RESEARCH ARTICLE

Impact of glucose and lipid markers on the correlation of calculated and enzymatic measured low-density lipoprotein cholesterol in diabetic patients with coronary artery disease

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Background and Aims: Low-density lipoprotein cholesterol (LDL-C) is widely estimated by Friedewald equation (FE) and Enzymatic test (ET), which are affected by several factors. The aim of this study was to observe the impact of diabetic lipid and glucose patterns on the correlation between FE LDL-C (F-LDL) and ET LDL-C (E-LDL) in patients with coronary artery disease (CAD).

Methods and Results: A total of 8155 CAD patients were consecutively enrolled and their lipid profiles were measured. The impacts of triglyceride (TG), glycosylated hemoglobin A1c (HbA1c), and high-density lipoprotein cholesterol (HDL-C) on the correlation of F-LDL and E-LDL were examined. The difference value (DV) between F-LDL and E-LDL was compared using ANOVA test. The CAD patients with DM were elder and had higher body mass index, plasma TG compared with those without DM ($P < .05$ separately). In the whole population, F-LDL was lower than E-LDL but showed a high correlation with E-LDL ($r = .970$, $P = .000$). Moreover, as the TG concentrations increased, the DV increased accordingly but the correlation between F-LDL and E-LDL decreased ($P < .01$). The similar trend was also found in both DM and non-DM patients comparing with different TG groups. However, in patients with DM, there was no significant difference of DV in different HbA1c groups or HDL-C concentrations ($P > .05$).

Conclusion: Although F-LDL might underestimate the value of LDL-C, the correlation between F-LDL and E-LDL was clinically acceptable ($r = .97$), suggesting the LDL-C values measured by two methods were similarly reliable in CAD patients with or without DM.

KEYWORDS

diabetes mellitus, enzymatic test, Friedewald equation, LDL-C, triglycerides

1 | INTRODUCTION

Low-density lipoprotein cholesterol (LDL-C) is the primary target of therapy in patients with coronary artery disease (CAD), especially in patients combined with diabetes mellitus (DM).¹⁻⁴ Several methods of

LDL-C measurement are applied in research or clinical practice. Among them, the gold standard of LDL-C measurement is β -quantification after ultracentrifugation, which is expensive and inconvenient for routine laboratory. Recently, the direct homogeneous assays which have shown reasonable accuracy and precision are far more expensive in

most laboratories. The enzymatic test (ET), which means the selective solubilization method in this study, is the most common and cost-effective of LDL-C measurement applied in most hospitals worldwide.

Friedewald equation (FE) is the most widely used for LDL-C estimation in most clinical studies, but unreliable in extreme lipid values, such as triglyceride (TG) > 4.5 mmol/L or LDL-C < 1.8 mmol/L⁵; and in non-fasting conditions.⁶ Yet, the abnormalities in lipoprotein composition in patients with DM are characterized as elevated TG level. Thus, the assessment of LDL-C using FE may result in inaccuracies.

To our knowledge, few studies have paid attention to the reliability of FE on the patients with DM. Besides, ET is commonly used in DM, but few studies are available regarding the impact of diabetic lipid and glucose on the correlation between ET and FE. Moreover, as earlier as 1990s, Rubiés-Prat J and his colleagues⁷ discovered that FE might be inaccurate in patients with DM. However, the number of the study population is not large enough. Therefore, in this study, we assessed the difference between FE and ET of LDL-C value in hospitalized patients with CAD, especially focused on the patients with DM.

2 | METHODS

2.1 | Study population

The cross-sectional study was approved the hospital's ethical review board (Fuwai Hospital and National centre for

cardiovascular diseases, Beijing, China) and complied with the Helsinki Declaration. The informed written consent was obtained from each patient.

From the 1st January 2011 to the 30th June 2016, a total of 10 242 patients hospitalized in the department of dyslipidemia of Fuwai Hospital were continuously enrolled. All the patients were performed coronary angiography or coronary computed tomography angiography because of angina-like chest pain or positive treadmill exercise test. Data required for this study were collected from hospital records. Patients with acute coronary syndrome, heart failure, significant hematologic disorders, infectious or systemic inflammatory disease, thyroid dysfunction, severe liver and/or renal insufficiency, and malignant disease were excluded from the current study.

Of the 10 242 patients, 8523 (83.2%) had CAD as angiographic documented >50% diameter stenosis in more than one major epicardia coronary artery; 368 (3.6%) patients had the TG level > 4.5 mmol/L. At last, a total of 8155 patients with CAD and fasting serum TG levels < 4.5 mmol/L were enrolled in this study. The main demographic and clinical characteristics of the study population are summarized in Table 1.

2.2 | Laboratory measurements

The glycosylated hemoglobin A1c (HbA1c) and lipid profile were analyzed by the clinical chemistry department of Fuwai hospital.

Variables	Total (n = 8155)	DM (n = 2276)	Non-DM (n = 5879)	P-value
Age, y	58 ± 10.79	59 ± 10.35	57 ± 10.91	<.001
Male, % (n)				
Male	71.9 (5867)	71.1 (1618)	72.3 (4249)	.243
Female	28.1 (2288)	28.9 (658)	27.7 (1630)	.243
BMI, kg/m ²	25.79 ± 11.1	26.24 ± 3.1	25.64 ± 3.3	<.001
Hypertension	61.6 (5015)	69.8 (1578)	58.5 (3437)	<.001
Dyslipidaemia	75.3 (6115)	81.6 (1842)	72.8 (4273)	<.001
Lipid lowering drug	85.6 (6096)	88.0 (1735)	84.6 (4361)	.057
Glu, mmol/L	5.95 ± 1.8	7.49 ± 2.3	5.31 ± 1.0	<.001
HbA1c	6.3 ± 1.1	7.3 ± 1.3	5.90 ± 0.7	<.001
Cr, μmol/L	78.28 ± 17.8	79.21 ± 19.5	77.05 ± 17.2	.006
TG, mmol/L	1.47 (1.08-2.02)	1.5 (1.13- 2.1)	1.45 (1.07-1.99)	.007
TC, mmol/L	4.10 ± 1.2	3.99 ± 1.1	4.23 ± 1.2	<.001
HDL-C, mmol/L	1.01 (0.86-1.22)	0.98 (0.83-1.18)	1.03 (0.87-1.24)	<.001
E-LDL, mmol/L	2.53 ± 1.0	2.44 ± 1.0	2.57 ± 1.1	<.001
F-LDL, mmol/L	2.30 ± 1.0	2.20 ± 1.0	2.33 ± 1.1	<.001

TABLE 1 General characteristics of 8155 CAD patients

Data expressed as a mean ± standard deviation for variables of normal distribution, median (interquartile range) for variables of non-normal distribution; percentage (number) for categorical variables. BMI, body mass index; Glu, glucose; HbA1c, glycosylated hemoglobin A1c; Cr, creatinine; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated low-density lipoprotein cholesterol; Lp(a), lipoprotein a; hsCRP, highly sensitive C-reactive protein; CAD, coronary artery disease; DM, diabetes mellitus.

TABLE 2 Comparison of difference between E-LDL and F-LDL in CAD patients according to TG concentration

TG (mmol/L)	n	E-LDL	F-LDL	DV	P*	Pearson correlation
TG ≤ 1.1	2151	2.26 ± 1.14	2.13 ± 1.16	0.12 ± 0.21	<.001	0.983
1.11-2.3	4643	2.59 ± 0.96	2.36 ± 0.95	0.23 ± 0.23	NA	0.971
2.31-3.4	1087	2.80 ± 1.03	2.41 ± 1.04	0.40 ± 0.27	<.001	0.965
3.41-4.5	274	2.62 ± 1.06	2.11 ± 1.11	0.52 ± 0.28	<.001	0.966
Total	8155	2.53 ± 1.04	2.30 ± 1.04	0.23 ± 0.26	-	0.970

CAD, coronary artery disease; LDL-C, low-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated LDL-C; DV, difference value between E-LDL and F-LDL; NA, not applicable.

*Compared the DV in 1.11-2.3 mmol/L TG group within the other TG groups.

Blood samples were obtained for all patients from the cubital vein after 10 hours overnight fast. The blood was collected into EDTA-containing tubes.

Serum concentrations of total cholesterol (TC, mmol/L), TG (mmol/L), and high-density lipoprotein cholesterol (HDL-C, mmol/L) were measured using the enzymatic methods with an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). E-LDL (mmol/L) was directly tested by the selective solubilization methods using reagent kit of MetaboLead LDL-C (Kyowa Medex, Tokyo, Japan). F-LDL was calculated by the FE: LDL-C (mmol/L) = (TC - HDL-C) - (TG/2.2).⁸ HbA1c was measured using high-performance liquid chromatography by a certified automated analyzer (HPLC; HLC-723G7 hemoglobin HPLC analyzer; Tosoh Corp).

All the patients were classified into four groups according to serum TG concentrations as follows: ≤1.1 mmol/L, 1.11-2.3 mmol/L, 2.31-3.4 mmol/L, 3.41-4.5 mmol/L; and six groups according to LDL-C concentration as follows: ≤1.4 mmol/L, 1.41-1.8 mmol/L, 1.81-2.6 mmol/L, 2.61-3.4 mmol/L, 3.41-4.1 mmol/L, >4.1 mmol/L; and three groups according to HbA1c levels as follows: ≤6.5%, 6.51%-7.0%, and >7.0%; and four groups according to HDL-C concentration as follows: ≤1.0 mmol/L, 1.01-1.2 mmol/L, 1.21-1.4 mmol/L, >1.4 mmol/L.

2.3 | Statistical analysis

The continuous variables were described as means with standard deviations (SD, for normally distributed variables) or as a median with interquartile range (for skewed variables), and compared using the one-way ANOVA and Wilcoxon rank sum test, respectively. Categorical variables are described as frequency and percentages, and compared using chi-square test. To compare measured and calculated LDL-C levels, the difference value (DV) between F-LDL and E-LDL for each patient and the LDL-C mean [(E-LDL + F-LDL)/2] were derived. Pearson correlation was performed for E-LDL and F-LDL. In the subgroup analysis of difference value (DV) between E-LDL and F-LDL, one-way ANOVA test was used in comparing with different TG, HDL-C, and HbA1c groups. All statistical analyzes were performed using SPSS software (version 22, IBM SPSS Inc., USA). Statistical significance was defined as a two-sided *P*-value of < .05.

3 | RESULTS

The general characteristics of the 8155 patients were presented in Table 1. The patients with DM were found elder and more overweight than the non-DM patients (*P* < .05, respectively). But there was no significant difference of gender and treatment of lipid-lowering drug between DM and non-DM patients. The mean levels of TC, HDL-C, E-LDL, and F-LDL were lower in the DM group than in the non-DM group. F-LDL was lower than E-LDL with the mean DV of 0.23 mmol/L (95% CI: -0.28 to 0.74 mmol/L) in the whole population; and of 0.24 mmol/L (95% CI: -0.25 to 0.73 mmol/L) in the patients with DM. However, the mean levels of TG were higher in the DM group than in the non-DM group (*P* < .05, respectively).

In the whole population, the DV in different TG groups were increased along with the TG concentration while the correlation between E-LDL and F-LDL was decreased as shown in Table 2 (*P* < .01). The correlation between E-LDL and F-LDL was the highest in the TG ≤ 1.1 mmol/L group (Pearson correlation = 0.983, *P* < .01).

When stratified by LDL-C categories, the absolute differences between E-LDL and F-LDL were increased along with the LDL-C concentrations in both DM and non-DM patients. However, the differences value had no significant in LDL-C ≤ 1.4 mmol/L group and 1.41-1.8 mmol/L group (*P* > .05, Table 3).

In patients with DM, the similar trend of DV changes in different TG group was found in Table 4. As the TG level increasing, the mean of DV increased from 0.12 to 0.52 mmol/L (*P* < .01), and the Pearson correlation decreased from 0.975 to 0.960. In CAD patients without DM, it also displayed the similar trend of DV changes in different TG group (Table 4).

As comparing with the DV in different HbA1c level, there was no significant difference in the DM group and non-DM group (*P* > .05, Table 5). However, along with the increase of HbA1c, the Pearson correlation between E-LDL and F-LDL increased from 0.961 to 0.969. It was the opposite trend in the non-DM patients. As shown in Table 4, the correlation between E-LDL and F-LDL decreased from 0.967 to 0.960 following the increase of HbA1c level.

In the different HDL-C group, the HDL-C ≤ 1 mmol/L group had the minimum of mean of DV in both DM (*P* = .49) and non-DM patients (*P* = .087), but there was no statistically significant difference. The Pearson correlation increased along with the increase of HDL-C

LDL-C (mmol/L)	n	E-LDL	F-LDL	DV	P*
DM					
≤1.4	225	1.19 ± 0.15	1.00 ± 0.25	0.18 ± 0.20	NA
1.41-1.8	370	1.62 ± 0.11	1.43 ± 0.23	0.18 ± 0.20	.988
1.81-2.6	883	2.19 ± 0.23	1.97 ± 0.31	0.21 ± 0.22	.109
2.61-3.4	493	2.96 ± 0.23	2.69 ± 0.32	0.25 ± 0.27	.001
3.41-4.1	167	3.73 ± 0.19	3.43 ± 0.38	0.30 ± 0.34	<.001
>4.1	138	4.85 ± 1.04	4.48 ± 1.18	0.38 ± 0.39	<.001
Non-DM					
≤1.4	447	1.20 ± 0.15	1.05 ± 0.23	0.15 ± 0.19	NA
1.41-1.8	873	1.63 ± 0.15	1.44 ± 0.22	0.18 ± 0.20	.134
1.81-2.6	2163	2.16 ± 0.21	1.98 ± 0.32	0.21 ± 0.24	.025
2.61-3.4	1442	2.92 ± 0.23	2.72 ± 0.34	0.25 ± 0.27	<.001
3.41-4.1	541	3.70 ± 0.19	3.37 ± 0.36	0.30 ± 0.38	<.001
>4.1	413	5.09 ± 1.57	4.77 ± 1.68	0.28 ± 0.51	<.001

CAD, coronary artery disease; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated LDL-C; NA, not applicable.

*Compared the DV in ≤1.4 mmol/L LDL-C group within the other TG groups.

TABLE 3 Comparison of difference between E-LDL and F-LDL in CAD patients with or without DM according to LDL-C concentration

TABLE 4 Comparison of difference between E-LDL and F-LDL in CAD patients combined with or without DM according to TG concentration

TG (mmol/L)	n	E-LDL	F-LDL	DV	P*	Pearson correlation
DM						
TG ≤ 1.1	543	2.12 ± 0.90	2.00 ± 0.90	0.12 ± 0.19	<.001	0.975
1.11-2.3	1298	2.49 ± 0.94	2.27 ± 0.94	0.22 ± 0.21	NA	0.974
2.31-3.4	332	2.75 ± 0.99	2.34 ± 0.98	0.41 ± 0.28	<.001	0.961
3.41-4.5	103	2.49 ± 1.06	1.97 ± 1.15	0.52 ± 0.28	<.001	0.960
Total	2276	2.44 ± 0.96	2.20 ± 0.95	0.24 ± 0.25	-	0.966
Non-DM						
TG ≤ 1.1	1608	2.28 ± 1.14	2.18 ± 1.20	0.11 ± 0.25	<.001	0.984
1.11-2.3	3345	2.62 ± 0.96	2.39 ± 0.96	0.22 ± 0.26	NA	0.969
2.31-3.4	755	2.82 ± 1.04	2.43 ± 1.07	0.39 ± 0.30	<.001	0.968
3.41-4.5	171	2.70 ± 1.06	2.18 ± 1.08	0.52 ± 0.27	<.001	0.964
Total	5879	2.55 ± 1.05	2.33 ± 1.05	0.22 ± 0.28	-	0.971

CAD, coronary artery disease; DM, diabetes mellitus; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated LDL-C; DV, difference value between E-LDL and F-LDL; NA, not applicable.

*Compared the DV in 1.11-2.3 mmol/L TG group within the other TG groups.

level in the DM patients, whereas in the non-DM patients, it showed the opposite trend of correlation (Table 6).

4 | DISCUSSIONS

In the present study focusing on CAD patients whose TG ≤ 4.5 mmol/L, we found that the lipid profile of CAD patients with DM is characterized by increased TG level and decreased HDL-C level, which was different from those without DM and consistent with the previous studies.^{9,10} Moreover, the data indicated

that the FE estimated LDL-C levels were lower than the values obtained by ET, but had high correlation with the ET generally. In addition, the difference between the two methods increased with the TG concentration but the correlation decreased. However, the HbA1c and HDL-C level had no effect on the difference of the two methods of LDL-C measurement in the DM and non-DM patients, suggesting that the both of the enzymatic method and FE could apply in CAD patients with TG ≤ 4.5 mmol/L.

The accuracy and reliability of LDL-C measurement is essential in clinical practice, because it is not only the most important independent risk factor of CAD especially in patients with DM but also the strongly

TABLE 5 Comparison of difference between E-LDL and F-LDL according to different levels of HbA1c in CAD patients combined with or without DM

DM						
HbA1c (%)	n	E-LDL	F-LDL	DV	P*	Pearson correlation
HbA1c ≤ 6.5	723	2.36 ± 0.89	2.14 ± 0.87	0.23 ± 0.24	.248	0.961
6.51-7.0	399	2.43 ± 1.00	2.19 ± 0.99	0.25 ± 0.26	.458	0.966
>7.0	1105	2.48 ± 0.99	2.25 ± 0.92	0.24 ± 0.25	NA	0.969
Total	2227	2.44 ± 0.96	2.20 ± 0.95	0.24 ± 0.25	-	0.966
Non-DM						
HbA1c (%)	n	E-LDL	F-LDL	DV	P**	Pearson correlation
HbA1c ≤ 6.5	5147	2.54 ± 1.01	2.31 ± 1.00	0.23 ± 0.26	NA	0.967
6.51-7.0	336	2.65 ± 1.00	2.42 ± 0.99	0.23 ± 0.27	.443	0.964
>7.0	268	2.62 ± 0.89	2.38 ± 0.85	0.24 ± 0.25	.530	0.960
Total	5751	2.55 ± 1.00	2.32 ± 0.99	0.23 ± 0.26	-	0.966

CAD, coronary artery disease; DM, diabetes mellitus; HbA1c, glycosylated hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated LDL-C; DV, difference value between E-LDL and F-LDL; NA, not applicable.

*Compared the DV in HbA1c > 7.0% group within the other HbA1c groups.

**Compared the DV in HbA1c < 6.5% group within the other HbA1c groups.

TABLE 6 Comparison of difference between E-LDL and F-LDL according to different levels of HDL-C in CAD patients combined with or without DM

HDL-C (mmol/L)	n	E-LDL	F-LDL	DV	P*	Pearson correlation
DM						
HDL-C ≤ 1	466	2.11 ± 0.78	1.87 ± 0.80	0.24 ± 0.25	.490	0.962
1.01-1.2	527	2.54 ± 0.94	2.28 ± 0.95	0.26 ± 0.25	NA	0.964
1.21-1.4	302	2.68 ± 1.04	2.43 ± 1.00	0.25 ± 0.25	.537	0.970
>1.4	214	2.61 ± 1.00	2.35 ± 0.97	0.26 ± 0.24	.828	0.970
Total	1509	2.44 ± 0.95	2.21 ± 0.94	0.24 ± 0.25	-	0.965
Non-DM						
HDL-C ≤ 1	946	2.38 ± 1.27	2.15 ± 1.31	0.23 ± 0.25	.087	0.981
1.01-1.2	1488	2.61 ± 1.08	2.37 ± 1.06	0.24 ± 0.26	NA	0.970
1.21-1.4	893	2.67 ± 0.98	2.40 ± 0.92	0.26 ± 0.25	.100	0.966
>1.4	753	2.79 ± 1.01	2.53 ± 1.00	0.26 ± 0.27	.389	0.965
Total	4080	2.60 ± 1.10	2.37 ± 1.10	0.24 ± 0.26	-	0.972

CAD, coronary artery disease; DM, diabetes mellitus; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; E-LDL, enzymatic measured low-density lipoprotein cholesterol; F-LDL, Friedewald equation estimated LDL-C; DV, difference value between E-LDL and F-LDL; NA, not applicable.

*Compared the DV in 1.01-1.2 mmol/L HDL-C group within the other HDL-C groups.

emphasized target for dyslipidemia treatment.¹¹⁻¹⁴ There are different methods of LDL-C measure. Among them, the enzymatic method of LDL-C measurement is the mainstream of clinical laboratory test with applicable accuracy and stability using in the majority of the world.

FE as the most widely applied method in clinical practice is recommended in several guidelines related to the therapy of dyslipidemia.^{11,12,15,16} It assumes the ration of the mass of TG to very low-density lipoprotein cholesterol (VLDL-C) to be relatively constant.⁸ However, in the real world, the ratios are variable in different

individuals leading to less accuracy of FE, especially in the population with TG > 4.5 mmol/L and non-fasting state.^{8,10,17,18}

The dyslipidemia of DM is primarily characterized as high level of TG and low level of cholesterol,¹⁹⁻²¹ which might imply the unreliability of FE applying in the patients with DM. Hirany S and Whiting M et al observed that FE in comparison with direct assay was underestimated the LDL-C level.^{19,20} Chaen et al revealed that the FE showed the divergence from direct method in Japanese patients with DM.²² Although several formulas were derived from different population

in order to improve the accuracy and reliability of FE, they were not found to be the suitable replacements.²³⁻²⁷

Based on the above findings, we enrolled the patients with angiographic proven CAD and investigated the correlation between E-LDL and F-LDL and the associated impact factors. Similar to the previous studies,²⁸⁻³⁰ we found there was significant difference between the overall mean of E-LDL compared with F-LDL, and the FE underestimated the LDL-C in all TG ranges. We also found that the DV increased with the TG level and the correlation between E-LDL and F-LDL decreased in both DM and non-DM patients. However, HbA1c and HDL-C had no impact on the DV between F-LDL and E-LDL in both DM and non-DM patients.

With regard to the significance of the present study, following reasons may suggest the clinical importance for our study. (1) Although two methods of LDL-C measurement are frequently used in the real world, while its reliability is a key concern, especially in the era of intensive lipid control and in the highest risk patients; However, to our knowledge, the comparison study on these two methods in CAD patients are less common or limited by small sample size; (2) In China, there are a huge number of hospitals using only FE to estimate LDL-C, while there have been no studies systematically evaluated the reliable of F-LDL in a cross-sectional patients with CAD in China. Furthermore, there are no recommendations that address the impact of glucose and lipid patterns on F-LDL. Thereby, we desire to provide related data to guide the practice in the real world.

Our study firstly observed the impact of glucose status and HDL-C levels on the difference and correlation of E-LDL and F-LDL in patients with DM. Although, there was no significant difference of DV between the two methods compared with different HbA1c and HDL-C level. The correlation between the two methods changed oppositely in patients with DM compared with patients with non-DM.

There are several limitations in the present study. First, we used E-LDL instead of β -quantification as the standard reference measurement. Second, this study is a cross-sectional study and on follow-up of the changes in lipid profile of the population is available. Third, the data were collected in single center. Therefore, further study is necessary to analyze the correlation of F-LDL and E-LDL in the large population.

In conclusion, the present study showed that the FE had high correlation of enzymatic method although it underestimated the LDL-C by 0.23 mmol/L. The TG level was the main impact factor of correlation between the two methods. It suggested the LDL-C values measured by two methods were similarly reliable in CAD patients with or without DM.

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REFERENCES

1. Cholesterol Treatment Trialists C, Baigent C, Blackwell L, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670-1681.
2. Cholesterol Treatment Trialists C, Mihaylova B, Emberson J, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet*. 2012;380:581-590.
3. Cholesterol Treatment Trialists C, Fulcher J, O'Connell R, et al. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet* 2015;385:1397-1405.
4. Silverman MG, Ference BA, Im K, et al. Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. *JAMA*. 2016;316:1289-1297.
5. Scharnagl H, Nauck M, Wieland H, Marz W. The Friedewald formula underestimates LDL cholesterol at low concentrations. *Clin Chem Lab Med*. 2001;39:426-431.
6. Langsted A, Nordestgaard BG. Nonfasting lipids, lipoproteins, and apolipoproteins in individuals with and without diabetes: 58 434 individuals from the Copenhagen General Population Study. *Clin Chem*. 2011;57:482-489.
7. Rubies-Prat J, Reverter JL, Senti M, et al. Calculated low-density lipoprotein cholesterol should not be used for management of lipoprotein abnormalities in patients with diabetes mellitus. *Diabetes Care*. 1993;16:1081-1086.
8. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18:499-502.
9. Sibal L, Neely RD, Jones A, Home PD. Friedewald equation underestimates low-density lipoprotein cholesterol at low concentrations in young people with and without Type 1 diabetes. *Diabet Med*. 2010;27:37-45.
10. Sathyapalan T, Atkin SL, Kilpatrick ES. LDL cholesterol variability in patients with Type 2 diabetes taking atorvastatin and simvastatin: a comparison of two formulae for LDL-C estimation. *Ann Clin Biochem*. 2015;52(Pt 1):180-182.
11. European Association for Cardiovascular P, Rehabilitation, Reiner Z, Catapano AL, et al. ESC/EAS guidelines for the management of dyslipidaemias: the task force for the management of dyslipidaemias of the European society of cardiology (ESC) and the European atherosclerosis society (EAS). *Eur Heart J* 2011;32:1769-1818.
12. Catapano AL, Graham I, De Backer G, et al. 2016 ESC/EAS guidelines for the management of dyslipidaemias. *Eur Heart J*. 2016;37:2999-3058.
13. Chen J, Zhang Y, Liu J, et al. Role of lipoprotein(a) in predicting the severity of new on-set coronary artery disease in type 2 diabetics: A Gensini score evaluation. *Diab Vasc Dis Res*. 2015;12:258-264.
14. Li S, Xu RX, Guo YL, et al. ABO blood group in relation to plasma lipids and proprotein convertase subtilisin/kexin type 9. *Nutr Metab Cardiovasc Dis*. 2015;25:411-417.
15. Chai Kheng EY, Chee Fang S, Chang S, et al. Low-density lipoprotein cholesterol levels in adults with type 2 diabetes: an alternative equation for accurate estimation and improved cardiovascular risk classification. *Diab Vasc Dis Res*. 2014;11:431-439.
16. Choi H, Shim JS, Lee MH, Yoon YM, Choi DP, Kim HC. Comparison of formulas for calculating low-density lipoprotein cholesterol in general population and high-risk patients with cardiovascular disease. *Korean Circ J*. 2016;46:688-698.
17. Sudhir K, Ports TA, Amidon TM, et al. Increased prevalence of coronary ectasia in heterozygous familial hypercholesterolemia. *Circulation*. 1995;91:1375-1380.

18. Schwab KO, Doerfer J, Naeke A, et al. Influence of food intake, age, gender, HbA1c, and BMI levels on plasma cholesterol in 29,979 children and adolescents with type 1 diabetes—reference data from the German diabetes documentation and quality management system (DPV). *Pediatr Diabetes*. 2009;10:184-192.
19. Hirany S, Li D, Jialal I. A more valid measurement of low-density lipoprotein cholesterol in diabetic patients. *Am J Med*. 1997;102:48-53.
20. Whiting MJ, Shephard MD, Tallis GA. Measurement of plasma LDL cholesterol in patients with diabetes. *Diabetes Care*. 1997;20:12-14.
21. Nesto RW. Beyond low-density lipoprotein: addressing the atherogenic lipid triad in type 2 diabetes mellitus and the metabolic syndrome. *Am J Cardiovasc Drugs*. 2005;5:379-387.
22. Chaen H, Kinchiku S, Miyata M, et al. Validity of a novel method for estimation of low-density lipoprotein cholesterol levels in diabetic patients. *J Atheroscler Thromb*. 2016;23:1355-1364.
23. Anandaraja S, Narang R, Godeswar R, Laksmi R, Talwar KK. Low-density lipoprotein cholesterol estimation by a new formula in Indian population. *Int J Cardiol*. 2005;102:117-120.
24. Anwar M, Khan DA, Khan FA. Comparison of friedewald formula and modified friedewald formula with direct homogeneous assay for low density lipoprotein cholesterol estimation. *J Coll Physicians Surg Pak*. 2014;24:8-12.
25. Chen Y, Zhang X, Pan B, et al. A modified formula for calculating low-density lipoprotein cholesterol values. *Lipids Health Dis*. 2010;9:52.
26. de Cordova CM, de Cordova MM. A new accurate, simple formula for LDL-cholesterol estimation based on directly measured blood lipids from a large cohort. *Ann Clin Biochem*. 2013;50(Pt 1):13-19.
27. Vujovic A, Kotur-Stevuljevic J, Spasic S, et al. Evaluation of different formulas for LDL-C calculation. *Lipids Health Dis*. 2010;9:27.
28. Kang M, Kim J, Lee SY, Kim K, Yoon J, Ki H. Martin's equation as the most suitable method for estimation of low-density lipoprotein cholesterol levels in Korean adults. *Korean J Fam Med*. 2017;38:263-269.
29. Li XL, Guo YL, Zhu CG, et al. Relationship of high-density lipoprotein cholesterol with periprocedural myocardial injury following elective percutaneous coronary intervention in patients with low-density lipoprotein cholesterol below 70 mg/dL. *J Am Heart Assoc*. 2015;4:e001412.
30. Nanda SK, Bharathy M, Dinakaran A, Ray L, Ravichandran K. Correlation of Friedewald's calculated low-density lipoprotein cholesterol levels with direct low-density lipoprotein cholesterol levels in a tertiary care hospital. *Int J Appl Basic Med Res*. 2017;7:57-62.

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