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Goals of non-high density lipoprotein cholesterol need to be adjusted in Chinese acute coronary syndrome patients: Findings from the CCC-ACS project

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ABSTRACT

Background: Guidelines recommended non-high density lipoprotein cholesterol (non-HDL-C) as a co-primary target, and set non-HDL-C goals as 30 mg/dl higher than low-density lipoprotein cholesterol (LDL-C) goals. However, the value is largely uncertain in Chinese patients.

Methods: We assigned non-HDL-C values at the same percentiles correspondent to LDL-C goals for patients from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome (CCC-ACS) Project. We calculated the differences between non-HDL-C and LDL-C and proposed appropriate adding values according to LDL-C and TG concentrations.

Results: Among 73,495 patients, 17.7% used lipid-lowering agents before admission. Of these, 27.2% achieved LDL-C < 70 mg/dl while 39.4% achieved non-HDL-C < 100 mg/dl. The mean difference between non-HDL-C and LDL-C was 23.2 mg/dl, which could be affected by LDL-C and TG concentrations. Importantly, of patients with LDL-C concentrations ≤100 mg/dl, the mean differences were 19.1 mg/dl in patients with TG ≤150 mg/dl and 24.6 mg/dl in patients with TG > 150 mg/dl.

Conclusions: There are significant differences between LDL-C and non-HDL-C in Chinese ACS patients. For secondary prevention, on average, the adding values should be 20 mg/dl for patients with TG ≤150 mg/dl and 25 mg/dl for patients with TG > 150 mg/dl when LDL-C goals of 70 mg/dl is achieved.

1. Introduction

The prevalence of atherosclerotic cardiovascular disease (ASCVD) in China has risen markedly in past three decades [1]. Acute coronary syndrome (ACS), an acute manifestation of ASCVD, has already resulted in a substantial increase of mortality in Chinese patients. The number of ACS deaths was 3.8 million in 2013 [2], and the growing prevalence of modifiable atherogenic risk factors, like dyslipidemia, has imposed great burden on morbidity and mortality of ACS [3]. Previous investigations indicated that increased plasma cholesterol concentrations contributed to 77% of increase in fatal myocardial infarction in Chinese population, posing serious risks to present and future health [4].

The relationship between dyslipidemia and ACS has been well established. According to the national survey, the prevalence of dyslipidemia in Chinese population was 34.0% (35.1% and 26.3% in urban and rural areas, respectively) [5], and the hallmark of dyslipidemia was high plasma triglyceride (TG), high plasma low-density lipoprotein cholesterol (LDL-C) and low plasma high-density lipoprotein cholesterol (HDL-C) [6]. So far, LDL-C has been recommended as the primary treatment target, but the importance of non-HDL-C has attracted more attention recently, especially in those with hypertriglyceremia [7,8]. Indeed, non-HDL-C encompasses all of the atherogenic apolipoprotein B-containing lipoproteins, including LDL, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), lipoprotein (a) and chylomicrons (CM) [9]. Prospective observation studies found that non-HDL-C was much better than LDL-C in predicting cardiovascular risks [10–12]. The advantages of non-HDL-C over LDL-C has also been confirmed in patients with statin treatment. For instance, a meta-analysis found that patients with LDL-C < 100 mg/dl but non-HDL-C > 130 mg/dl had higher risk of ASCVD compared to those reaching both targets; in

Abbreviations: CCC-ACS project, the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Project; ACS, acute coronary syndrome

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contrast, patients with LDL-C > 100 mg/dl but non-HDL-C < 130 mg/dl had similar risk of ASCVD as those reaching both targets [13], suggesting that non-HDL-C was superior to LDL-C in predicting ASCVD risk.

As accumulating evidence supporting the significance of non-HDL-C in predicting ASCVD risks, guidelines have flagged non-HDL-C as a co-primary target associated with LDL-C for lipid-lowering therapy and recommended non-HDL-C goals as 30 mg/dl higher than the corresponding LDL-C goals [14–17]. However, the fixed adding value of 30 mg/dl did not consider the population distribution of non-HDL-C, which could represent a more appropriate individual goal when two markers were discordant, and the true difference between non-HDL-C and LDL-C were still not tested in Chinese population.

2. Materials and methods

For the concern about intellectual property and patient privacy, the data, analytic methods, and study materials of this study will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

2.1. Study design and participating hospitals

The Improving Care for Cardiovascular Disease in China-Acute coronary syndrome (CCC-ACS) Project is a nationwide registry and quality improvement study with an ongoing database focusing on quality of ACS care in Chinese patients. This study was launched in 2014 as a collaborative initiative of the American Heart Association (AHA) and Chinese Society of Cardiology (CSC). Details of design and methodology of CCC-ACS project have been published [18]. In brief, the following steps were used to recruit hospitals in the CCC-ACS project. Firstly, mainland China was divided into 7 geographical regions (Northern, Northeastern, Eastern, Central, Southern, Southwestern, and Eastern China). Secondly, in each region, provinces were grouped into four groups according to gross domestic product per capita (low, medium-low, medium-high, and high). Thirdly, in each geographic-economic stratum, 10% of the tertiary hospitals were recruited. Hospitals with ACS case volume > 20 per month and were willing to participate in the project were recruited. Finally, a total of 191 hospitals were recruited across 30 provinces in China (Table A.1). The laboratories of 191 participating hospitals, before enrolled in CCC-ACS Project, all passed the External Quality Assessment (EQA) conducted by the National Ministry of Health Clinical Laboratory Center and passed the Medical Laboratory-Quality and Competence Requirements (ISO15189) China National Accreditation Service for Conformity Assessment (CNAS) to guarantee the consistency of results and to make sure that the data results are comparable between different medical laboratories. This study was registered (URL: http://www.ClinicalTrials.gov. Unique identifier: NCT02306616).

2.2. Sampling transport and determination of blood lipids

Blood samples were collected after a 12-h fast in a tube with an activator gel. The serum was separated within 30 min and stored in tubes at 4 °C. Subsequently, the tubes were transported to the laboratories of the corresponding hospitals and performed the analysis. Serum concentrations of total cholesterol (TC) and TG were measured by automated enzymatic assays; serum concentrations of LDL-C and HDL-C were measured by a commercially available direct method (i.e., antibody blocking method and selective protection method, respectively) by a laboratory technician who had no idea of this study. The instruments and the supporting reagents used by laboratories of 191 participating hospitals were list in Table A.2. Non-HDL-C is calculated by subtracting HDL-C from TC. Body mass index (BMI) is calculated as weight in kilograms divided by height in meters squared. Classifications of TC, TG, HDL-C and LDL-C concentrations were based on the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP-III) guidelines [19].

2.3. Data collection

A standard data collection platform (Oracle Clinical Remote Data Capture, Oracle) was used. Multiple strategies were used to ensure the accuracy and completeness of the data. Regular on-site quality audits by third-party clinical research associates were performed to ensure enrollment of consecutive patients. Trained data abstractors in the participating hospitals reported the required data, which they abstracted from the patients' medical records. Eligible patients were consecutively reported to the CCC-ACS database for each month before the middle of the following month. Third-party clinical research associates were hired to perform quality audits to ensure that cases were reported consecutively rather than selectively. Additionally, about 5% of reported cases from every participating center were randomly selected every 3 months. Selected data were then compared with the original medical records to ensure accuracy and completeness. According to the quality audit reports, the data in this study were appropriately reported with a low incidence of missing data or error. The quality audit reports were also fed back to each center regularly to ensure data quality.

2.4. Study population

On the basis of principal discharge diagnosis, 88,561 patients with ACS from 191 hospitals across 30 provinces in China were registered from November 1, 2014, to October 31, 2018. Of these, 73,495 patients enrolled in our study, 15,066 patients were excluded, including 2764 patients with incorrect lipid values and 12,302 patients lacking important clinical data. Institutional review board approval was granted for this research by the ethics committee of Institute of Heart Lung and Blood Vessel Diseases in Beijing Anzhen Hospital, Capital Medical University. No informed consent was required.

2.5. Statistical analysis

Firstly, we assigned population percentiles to LDL-C and non-HDL-C concentrations and examined the differences between LDL-C and non-HDL-C. We also divided the patients into five groups by LDL-C concentrations and evaluated its agreements with the corresponding non-HDL-C concentrations by cross tabulations. Secondly, we listed the mean differences between LDL-C and non-HDL-C by different LDL-C and TG concentrations, and calculated the average differences in patients with different LDL-C and TG stratifications.

Laboratory findings were reported as (mean ± standard deviation) or median for continuous variables and as a proportion (%) for categorical variables. Continuous variables were compared using Mann-Whitney test and categorical variables were compared using the Chi-squared test. We consider $P < 0.05$ as statistically significant. All P values were 2-tailed and not adjusted for multiple testing. Statistical analyses were performed using IBM SPSS statistics 25, and STATA Version 13.0 software. The bar graph and the image scatter plot with color indicating density were generated in Graph-pad prism 6 and R Version 3.5.1 software.

3. Results

3.1. Basic demographic and lipids characteristics of patients

Characteristics of patients were shown in Table A.3. A total of 73,495 patients were enrolled in our study with a mean (SD) age of 63.4 (12.4) y and 74.5% of the patients were male. The proportion of different lipids concentrations classified by ATP-III guideline were shown in Table A.4. The mean (SD) difference between LDL-C and non-HDL-C in all patients was 23.2 (9.2) mg/dl (Table A.5). Basic information of

Table 1
Differences of LDL-C and Non-HDL-C in all patients.

Population percentile	LDL-C (mg/dl)	Non-HDL-C (mg/dl)	Differences (mg/dl)
1	35.5	54.5	19.0
5	51.4	72.3	20.9
10	61.4	82.7	21.3
15	68.4	90.4	22.0
17	70.1	92.5	22.4
20	74.2	97.0	22.8
25	79.6	102.8	23.2
44	96.6	122.2	25.6
50	100.4	128.3	27.9
72	122.9	153.1	30.2
75	126.4	157.3	30.9
78	130.3	161.6	31.3
90	151.5	186.3	34.8
93	160.4	197.2	36.8
97	189.7	228.1	38.4
99	203.0	243.1	40.1

Abbreviations: LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol.

male patients and female patients were shown in Table A.6, and the differences distribution between LDL-C and non-HDL-C had no statistics significance between men and women patients ($p > 0.05$, Table A.7).

3.2. Percentage of patients achieving LDL-C or non-HDL-C target with prior lipid-lowering agents

In all patients, 13,042 took lipid-lowering drugs before admission (17.7%). Of these, 27.2% reached LDL-C target of < 70 mg/dl, however, nearly 39.4% reached non-HDL-C target of < 100 mg/dl (Fig. A.1).

3.3. Patients-concentration discordance and distribution of non-HDL-C and LDL-C

The LDL-C cut-points of 70, 100, 130, 160, 190 mg/dl were at 17th, 50th, 78th, 93th, 97th percentile, and the corresponding concentrations of non-HDL-C were 93, 128, 161, 197, 228 mg/dl, respectively. The differences between non-HDL-C and LDL-C were < 30 mg/dl below 72nd percentile, suggesting that about 72% patients could not use non-LDL-C as therapeutic target (Table 1). Use of prior lipid-lowering agents had no obvious effect on difference distribution between non-HDL-C and LDL-C ($p > 0.05$, Tables A.8 and A.9).

3.4. Comparison of overlap between LDL-C concentrations and corresponding non-HDL-C concentrations based on different adding values

The rate of overlap between different LDL-C concentrations and corresponding non-HDL-C concentrations was calculated, based on an adding value of 30 mg/dl. We divided the patients into five groups by LDL-C concentrations and observed that the lowest LDL-C concentration (< 70 mg/dl) presented a greatest overlap with the corresponding non-HDL-C concentration. However, the discordance appeared obviously in patients with LDL-C 70–160 mg/dl (Table 2). Next, we examined the rate of overlap between LDL-C concentrations and corresponding non-HDL-C concentrations based on the adding values of 20 and 25 mg/dl. In patients with LDL-C < 70 mg/dl, the rate was slightly greater when the adding value was 30 mg/dl, compared to that when the adding value was 20 or 25 mg/dl. However, in patients with LDL-C > 70 mg/dl, the overlap was greater when the adding value was 20 mg/dl or 25 mg/dl (Tables A.10-1 and A.10-2). The average rates of overlap were similar when adding value was 20 or 25 mg/dl, but higher than that when adding value was 30 mg/dl (Fig. A.2).

3.5. Mean differences between LDL-C and non-HDL-C stratified by different LDL-C and TG concentrations

Next, we investigated the mean differences between LDL-C and non-HDL-C according to different LDL-C and TG concentrations. After analysis, we found that the magnitude of differences could be affected by LDL-C and TG concentrations (Fig. A.3). Of patients with LDL-C concentrations ≤100 and > 100 mg/dl, the mean differences were 20.4 and 25.8 mg/dl, respectively (Fig. A.3). Furthermore, among the patients with LDL ≤100 mg/dl, the mean differences were 19.1 mg/dl in patients with TG ≤150 and 24.6 mg/dl in patients with TG > 150 mg/dl, respectively (Table 3).

3.6. Non-HDL-C and LDL-C percentile discordance by different TG concentrations

We visually assessed the discordance between LDL-C and non-HDL-C percentiles. At low TG concentrations (TG < 100 mg/dl), non-HDL-C percentile was lower than LDL-C percentile, while at high TG concentrations (TG > 150 mg/dl), non-HDL-C percentile was higher than LDL-C percentile. The higher TG concentrations, the greater discordance could be observed (Fig. 1).

4. Discussion

Our study highlights the magnitude of differences between LDL-C and non-HDL-C concentrations in Chinese ACS patients. To our knowledge, this is the first and largest study to evaluate characteristics of Chinese ACS patients with differences between those two markers.

In our present study, we found the non-HDL-C values with percentile equivalence to LDL-C cut-points of 70, 100, 130, 160, 190 mg/dl were 93, 128, 161, 197, 228 mg/dl, and difference of 30 mg/dl between non-HDL-C and LDL-C was at 72nd percentile of patients. These results were similar with several previous published findings. For instance, an analysis revealed that LDL-C cut-points of 70, 100, 130, 160, and 190 mg/dl were in the same population percentiles as non-HDL-C values of 93, 125, 157, 190, and 223 mg/dl in American population [20]; additionally, a cross-sectional designed study also demonstrated that difference between non-HDL-C and LDL-C in Japanese population was lower than 30 mg/dl [21]. Similar differences were observed in a study of Brazilian population [22], suggesting that the adding value of 30 mg/dl seems not appropriate.

Then we observed that about 27.2% of Chinese ACS patients reached the goal of LDL-C < 70 mg/dl with prior lipid-lowering agents, but when non-HDL-C < 100 mg/dl was employed as target, > 39.4% could reach the goal, revealing that the adding of 30 mg/dl to LDL-C goals as non-HDL-C goals may over-estimate the goal-reaching rate in Chinese ACS patients. Therefore, conventional goals of non-HDL-C recommended by guidelines may need to be lowered to better match the percentiles of LDL-C goals. Reliance on either single measure in non-HDL-C or LDL-C might result in failure to classify risks and treatment effects of ACS.

As mentioned above, non-HDL-C represents the cholesterol mass contained in all atherogenic lipoproteins. The rationale for the difference of 30 mg/dl between LDL-C and non-HDL-C goals is a theoretical calculation estimated from percentile distributions derived from the Framingham study [23] and is based on the assumption that VLDL-C is the principal atherogenic lipoprotein after LDL-C [24]. It is proposed that, on the average, the weight ratio of TG to cholesterol in VLDL particle is 5 to 1; that is, if the weight of TG is 150 mg in VLDL particle, the weight of cholesterol content in VLDL particle should be around 30 mg. However, evidence revealed that a biologically optimal fasting TG concentration was < 150 mg/dl, so a normal VLDL-C concentration was likely < 30 mg/dl [25]. On the other hand, LDL particles carry approximately 75%~85% of total cholesterol while VLDL particles carry approximately 5%~25% of cholesterol [26]. When LDL-C is

Table 2
Cross-table between non-HDL-C and LDL-C categories according to cut-off points of LDL-C with 30 mg/dl difference.

		Non-HDL-C (mg/dl)				
		< 100	100–130	130–160	160–190	> 190
LDL-C (mg/dl)	< 7 < 70 < 70 *n* = 12,058	80.5%	14.9%	4.6%	0%	0%
	70–100 *n* = 23,239	27.4%	55.3%	15.0%	2.3%	0%
	100–130 *n* = 21,944	0%	29.1%	54.6%	14.3%	2.0%
	130–160 *n* = 10,997	0%	0%	31.4%	51.0%	17.6%
	> 160 *n* = 5257	0%	0%	1.0%	23.6%	75.4%

Abbreviations: LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol.

Table 3
Mean differences between LDL-C and non-HDL-C stratified by different LDL-C and TG concentrations.

		TG (mg/dl)	
		≤150	> 150
LDL-C (mg/dl)	≤100	19.1 mg/dl	24.6 mg/dl
	> 100	22.8 mg/dl	29.4 mg/dl

Abbreviations: LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density lipoprotein cholesterol; TG, triglyceride.

decreased by lipid-lowering agents, the concentration of VLDL-C should be lowered, also suggesting that concentrations of VLDL-C was < 30 mg/dl. Furthermore, both LDL and VLDL contribute significantly to the atherogenesis. Thus, in order to further reduce the risk of ACS and major adverse cardiovascular events (MACE), LDL-C and VLDL-C should be lowered simultaneously. When LDL-C target is set to a lower value (< 70 mg/dl) in patients with very high risk based on the number of risk factors, the VLDL-C target should be lowered synchronously (< 30 mg/dl). Actually, evidence from the Limiting UNdertreatment of lipids in ACS With Rosuvastatin (LUNAR) Trial have already shown that to better match LDL-C, the current non-HDL-C goal should be lowered by 8 to 10 mg/dl [27]; another meta-analysis of 8 major statin trials also demonstrated that compared with patients who achieved an LDL-

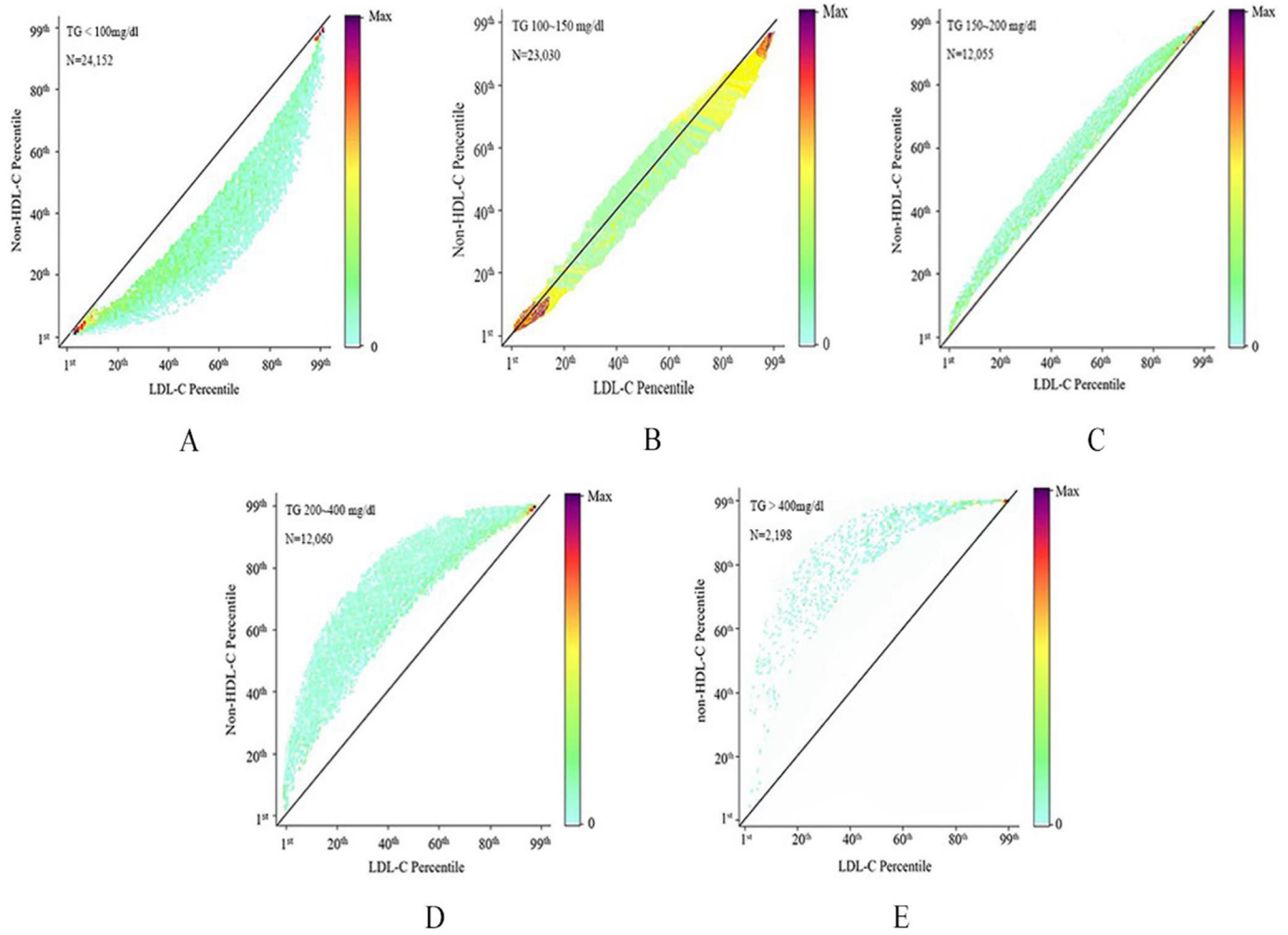

Fig. 1. Patient-Concentration Discordance Between Population Percentiles of LDL-C and non-HDL-C. The 5 groups according to different TG concentrations (A~E). The density of data is expressed by different shades of color, which represent increasing densities of patients per pixel, from light green to purple. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

C > 175 mg/dl, those who reached LDL-C < 50 mg/dl and non-HDL-C < 75 mg/dl targets had the lowest ASCVD events [28]. Additionally and importantly, 2017 American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Clinical Practice Guideline recommended, for the first time, that the targets of patients with diabetes was LDL-C < 55 mg/dl and non-HDL-C targets of < 80 mg/dl, demonstrating that the adding value should be 25 mg/dl [29]. Taken together, it is obviously that the fixed value of 30 mg/dl for adding to LDL-C target as non-HDL-C target is not appropriate. Herein, in our study, the mean difference between the non-HDL-C and LDL-C was 23.2 mg/dl, and the magnitudes of difference are affected by the concentrations of LDL-C and TG. As mentioned above, of patients with LDL-C concentrations ≤100 mg/dl and with LDL-C concentrations > 100 mg/dl, the mean differences were 20.4 mg/dl and 25.8 mg/dl, respectively. Furthermore, among the patients with LDL ≤100 mg/dl, the mean differences were 19.1 mg/dl in patients with TG ≤150 mg/dl and 24.6 mg/dl in patients with TG > 150 mg/dl, respectively. Thus, different adding values for Chinese ACS patients should be based on the concentrations of LDL-C and TG after using lipid-lowering agents, so setting the targets based on LDL-C and TG concentrations is necessary.

It is no doubt about the relationship between plasma concentrations of LDL-C and risks of ACS, as well as about the benefits of lipid-lowering therapy such as statin treatment. However, despite achieving LDL-C target, it is also clear from the evidence that the persistence of a high cardiovascular disease risks, as a concept called residual risk, are notable. Currently, accumulating evidence showed that there were divergences with using of LDL-C for treatment and prevention target of ASCVD or ACS patients. Firstly, in many hospitals, LDL-C was still obtained using the Friedewald-estimated formula (F-formula) that LDL-C was calculated as [TC – (HDL-C) – (TG/5)] [30]. Since LDL-C relies on the detection of three other variables, it was easier to generate systematic errors of LDL-C. Secondly, the F-formula requires assumptions that ratio of cholesterol to TG carried in VLDL particles is constant. However, when TG concentration is high, it is apparent that LDL-C concentration is often underestimated by the increased proportion of cholesterol in the VLDL. Thirdly, there were evidence that even achieving lower LDL-C targets (< 70 mg/dl) in very high-risk patients left a high residual risk. For example, in 4S trials, patients treated with lipid-lowering agents presented 20% of cardiovascular events rates over the 5-years period [31]; in TNT trials, patients treated with atorvastatin 80 mg daily was associated with a 22% risk reduction of major cardiovascular events compared with those taking atorvastatin 10 mg daily, about 9.9% of patients still experienced a cardiovascular event during 5-years follow-up [32].

Indeed, it is worth noting that current available guidelines have demonstrated that adding VLDL-C to LDL-C as non-HDL-C could provide an additional power to predict risk of ASCVD [19]. Evidence have also verified that non-HDL-C was a better marker for ASCVD and MACE risk prediction and a more effective target for lipid-lowering therapy. For instance, a meta-analysis including 8 trials found that patients with on statin treatment LDL-C ≤100 mg/dl but non-HDL-C ≥130 mg/dl had a higher hazard ratio (HR) for future ACS of 1.32 (95% CI, 1.17–1.50) compared to those reaching both targets (HR = 1). However, those patients with LDL-C ≥100 mg/dl but non-HDL-C ≤130 mg/dl had HR for future ACS of 1.02 (95% CI, 0.92–1.12) [33]. In 2017, a retrospective study investigated the predictability of attaining non-HDL-C goal and long-term MACE in Thai patients after acute myocardial infarction (AMI). The results showed that compared to patients with non-HDL-Cconcentration ≤100 mg/dl, patients with non-HDL-C ≥130 mg/dl had a HR for MACE of 3.15 (95% CI, 1.46–6.80). While compared to those with LDL-C concentration ≤70 mg/dl, patients with LDL-C ≥100 mg/dl was associated with a HR for MACE of 0.42 (95% CI, 0.18–0.98), indicating that non-HDL-C was a better predictor of future MACE following AMI [33]. On the other hand, Lee et al. investigated 1792 individuals who underwent percutaneous coronary intervention (PCI) and demonstrated that each one standard deviation (1-SD) increase in corrected variability independent of mean (cVIM) of LDL-C and non-HDL-C could increase the risk of MACE by 34% and 37%, respectively, revealing that non-HDL-C treatment goals could be a better target of lipid-lowering therapy [34]. Because non-HDL-C was not routinely reported in laboratory results, persons with normal LDL-C but high non-HDL-C might be excluded for lipid-lowering therapy. Actually, patients with high non-HDL-C but normal LDL-C were more likely to have metabolic syndromes, so ignoring non-HDL-C may result in missed treatment opportunities for these persons with a high ASCVD risks [35]. Furthermore, the concentration of non-HDL-C is not influenced by fasting conditions, which could provide convenience for patients in clinical practice [10].

Our study focused on the ACS patients and the lipid-lowering therapeutic target for secondary prevention. Regarding when we could use the non-HDL-C goals, it is reasonable to use non-HDL-C goal in the secondary prevention. Moreover, the decreased adding value (< 30 mg/dl) is applicable to the secondary prevention after the LDL-C target of 70 mg/dl is reached. On the other hand, is routinely measurement of LDL-C necessary? It is true that non-HDL-C is easily calculated as [TC – (HDL-C)] without LDL-C measurement, and it seems not necessary to routinely measure LDL-C. But it is worth noting that the current guidelines recommended LDL-C as the primary target and non-HDL-C as the secondary target, meaning that we need know first whether LDL-C target has reached after lipid-lowering therapy in clinical practice. Thus, LDL-C measurement is necessary to evaluate the effect of treatment.

Limitations were described as followed. Firstly, even we have provided appropriate values for adding to LDL-C goals as non-HDL-C goals, we still need a large-scale prospective study in Chinese ACS patients to determine the validity of the values. Secondly, values of lipid concentrations in our study were collected from ACS patients, which could subject to the effect of acute stress response, leading to a relatively lower LDL-C concentration and higher TG concentration compared to those in pre-attack status. Thirdly, the confusion factors in our study caused by the methodological differences among 191 hospitals is inevitable. However, despite these limitations, our study included a significant number of patients, and data of patients were collected through standardized laboratory parameters. The rigorous pre-analytical and analytical protocols guaranteed the uniformity of the methodology.

5. Conclusions

There are significant differences between LDL-C and non-HDL-C in Chinese ACS patients, and adding the fixing value of 30 mg/dl to LDL-C goals as non-HDL-C goals may over-estimate goal-reaching rate. Thus, lowering 5–10 mg/dl of conventional non-HDL-C cut-points may match percentiles of LDL-C cut-points better. Our findings could provide significant implications for guideline modifications on non-HDL-C goal in clinical practice. According to our results, for secondary prevention, different adding values should be employed to set non-HDL-C goals based on the TG concentrations after the LDL-C goal of 70 mg/dl is achieved. On average, the adding values might be 20 mg/dl for patients with TG ≤150 mg/dl and 25 mg/dl for patients with TG > 150 mg/dl.

Author contributions

X.S. and D.Q.P. contributed to the study design; X.S., M.D.L., Y.H.L., X.Y.T. and X.Y.Z. performed research, analyzed and interpreted data; X.S. and D.Q.P. wrote the manuscript. All authors reviewed drafts and approved the final version of the manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cca.2019.06.022.

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