similar to the Friedewald equation, although in general smaller fixed biases were observed (intercept=-0.29 to 7.43 mg/dl) for the various dHDL-C assays. For 3 of the dHDL-C assays, namely Denka, Kyowa and Wako, the % of results exceeding the total error goal for LDL-C was lower than that for the Friedewald equation but was still in the range of 6.9-10.3%.

The Anandaraja equation appeared to be inferior to the Friedewald equation and all the other equations in terms of its relatively poor R^2 (0.88), large negative proportional error (0.87), and large positive fixed bias (11.1 mg/dl) (Table 4). Using the Anandaraja equation for cLDL-C, 44% of the results exceeded the total error goal.

3.3. Comparison of cLDL-C equations for hypertriglyceridemic subjects

When samples with TG between 200 and 400 mg/dl were analyzed, none of the equations for cLDL-C, including the Friedewald equation, showed good agreement with rLDL-C (Tables 3 and 4). In general, 30-45% of the results exceeded the recommended total error for LDL-C, and none of the cLDL-C equations appeared to show a clear advantage over the others. The Chen and Vujovic equations were best for calculating LDL-C when the Wako dHDL-C test was used in hypertriglyceridemic samples, but in both cases over 20% of the results still exceeded the total error goal recommendation.

3.4. Cardiac risk factor misclassification with cLDL-C equations

3.4.1. Normotriglyceridemic samples—Percent misclassification for each cLDL-C equation was determined for normotriglyceridemic samples (TG <200 mg/dl) (Fig. 1A-1D).

Each subject was classified into a CVD risk category based on rLDL-C and compared to the risk classification obtained when LDL-C was calculated by the 4 equations. Depending on the dHDL-C assay used in the calculation, there was a wide variation (5.6-16.6%) in the degree of CVD risk misclassification when the Friedewald equation was used (Fig. 1A). The Vujovic and Chen equations also had a similar wide variation in the % of CVD risk misclassifications, depending on the dHDL-C assay used, although the Vujovic (Fig. 1B) equation tended to misclassify more subjects into a higher risk category, whereas the Chen equation (Fig. 1C) misclassified more subjects into a lower risk category. The Anandaraja equation showed the most misclassifications (27.6%) (Fig. 1D), and also displayed an overall bias for underestimating LDL-C, leading to misclassifying more patients into a lower CVD risk category.

In order to identify the best equation for each dHDL-C assay, rates of total misclassifications were compared for the combination of each one of the eight dHDL-C assays with each one of three equations (Friedewald, Vujovic and Chen). Roche, Serotec, Daiichi, Denka and UMA dHDL-C assays all had the lowest rates of total misclassifications (5.6%, 6.9%, 7.6%, 9.7% and 15.8%, respectively) when cLDL-C was estimated with Friedewald equation. In only 3 cases did one of the alternative equations yield a lower rate of misclassification with a particular dHDL-C assay than the Friedewald equation. The Sysmex dHDL-C assay yielded the lowest number of misclassifications when Chen equation was used (8.9%), but this difference was not statistically different compared to the misclassification rate obtained with Friedewald equation (10.4%). The Wako and Kyowa dHDL-C assays showed a trend toward less misclassifications (10.3% and 11.1%, respectively) when used in the Vujovic equation compared to the Friedewald equation, but again the difference was not statistically significant. The Anandaraja equation misclassified a total of 27.6% of normotriglyceridemic subjects, which was statistically the highest among the 4 equations investigated.

In hypertriglyceridemic (200 mg/dl >TG< 400 mg/dl) samples (Fig. 2A-2D), a much greater % of total misclassifications, typically more than 40%, were observed for all cLDL-C equations. There was no statistical advantage for 1 cLDL-C equation over another, in terms of total % misclassification, in this population.

4. Discussion

The following are the 3 main findings from this study: (1) the use of different dHDL-C assays has a profound effect on the accuracy of calculated LDL-C, (2) the different equations for cLDL-C can produce variable results and the optimum equation for calculating cLDL-C depends on which dHDL-C assay is used, and (3) the Friedewald equation has the best overall performance for calculating LDL-C.

Because 3 measurements, namely TC, HDL-C and TG, are typically used in the calculation of LDL-C, errors from any of these measurements can affect the accuracy of cLDL-C [2,6]. Based on College of American Pathologists participant summary reports for the Accuracy Based Lipid Survey (ABL-A 2011), which uses commutable fresh frozen serum samples as survey material, most TC and TG assays showed relatively good agreement with their reference methods, but dHDL-C assays do not as closely agree with rHDL-C. Even greater

discrepancies between dHDL-C assays and rHDL-C were found in a recent study [10] when samples from patients with dyslipidemias were analyzed. Most dHDL-C assays were found to yield results that exceed their recommended total error goal of 13% [16]. It is not surprising, therefore, that a wide range of misclassification was found for the different cLDL-C equations, depending on the dHDL-C used (Fig. 1A-1C, 2A-2C). As would be expected, the dHDL-C assays that best matched their reference method appeared, in general, to yield more accurate cLDL-C results. Interestingly, however, there were some exceptions when a poorer performing dHDL-C assay performed better with a particular cLDL-C equation. For example, the Wako dHDL-C test, which had the greatest % of results that exceeded the total error goal (Table 3), showed the most % misclassifications for cLDL-C by the Friedewald and Chen equations but the least misclassifications for the Vujovic equation (Fig. 1A-1C). Because the Vujovic equation tended to have a positive bias and overestimated cLDL-C (Fig. 1B), this bias was partially compensated by the negative bias in the Wako dHDL-C test.

Overall, the Friedewald equation for calculating LDL-C was either the best or equivalent to the other equations, in terms of CVD risk classification (Fig. 1A-1D). Only in the cases of the Wako and Kyowa dHDL-C assays with the Vujovic equation and the Sysmex dHDL-C assay with the Chen equation, were fewer misclassifications observed with these equations compared to the Friedewald equation, although the differences were not statistically significant (Fig. 1A-1C). The Anandaraja equation was the least accurate for calculating cLDL-C, most likely because it does not contain a variable for HDL-C and only uses TC and TG. The Anandaraja equation does have a large constant negative term (Table 2), but this fixed term does not fully compensate for the variable amounts of HDL-C present in patient samples. Based on our analysis, there does not appear to be any advantage of the Anandaraja equation over the other cLDL-C equations except for perhaps its simplicity and reduced cost (no need for HDL-C testing). This potential advantage, however, is limited by the fact that HDL-C is frequently measured in CVD risk assessment and in the monitoring of lipid-lowering therapy.

It is well known that the Friedewald equation performs poorly in hypertriglyceridemic samples and is not recommended when TG >400 mg/dl [6]. Others have shown, however, that its performance steadily decreases with increasing TG [17,18]. For subjects with TG between 200 and 400 mg/dl, the Friedewald equation and all other equations in this study yielded relatively inaccurate cLDL-C results (Table 3 and 4, Fig. 2A-2D), with 21-47% of the results exceeded the total error goal. dLDL-C tests are not as adversely affected by high TG and have been shown to be superior for CVD risk classification compared to cLDL-C by the Friedewald equation in hypertriglyceridemic samples [11]. The results from this study and previous findings, therefore, suggest that it may be best not to use any of the equations for calculating LDL-C in patients when TG >200 mg/dl, and instead use a dLDL-C assay. Alternatively, one could use Non-HDL-C ($TC - HDL-C$) or apolipoprotein B, which, as other studies have shown, may be better cardiovascular biomarkers than LDL-C in hypertriglyceridemic subjects [4,15,19,20].

There are several limitations to this study that are important to note. First, only one specific assay was used for TC and TG (Roche and Siemens Advia reagents, respectively) in the

calculations for LDL-C. As discussed above, the use of different TC and TG methods are not as likely, however, to significantly affect the calculation of LDL-C as much as dHDL-C assays because of their better standardization. The TC and TG methods used in this study also did not differ from their respective reference methods by more than 2% [10,11]. Another limitation is that only a small number of subjects with hypertriglyceridemia were examined, although based on the relatively poor accuracy observed in this small subset (Fig. 2A-2D), it is unlikely that any of the equations for calculating LDL-C even in patients with a moderate increase in TG (200mg/dl >TG < 400mg/dl) will be fully satisfactory. Most of the direct HDL-C assays begin to show errors in samples with TG > 200 mg/dl [10,11], and hence this cutpoint was used in this study but comparing the cLDL-C equations at a lower TG thresholds may reveal an advantage for some equations for over the others. Another limitation of this study is that other equations besides the ones tested have been described for estimating LDL-C [17,18,21], but we have tried to focus here on the more recent and more popularly used cLDL-C equations. Finally, the samples collected for this study were largely obtained from patients with dyslipidemia and cardiovascular disease and may not be representative of the general population. The accurate determination of LDL-C in subjects with dyslipidemia, however, is obviously critical for the effective use of LDL-C in identifying and managing patients at risk for CVD.

Acknowledgments

We thank Kara Dobbin and Selvin Edwards at the CDC for performing the cholesterol reference method measurements and Tonya Mallory for arranging support from the US distributors. We also appreciate the assistance of Drs. Todd Gehr, Daniel Carl, Anna Vinnikova, and Velimir Luketic and Carol Sargeant with recruiting patients at Virginia Commonwealth University.

Research Funding: M.J. Oliveira, A.T. Remaley and H.E. van Deventer: Warren Grant Magnuson Clinical Center, Intramural Research Program of the National Institutes of Health. G. Miller: Denka Seiken, Kyowa Medex, Sekisui Medical, Serotec, Sysmex International Reagents, UMA, and Wako Pure Chemical Industries donated reagents, calibrators, and controls and contributed financial support to Pacific Biometrics Research Foundation. Genzyme and Pointe Scientific contributed financial support to Pacific Biometrics Research Foundation. Pacific Biometrics Research Foundation provided a grant to Virginia Commonwealth University (funded by the financial contributions noted above). Roche Diagnostics donated reagents, calibrators, controls, and a Hitachi 917 instrument.

Abbreviations

dLDL-C	direct LDL cholesterol
dHDL-C	direct HDL cholesterol
rHDL-C	HDL cholesterol measured by the reference method
rLDL-C	LDL cholesterol measured by the reference method
cLDL-C	calculated LDL cholesterol
NCEP	National Cholesterol Education Program

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Highlights of the paper

- The Friedewald equation is the most used method for calculating LDL-C. It is dependent upon the accurate assays for HDL-C, which have recently undergone considerable changes with the development of direct assays. Three other alternative equations (Vujovic, Chen and Anandaraja) for calculating LDL-C have recently been proposed, but they have not been systematically examined with all the different types of direct HDL-C assays or compared, in all cases, to the beta quantification reference method procedure for LDL-C.
- Using 8 different dHDL-C assays, LDL-C was calculated by all 4 equations (Friedewald, Vujovic, Chen and Anandaraja) in 164 samples and compared to the beta quantification reference procedure. The % of results that exceeded the total error goal for LDL-C in normotriglyceridemic ($TG < 200$ mg/dL) samples varied widely (6.4 to 24.8%) and depended upon the equation and dHDL-C assay used. Overall, the Friedewald equation showed the best correspondence to the reference method but for some dHDL-C assays either the Vujovic or Chen equation showed slightly better results. The Anandaraja equation was clearly inferior to the other equations in accurately estimating LDL-C.
- In the hypertriglyceridemic samples ($200\text{mg/dL} < TG < 400\text{mg/dL}$) none of the equations, including the Friedewald equation showed a close correspondence to the reference method procedure for LDL-C and misclassified between 20-40% subjects into a different CVD risk score based on LDL-C. It is recommended that direct LDL-C or alternative CVD risk biomarkers should be used in this population.

Figure 1. Cardiovascular disease risk misclassification by various equations for cLDL-C in samples with TG < 200 mg/dL

Subjects (n=145) with normal serum triglycerides (< 200 mg/dL) were classified into cardiovascular risk categories based on LDL-C performed by the reference method and by the indicated equation and dHDL-C assay. Results are shown as % of participants who were misclassified by cLDL-C into either a lower risk category (hatched bars) or higher risk category (open bars). dHDL-C assays are displayed in ascending order according to increasing total misclassifications. Asterisks (*) indicate the equation that produced the lowest total % misclassification for the indicated dHDL-C assay when compared to other equations, using the same dHDL-C assay. dHDL-C assays: Da, Daiichi; De, Denka; Ky; Kyowa; Ro; Roche; Se; Serotec; Sy, Sysmex; Um, UMA; Wa, Wako.

Figure 2. Cardiovascular disease risk misclassification by various equations for cLDL-C in samples with TG between

200 mg/dL and 400 mg/dL. Subjects (n=19) with serum triglycerides between 200 and 400 mg/dL were classified into cardiovascular risk categories based on LDL-C performed by the reference method and by the indicated equation and dHDL-C assay. Results are shown as % of participants who were misclassified by cLDL-C into either a lower risk category (hatched bars) or a higher risk category (open bars). dHDL-C assays are displayed in ascending order, according to increasing total misclassification. dHDL-C assays: Da, Daiichi; De, Denka; Ky, Kyowa; Ro, Roche; Se, Serotec; Sy, Sysmex; Um, UMA; Wa, Wako.

Table 1

Mean lipid and lipoprotein values in study participants.

Test	Triglycerides < 200 mg/dl (n=145)	Triglycerides 200 and < 400 mg/dl (n=19)
TG (mg/dl)	101 (41.2; 10 - 190)	263 (57.4; 208 - 386)
TC (mg/dl)	169 (55.2; 19 - 409)	198 (49.4; 120 - 275)
HDL-C (mg/dl)	49 (17.5; 20 - 126)	38 (8.7; 24 - 57)
LDL-C (mg/dl)	103 (45.1; 3 - 301)	112 (41.6; 49 - 196)

Numbers in parentheses refer to standard deviation and range of measured values. LDL-C and HDL-C values were determined by their respective reference methods.

Table 2

Formulas for calculation of LDL-Cholesterol.

Formula Name	Original Equation	Alternative Form of Equation
Friedewald	$\text{cLDL-C} = \text{TC} - \text{HDL-C} - (\text{TG}/5)$	$\text{cLDL-C} = \text{TC} - \text{HDL-C} - (0.2 \times \text{TG})$
Vujovic	$\text{cLDL-C} = \text{TC} - \text{HDL-C} - (\text{TG}/6.58)$	$\text{cLDL-C} = \text{TC} - \text{HDL-C} - (0.152 \times \text{TG})$
Chen	$\text{cLDL-C} = (0.9 \times \text{Non-HDL-C}) - (0.1 \times \text{TG})$	$\text{cLDL-C} = (0.9 \times \text{TC}) - (0.9 \times \text{HDL-C}) - (0.1 \times \text{TG})$
Anandaraja	$\text{cLDL-C} = (0.9 \times \text{TC}) - (0.9 \times \text{TG}/5) - 28$	$\text{cLDL-C} = (0.9 \times \text{TC}) - 28 - (0.18 \times \text{TG})$

Formulas are in form for units mg/dl

Table 3

Comparison of cLDL-C by various equations to rLDL-C.

TG < 200 mg/dl (n=145)								
Direct HDL-C Assay	Daiichi	Denka	Kyowa	Roche	Serotec	Sysmex	UMA	Wako
Friedewald Equation								
R ²	0.98	0.98	0.98	0.98	0.98	0.98	0.96	0.97
Slope	0.95 ^a	0.98 ^a	0.96 ^a	0.95 ^a	0.95 ^a	0.95 ^a	0.94 ^a	0.94 ^a
Intercept (mg/dl)	5.58 ^a	5.52 ^a	7.99 ^a	6.10 ^a	6.10 ^a	3.95 ^a	9.24 ^a	11.59 ^a
Mean total error, % (SD)	-1.4 (8.3)	-4.3 (11.7)	-5.9 (12.7)	-2.9 (10.7)	-2.6 (15.7)	0.6 (8.3)	-4.0 (12.2)	-8.7 (18.1)
% > total error %goal ^b	8.3	12.4	13.8	10.3	7.6	9	14.5	24.8
Chen Equation								
R ²	0.98	0.97	0.98	0.98	0.98	0.98	0.95	0.97
Slope	1.04 ^a	1.06 ^a	1.04 ^a	1.04 ^a	1.03 ^a	1.04 ^a	1.02 ^a	1.03 ^a
Intercept (mg/dl)	-1.05	-1.11	1.59	-0.36	-0.32	-2.76	3.18	5.01 ^a
Mean total error, % (SD)	-2.0 (7.4)	-4.7 (9.7)	-6.1 (10.3)	-3.4 (8.8)	-3.2 (13.1)	-0.3 (8.4)	-4.4 (13.0)	-8.6 (14.3)
% > total error %goal ^b	6.2	9	16.6	9	9.7	7.6	22.8	24.8
Vujovic Equation								
R ²	0.98	0.98	0.98	0.98	0.98	0.98	0.95	0.97
Slope	0.94 ^a	0.96 ^a	0.95 ^a	0.94 ^a	0.94 ^a	0.95 ^a	0.93 ^a	0.93 ^a
Intercept (mg/dl)	1.38	1.32	3.94 ^a	2.01	2.04	-0.29	5.39 ^a	7.43 ^a
Mean total error, % (SD)	4.8 (7.7)	1.9 (10.7)	0.3 (11.6)	3.3 (9.7)	3.6 (14.7)	6.8 (8.4)	2.2 (13.3)	-2.5 (16.5)
% > total error %goal ^b	9.7	6.9	10.3	12.4	13.8	17.9	19.3	10.3
200 mg/dl < TG < 400 mg/dl (n=19)								
Friedewald Equation								
R ²	0.94	0.94	0.95	0.95	0.95	0.94	0.94	0.94
Slope	0.91 ^a	0.92 ^a	0.91 ^a	0.90 ^a	0.89 ^a	0.91 ^a	0.91 ^a	0.91 ^a
Intercept (mg/dl)	14.39 ^a	15.96 ^a	15.53 ^a	13.29 ^a	13.83 ^a	12.50	12.61	17.98 ^a
Mean total error, % (SD)	-5.1 (11.3)	-8.0 (11.6)	-5.6 (11.0)	-3.8 (10.7)	-3.7 (11.0)	-3.0 (10.6)	-3.1 (11.4)	-9.8 (12.8)
% > total error %goal ^b	42.1	36.8	36.8	36.8	36.8	31.6	36.8	47.4
Chen Equation								
R ²	0.93	0.93	0.93	0.94	0.93	0.93	0.92	0.93

TG < 200 mg/dl (n=145)								
Direct HDL-C Assay	Daiichi	Denka	Kyowa	Roche	Serotec	Sysmex	UMA	Wako
Slope	1.00 ^a	1.02 ^a	1.01 ^a	1.00 ^a	0.99 ^a	1.00 ^a	1.00 ^a	1.01 ^a
Intercept (mg/dl)	-6.43	-5.61	-6.13	-7.57	-6.42	-7.91	-8.03	-3.12
Mean total error, % (SD)	7.5 (12.2)	4.8 (10.8)	7.0 (11.7)	8.6 (11.5)	8.7 (11.6)	9.3 (12.4)	9.3 (13.0)	3.2 (10.4)
% > total error %goal ^b	42.1	31.6	36.8	31.5	36.8	42.1	42.1	21.1
Vujovic Equation								
R ²	0.93	0.94	0.94	0.95	0.94	0.94	0.93	0.94
Slope	0.91 ^a	0.92 ^a	0.91 ^a	0.91 ^a	0.89 ^a	0.91 ^a	0.91 ^a	0.91 ^a
Intercept (mg/dl)	1.37	2.51	1.59	0.25	1.16	-0.29	-0.31	4.81
Mean total error, % (SD)	9.8 (10.9)	6.9 (10.0)	9.2 (10.4)	11.1 (10.2)	11.2 (10.4)	11.9 (10.9)	11.8 (11.6)	5.1 (10.2)
% > total error %goal ^b	42.1	31.6	42.1	42.1	47.4	42.1	42.1	26.3

^a *P* value < .05;

^b Percent of results that exceeded the error goal of 12% for LDL-C determination as recommended by the National Cholesterol Education Program.

Table 4

Comparison of cLDL-C by Anandaraja equation to rLDL-C.

	TG < 200 mg/dl (n=145)	200 mg/dl < TG < 400 mg/dl (n=19)
R²	0.88	0.95
Slope	0.87 ^a	0.92 ^a
Intercept (mg/dl)	11.13 ^a	17.71 ^a
Mean total error, % (SD)	−1.4 (53.1)	−10.8 (12.6)
% > total error goal ^b	44.1	42.1

^a *P* value < .05;^b Percent of results that exceeded the error goal of 12% for LDL-C determination as recommended by the National Cholesterol Education Program.