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Original Article

Improvement of Goal Attainment of Low-Density Lipoprotein Cholesterol in High-Risk Patients by Individualized Target Value Reminding Approach

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SUMMARY

Background: The attainment of target serum low-density lipoprotein cholesterol (LDL-C) levels and the prescription rates of high-intensity stain (HIS) and ezetimibe among high-risk patients in Taiwan remain unsatisfactory. We hypothesized that reminding individualized target LDL-C values to physicians and patients improved the attainment.

Methods: Between July 2018 and December 2019, 214 high-risk patients with suboptimal LDL-C levels in the Lipid Clinic of our institution, including 100 patients with coronary artery disease (CAD), were enrolled. Each patient received prescription of lipid-lowering medications supported by an intelligent checklist-assisted reminding approach and informed individualized target serum LDL-C levels. The LDL-C goal attainment rates and the prescription rates of HIS/ezetimibe of patients were analyzed every 3 months.

Results: Patients with CAD at enrollment had a higher rate of stain prescription, lower baseline serum LDL-C levels, and a wider gap to reach serum LDL-C goals, compared to those without CAD. The prescription rates of HIS/ezetimibe at baseline, 3-month, 6-month, and 9-month follow-ups in patients with CAD were respectively 25.0%/8.0%, 78.6%/51.0%, 78.6%/69.0%, and 87.5%/82.1%, while those in patients without CAD were respectively 6.1%/9.6%, 70.8%/26.5%, 66.7%/33.3%, and 78.3%/43.5%. The LDL-C goal attainment rates at 3-month, 6-month, and 9-month follow-ups in patients with CAD were respectively 58.8%, 62.0%, and 62.5%, while those in patients without CAD were respectively 79.6%, 75.6%, and 73.9%.

Conclusion: The intelligent checklist-assisted reminding approach in electronic medical order system, accompanied by an increased prescription of HIS and ezetimibe in the Lipid Clinic effectively facilitate the improvement of LDL-C goal attainment rates in high-risk patients.

1. Introduction

Dyslipidemia is prevalent in Asia, including Taiwan, in both adults and the elderly.[1,2] Based on clinical and observational studies, low-density lipoprotein cholesterol (LDL-C) is an important treatment target to prevent the risk of atherosclerotic cardiovascular disease (ASCVD), and statin is the effective therapy to reduce serum LDL-C levels.[3–7] The intensity of statin therapy is divided into 3 categories: high-intensity, moderate-intensity, and low-intensity that typically lower LDL-C levels by ≥ 50%, 30% to 49%, and < 30%, respectively.[8,9] According to the latest American[8] and European[9] guidelines for management of dyslipidemia, high-intensity statin (HIS) is recommended in patients with ASCVD, and ezetimibe should be added when the optimal LDL-C goal is not reached. Despite these above-mentioned guidelines' recommendations, the use of HIS and ezetimibe, as well as the attainment rates of target serum LDL-C levels in high-risk patients are still suboptimal.[10–14]

In Taiwan, the management of dyslipidemia in high-risk patients remained to be improved. According to the CEntralized Pan-Asian survey on tHE Under-treatment of hypercholesterolemia (CEPHEUS Pan-Asian survey), the attainment rates of target serum LDL-C levels in Taiwan among patients whose LDL-C target levels should be lower than 100 mg/dL and 70 mg/dL were respectively 69% and 22%.[15] Additionally, the Taiwan Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) registry study showed that 73% of patients with ASCVD used statin therapy and only 54% of these patients reached serum LDL-C levels < 100 mg/dL.[16] In a cohort of patients with stable coronary artery disease (CAD) who were enrolled by National Taiwan Biosignature Research Investigators (Biosignature CAD cohort study),[17] there were 73% of patients with stable CAD receiving statin therapy at enrollment. These previous results were obtained more than three years ago and did not report the prescription rates of HIS and ezetimibe, thereby creating a bar-

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rier to infer the current status of lipid management in high-risk patients in Taiwan. Recently, the "2017 Taiwan lipid guidelines for high risk patients" has been issued and clearly recommended target serum LDL-C levels for high-risk patients;[18] however, the real-world data demonstrating the prescription rates of HIS and ezetimibe, as well as the goal attainment rates of LDL-C in high-risk patients, remained still unclear. To address this knowledge gap, the present study aimed to investigate the prescription of HIS and ezetimibe, and the LDL-C goal attainment rates in high-risk patients by analyzing data collected from the Lipid Clinic in a medical center. In addition, the present study would like to evaluate whether a reminding approach implemented in electronic medical order system improved the attainment of target serum LDL-C levels in high-risk patients.

2. Materials and methods

2.1. Study design, definition of high-risk comorbidities, and HIS

This study was a retrospective analysis of prospective enrolled patients in the Lipid Clinic which was established in our institution since July 2018 and included three cardiologists and one endocrinologist as the principal investigators. The principal investigator meeting has been held every two months to discuss any queries about the protocol setting and patient recruitment. All protocols of the present study were approved by the Institutional Review Board of our institution (Approval No. 18MMHIS083e), and written informed consent was obtained from all participants.

The definition of high-risk comorbidities, intensity of statins, and the target serum LDL-C levels of high-risk patient were according to "2017 Taiwan lipid guidelines for high risk patients".[18] High-risk patients were identified if patients had at least one of the following medical histories: CAD, ischemic stroke (IS), peripheral artery disease (PAD), diabetes mellitus (DM), or familial hypercholesterolemia (FH). Patients with CAD were defined as those who had > 50% diameter stenosis of major epicardial coronary arteries confirmed by coronary computed tomography (CT) angiography or coronary angiography, or had a history of acute coronary syndrome (ACS) identified by medical records of hospitalization and urgent coronary revascularization. Diagnosis of IS was based on the neurologist's records with relevant image confirmation by brain CT or magnetic resonance imaging. Diagnosis of PAD was confirmed by ankle-brachial index < 0.9 or > 1.4 and/or > 50% diameter stenosis of peripheral arteries observed in CT angiography. Diagnosis of DM was based on medical records and prescribed medications. FH was identified when patients had a pathogenic genotype confirmed by gene test or had a Dutch Lipid Clinic Network (DLCN) score > 8.[19] Other medical histories, including hypertension (HTN), heart failure, and dialysis were identified based on medical records.

Atorvastatin 40–80 mg/day and rosuvastatin ≥ 20 mg/day were referred as HISs.[18] The target serum LDL-C levels of patients with CAD were < 70 mg/dL, while those of high-risk patients without CAD were < 100 mg/dL.[18]

2.2. Study population, data collection, and workflow in the Lipid Clinic

High-risk patients were eligible to be enrolled in the present study if they did not have an optimal serum LDL-C level determined by physicians according to the current Taiwan lipid guidelines.[18] We excluded patients who were contraindicated or intolerant to statin therapy, unable to receive regular blood examination, or disagreed with providing personal medical information. Finally, high-risk patients were divided into 2 groups: patients with CAD and patients without CAD (Figure 1). After enrollment, specially-trained study nurses collected all baseline data whenever feasible, including age, sex, weight, height, smoking habit, histories of comorbidities, laboratory data, and concurrent prescribed medications. Body mass index was defined as weight in kilograms divided by the square of height in meters. The concurrent medications were recorded in detail, including angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs), antiplatelets (i.e., aspirin and $P2Y_{12}$ inhibitors), beta-blockers, calcium-channel blockers, statins, ezetimibe, fibrates, and insulin. All participants in the present study were followed up and underwent blood examination every 3 months for a total duration of 9 months. Each high-risk patient received well-organized treatment and counselling in the Lipid Clinic, including suggestions of life-style modification with providing health education leaflets, lipid-lowering therapy (LLT) according to recommendations of the current Taiwan lipid guidelines,[18] and emphasis of drug adherence. All patients in the present study received initiation or adjustment of statin therapy after enrollment. Other LLT, includ-

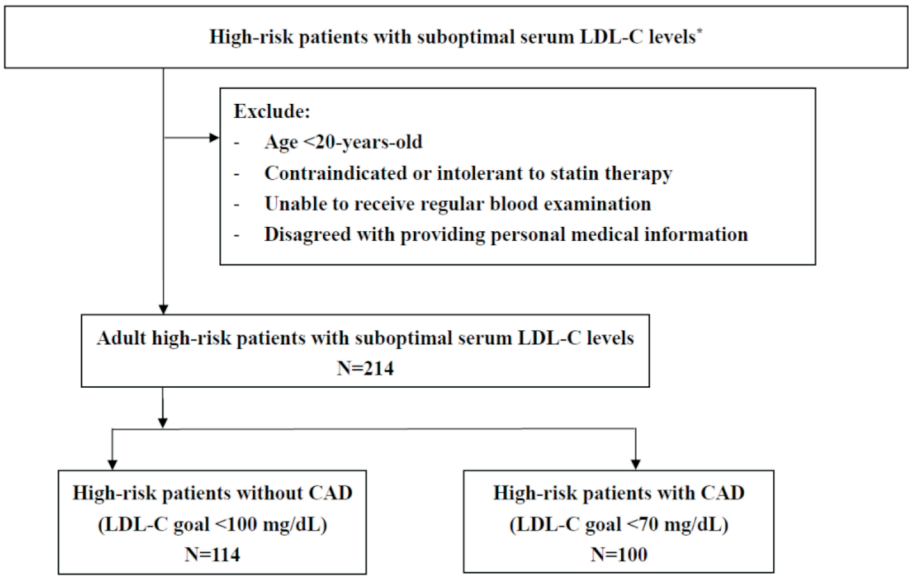

Figure 1. Diagram of high-risk patient selection. (* According to "2017 Taiwan lipid guideline in highrisk patients")

ing ezetimibe, fibrates, and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, were prescribed according to actual clinical situation and physician-patient discussion. At each visit, the patients' prescribed LLT and lipid profiles, including total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and LDL-C were recorded.

2.3. Integrated electronic checklist in medical order system

An electronic checklist was implemented in medical order system and appeared whenever the physicians prescribed any LLT, including statins, ezetimibe, fibrates, or PCSK9 inhibitors. Unlike the artificial intelligence (AI)-based system that could actively inform suboptimal results of blood lipid tests to physicians and patients, the electronic checklist was initially designed to assist physicians to evaluate patients' risk factors of ASCVD and medical histories of comorbidities, thereby reminding physicians whether the patients achieved their target serum LDL-C levels and whether adjustment of LLT was needed. The risk factors of ASCVD and medical histories of comorbidities listed in the electronic checklist were according to the recommendations of Taiwan's National Health Insurance Administration and Taiwan lipid guidelines.[18] The first part of the checklist was to remind physicians whether the patients had the following risk factors of ASCVD: current cigarette smoker, family history of premature CAD, age $\geq$ 45 years for males, age $\geq$ 55 years or menopause for females, and serum HDL-C < 40 mg/dL. The second part of the checklist was to remind physicians whether the patients had the following medical histories: HTN, ACS, CAD, IS, DM, PAD, and FH. The checkboxes of above-mentioned risk factors and medical histories were automatically checked according to patients' diagnostic codes and relevant prescribed medications. Finally, the physicians were required to confirm that the content of each patient's checklist was correct before they completed the electronic prescription orders. In addition, the individualized guideline-recommended serum LDL-C levels of each patient were informed and listed in the patient's laboratory report printout.

2.4. Study outcomes

The study outcomes in the present study were the prescription rates of HIS and ezetimibe, and the LDL-C goal attainment rates in high-risk patients at every 3-month follow-up.

2.5. Statistical methods

Continuous and categorical variables were presented with means ($\pm$standard deviations) or numbers (percentages), respectively. Comparisons were performed using the unpaired Student t test or Wilcoxon rank sum test for continuous variables, and the chi-square or Fisher's exact test for categorical variables as appropriate. The baseline characteristics of patients with CAD were compared with those without CAD. The prescription rates of HIS and ezetimibe, and LDL-C goal attainment rates were analyzed at every 3-month follow-up. Significance was set at $p < 0.05$ (2-tailed). SAS statistical software (version 9.2 for Windows; SAS Institute, Cary, NC, USA) was used for all analyses.

3. Results

Between July 2018 and December 2019, 214 high-risk patients who visited the Lipid Clinic and had a suboptimal serum LDL level were enrolled in the present analysis. Of them, 100 high-risk patients had histories of CAD, while the remaining 114 high-risk patients were without CAD. The baseline characteristics of all patients were listed in Table 1. Patients with CAD were older, more males, had a lower BMI, HbA1c, and eGFR, and less frequent to have diabetes and FH, but more frequent to receive antiplatelets, ACEIs/ARBs, and beta-blockers, compared to those without CAD (Table 1). The prescription rates of statin therapy and HIS at baseline were higher in patients with CAD (72.0% and 25.0%, respectively) compared to patients without CAD (37.7% and 6.1%, respectively) (Table 1). In addition, patients with CAD had lower baseline serum levels of TC, LDL-C, and HDL-C, compared to those without CAD (Table 1).

Compared to the patients without CAD, those with CAD had a wider gap to reach serum LDL-C goals irrespective of statin use at enrollment (percentage reduction to attain target serum LDL-C levels for patients with statin therapy at baseline, CAD vs. non-CAD, $30.6 \pm 15.9\%$ vs. $24.4 \pm 16.2\%$, $p = 0.048$; percentage reduction to attain target serum LDL-C levels for patients without statin therapy at baseline, CAD vs. non-CAD, $46.7 \pm 11.2\%$ vs. $34.1 \pm 16.1\%$, $p < 0.001$, see Table 1).

The prescription rates of statin therapy in high-risk patients increased and reached 100% after enrollment throughout 9-month follow-up (Figure 2). In addition, the use of HIS and ezetimibe in high-risk patients increased with time. The prescription rates of HIS in patients with CAD at baseline, 3-month, 6-month, and 9-month follow-ups were respectively 25.0%, 78.6%, 78.6%, and 87.5%, while those in patients without CAD were respectively 6.1%, 70.8%, 66.7%, and 78.3% (Figure 2). The prescription rates of ezetimibe in patients with CAD at baseline, 3-month, 6-month, and 9-month follow-ups were respectively 8.0%, 51.0%, 69.0%, and 82.1%, while those in patients without CAD were respectively 9.6%, 26.5%, 33.3%, and 43.5% (Figure 2).

Overall, the LDL-C goal attainment rates in these high-risk patients tended to reach a plateau after the first 3 months (Figure 3). The goal attainment rates of serum LDL-C in patients with CAD at 3-month, 6-month, and 9-month follow-ups were respectively 58.8%, 62.0%, and 62.5%, while those in patients without CAD were respectively 79.6%, 75.6%, and 73.9% (Figure 3). The use of HIS and ezetimibe in high-risk patients who did not attain their serum LDL-C goals increased with time. Of patients without LDL-C goal attainment, the prescription rates of HIS at 3-month, 6-month, and 9-month follow-ups were respectively 74.3%, 72.5%, and 75.8%, and the prescription rates of ezetimibe at 3-month, 6-month, and 9-month follow-ups were respectively 49.2%, 64.7%, and 72.7% (Figure 4).

4. Discussion

The main findings of our present study showed that a checklist-assisted reminding approach implemented in electronic medical order system was associated with an increased prescription of HIS and ezetimibe in high-risk patients, which subsequently led to an improvement of LDL-C goal attainment rates compared with those reported in previous studies.[10–16] Additionally, the LDL-C goal attainment rates in high-risk patients tended to reach a plateau irrespective of an increased use of HIS and ezetimibe after the first 3 months. To the best of our knowledge, this is the first study to demonstrate not only the status of prescription rates of HIS and ezetimibe, but also the LDL-C goal attainment rates among high-risk patients in Taiwan.

The use of HIS and the LDL-C goal attainment rates in high-risk patients are globally suboptimal. According to a recent analysis of a large-scale database in United States in 2017, only 15.3% and 25.2%

Table 1
Baseline characteristics of high-risk patients in Lipid Clinic.

	Total (N = 214)	CAD (-) (N = 114)	CAD (+) (N = 100)	*p**
Age	58.9 (11.1)	57.2 (12.4)	60.9 (9.2)	0.013
Male	151 (70.6)	64 (56.1)	87 (87.0)	< 0.001
BMI (Kg/m^2)	27.0 (4.8)	27.9 (5.4)	26.1 (4.0)	0.006
Medical history				
Current smoker	42 (19.6)	23 (20.2)	19 (19.0)	0.829
Hypertension	131 (61.2)	63 (55.3)	68 (68.0)	0.056
Diabetes	128 (59.8)	87 (76.3)	41 (41.0)	< 0.001
PAD	15 (7.0)	6 (5.3)	9 (9.0)	0.171
Ischemic stroke	7 (3.3)	3 (2.6)	4 (4.0)	0.708
Dialysis	3 (1.4)	1 (0.9)	2 (2.0)	0.600
Heart failure	27 (12.6)	11 (9.6)	16 (16.0)	0.163
FH	10 (4.7)	9 (7.9)	1 (1.0)	0.021
Prescribed medications				
Antiplatelets	109 (50.9)	16 (14.0)	93 (93.0)	< 0.001
Aspirin	87 (40.7)	15 (13.2)	72 (72.0)	< 0.001
$P2Y_{12}$ inhibitor	58 (27.1)	1 (0.9)	57 (57.0)	< 0.001
Beta-blocker	117 (54.7)	42 (36.8)	75 (75.0)	< 0.001
Calcium channel blocker	51 (23.8)	33 (28.9)	18 (18.0)	0.061
ACEI/ARB	126 (58.9)	60 (52.6)	66 (66.0)	0.047
Insulin	23 (10.7)	14 (12.3)	9 (9.0)	0.440
Any statin	115 (53.7)	43 (37.7)	72 (72.0)	< 0.001
HIS	32 (15)	7 (6.1)	25 (25.0)	< 0.001
Ezetimibe	19 (8.9)	11 (9.6)	8 (8.0)	0.672
Fibrate	16 (7.5)	12 (10.5)	4 (4.0)	0.070
Laboratory and physiological data				
LVEF (%)	62.0 (9.7)	63.5 (11.4)	60.8 (8.2)	0.091
Hb (g/dL)	13.9 (1.8)	13.7 (1.9)	14.1 (1.6)	0.065
Fasting glucose (mg/dL)	122.6 (35.4)	125.5 (36.1)	119.3 (34.4)	0.200
HbA1c (%)	6.8 (1.4)	7.1 (1.4)	6.6 (1.4)	0.013
Cr (mg/dL)	1.1 (1.0)	1.1 (1.0)	1.2 (1.1)	0.263
eGFR (ml/min)	75.6 (24.8)	79.2 (27.0)	71.6 (21.3)	0.023
AST (U/L)	25.9 (12.3)	26.3 (12.5)	25.6 (12.1)	0.673
Lipid profiles				
TC (mg/dL)	212.8 (74.2)	234.8 (88.2)	187.8 (42.1)	< 0.001
TG (mg/dL)	200.0 (495.1)	235.9 (674.0)	159 (74.4)	0.229
HDL-C (mg/dL)	44.6 (14.1)	46.6 (16.8)	42.4 (9.6)	0.025
LDL-C (mg/dL)	137.0 (48.5)	155.3 (50.8)	116.2 (35.9)	< 0.001
LDL-C in statin nonusers	156.3 (48.4)	163.7 (51.9)	137.6 (32.0)	0.003
LDL-C in statin users	120.4 (42.1)	141.4 (46.3)	107.8 (34.0)	< 0.001
% LDL-C need to reduce				
Statin users	28.2 (16.2)	24.4 (16.2)	30.6 (15.9)	0.048
Statin nonusers	37.7 (15.9)	34.1 (16.1)	46.7 (11.2)	< 0.001

ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AST = aspartate aminotransferase; BMI = body mass index; CAD = coronary artery disease; Cr = creatinine; eGFR = estimated glomerular filtration rate; FH = familial hypercholesterolemia; Hb = hemoglobin; HDL-C = high-density lipoprotein cholesterol; HIS = high-intensity statin; LDL-C = low-density lipoprotein cholesterol; LVEF = left ventricular ejection fraction; SD = standard deviation; TC = total cholesterol; TG = triglyceride.

* Patients with CAD vs. patients without CAD.

Data are number (%) in male, medical history, and prescribed medications, and in mean (SD) for the others.

of patients with ASCVD received a HIS and achieved serum LDL-C levels < 70 mg/dL, respectively.[13] The EUROASPIRE IV study also showed that only 32.7% of patients with CAD were prescribed a HIS and 19.3% of these patients achieved serum LDL-C levels < 70 mg/dL at 6-month follow-up.[14] In the present study, the use of HIS and the LDL-C goal attainment rates in high-risk patients were higher than that reported in the above-mentioned studies.[13,14] Our results were also superior to those obtained from CEPHEUS Pan-Asian survey[15] and T-SPARCLE registry study.[16] Notably, the baseline prescription rates of any statins among patients with CAD in the present study were similar to those in the Biosignature CAD cohort study in Taiwan.[17] Moreover, we further provided valuable data showing the prescription rates of HIS in all high-risk patients during follow-ups, which have not been mentioned in the Biosignature CAD cohort study. The improvement of LDL-C goal attainment rates observed in our present study can be explained by an aggressive prescription of HIS. Furthermore, the increased patients' awareness of their LDL-C goals and an effective assistance in prescribing LLT by electronic checklist in medical order system may also facilitate the improvement of attainment rates in high-risk patients.

The maximum efficacy of statin therapy to reduce serum LDL-C levels will occur by 4 weeks to 3 months,[8,9] implicating that the reduction of serum LDL-C levels and whether patients can achieve their LDL-C goals should be closely evaluated and monitored within 3 months after initiation or adjustment of statin therapy. In our present study, we observed that the LDL-C goal attainment rates in high-risk patients tended to reach a plateau after the first 3 months irrespective of an increased use of HIS. Additionally, we also observed that the aggressiveness in prescribing HIS among patients without LDL-C goal attainment increased with time during follow-

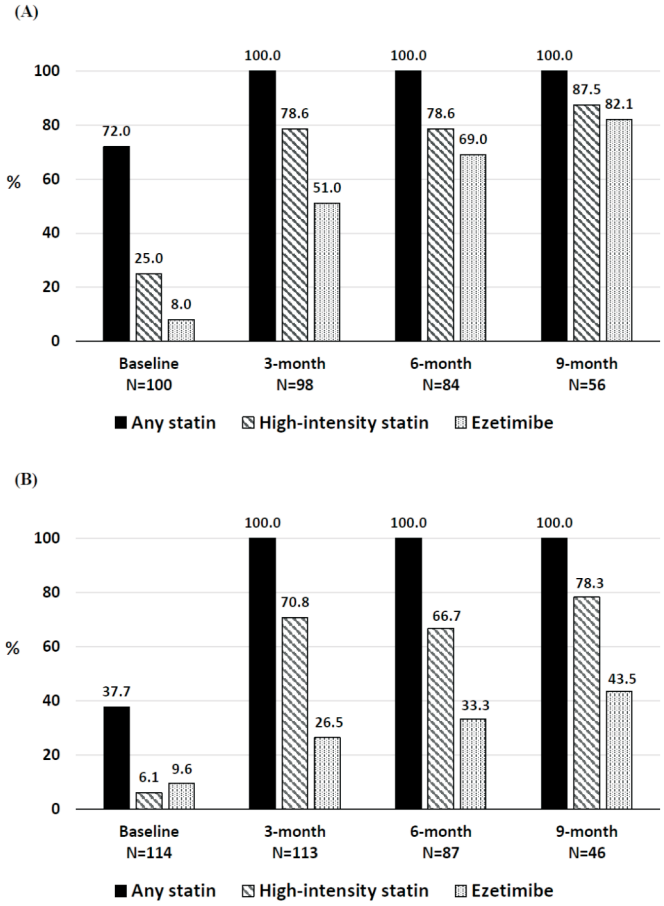

Figure 2. (A) Drug prescription among patients with CAD; (B) Drug prescription among patients without CAD.

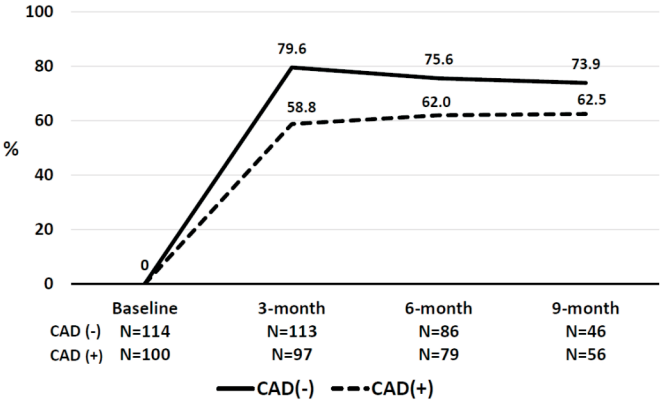

Figure 3. The goal attainment rate of LDL-C in patients with CAD and patients without CAD at every 3-month follow-up.

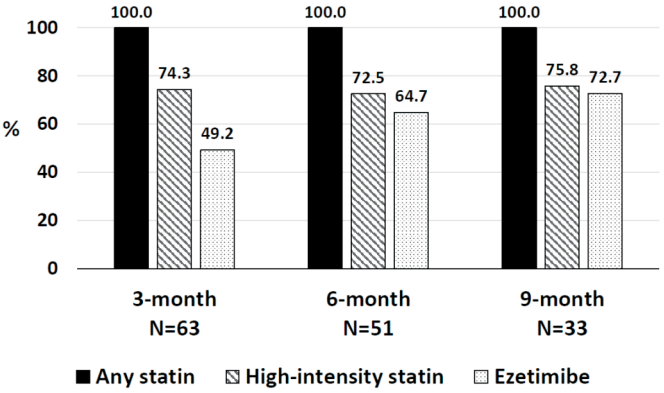

Figure 4. The prescription rates of high-intensity statin and ezetimibe among patients who did not reach their target serum LDL-C goals.

ups. These above-mentioned results in our present study were similar to those of the Return on Expenditure Achieved for Lipid Therapy in Asia (REALITY-Asia) study.[20] Our findings indicated that an increased frequency of blood lipid tests and an early prescription of HIS within 3 months in high-risk patients could not only improve LDL-C goal attainment rates, but also assist physicians to early identify whether a further nonstatin treatment such as ezetimibe or PCSK9 inhibitor was needed. This above-mentioned strategy is especially important for patients with ACS because data from randomized clinical trials and meta-analyses have shown that routine early use of HIS is associated with a rapid stabilization of coronary plaques and a reduced risk of short-term adverse cardiovascular events.[9,21]

The use of ezetimibe in combination with statin therapy plays a synergistic role in high-risk patients based on the evidence of IMPROVE-IT study.[22] The latest American[8] and European[9] lipid guidelines, as well as the current Taiwan lipid guidelines,[18] recommend that ezetimibe should be used as a combination therapy with statins when the LDL-C therapeutic goal is not achieved at the maximal tolerated statin dose. Additionally, previous studies showed that addition of ezetimibe to statin therapy will lower LDL-C to < 70 mg/dL in the majority of high-risk patients.[13,23] Despite these above-mentioned guidelines' recommendations, the use of ezetimibe in high-risk patients in clinical practice was still suboptimal.[24–26] In Taiwan, there was few data reporting the use of ezetimibe in high-risk patients. The T-SPARCLE study showed that less than 5% of patients with ASCVD received ezetimibe,[26] while the CEPHEUS Pan-Asian survey[15] and Biosignature CAD cohort study did not mention about the prescription rates of ezetimibe.[17] Compared with previous studies,[15,17,26] the present study showed a more aggressive prescription of ezetimibe and a better LDL-C goal attainment rate in high-risk patients. The results of our present study provided a valuable evidence to support the role of ezetimibe in facilitating LDL-C goal attainment in high-risk patients, as recommended by current guidelines.[8,9,18]

A recent study analyzing treatment patterns in more than 14,000 patients with ASCVD[27] showed that 87.9% and 90% of patients who failed to reach their serum LDL-C goals did not receive HIS and ezetimibe at 1-year follow-up, respectively. Despite a more aggressive prescription of HIS and ezetimibe in the present study compared to that of above-mentioned study, we still observed that 24.2% and 27.3% of high-risk patients who failed to reach their serum LDL-C goals did not receive HIS and ezetimibe at 9-month follow-up, respectively. Some factors may lead to underutilization of HIS and ezetimibe. Drug-related adverse effects and patients' intolerance are potential reasons. In addition, insufficient physician-patient discussion may result in a disagreement with statin intensity up-titration and receiving combination therapy with ezetimibe.[27] These above-mentioned factors may also contribute to a suboptimal medical adherence of patients and missing data for analysis at follow-ups, as noted in the present study. Taken together, routine assessment of treatment adherence and efficacy through laboratory examination of serum LDL-C levels[7,27] and an increased awareness by sufficient physician-patient discussion are suggested to improve underutilization of HIS and ezetimibe. Meanwhile, the early use of PCSK9 inhibitors in patients who are intolerant to HIS and ezetimibe is also suggested to further improve the LDL-C goal attainment rates.

In the present study, patients with CAD had a lower LDL-C goal attainment rate despite they had a lower baseline LDL-C level and more frequently received HIS during follow-ups compared with pa-

tients without CAD. An obvious reason to explain our findings was that patients with CAD had a stricter serum LDL-C target and a wider gap to reach goals compared with patients without CAD. In addition, the individual's suboptimal responsiveness to statins should be also considered.[28] This above-mentioned issue has becomes increasingly relevant because a suboptimal responsiveness to statins posed an increased risk of atherosclerosis and future ASCVD, especially in patients with CAD.[29] Detailed evaluation of patients' extrinsic factors (e.g., background diet, time of administration of statins, and concomitant drugs) and intrinsic factors (e.g., genetic polymorphism, and interaction between absorptive and synthetic cholesterol pathways)[28] that may influence statin responsiveness is helpful to identify statin hyporesponders and further facilitate the improvement of LDL-C goal attainment.

Our study was subjected to some limitations. First, this was a single-center study with a small size of population. We did not evaluate and compare the differences between patients treated in the Lipid Clinic and patients treated in non-lipid clinics, which would introduce bias in the present study. Additionally, we did not observe and compare cardiovascular outcomes between patients with goal attainment and those patients without attainment. Further nationwide large-scale survey is necessary to clarify this above-mentioned issue. Second, the LDL-C goal attainment rates presented in our study might be overestimated because we did not count the missing data from patients who were lost to follow-ups. Third, we excluded patients who were contraindicated or intolerant to stains in this present analysis, therefore we could not evaluate the goal attainment rates of LDL-C in the above-mentioned patients. Fourth, there were few PCSK9 inhibitor users because the cost of PCSK9 inhibitors was not yet covered by National Health Insurance in Taiwan during the study period. Therefore, the role of PCSK9 inhibitors could not be evaluated. Finally, it is worthwhile to develop an AI-based system which can actively detect suboptimal results of blood lipid tests and aware both physicians and high-risk patients. Despite these limitations, our data present the current status of LDL-C control in Taiwan and demonstrate the importance of an aggressive strategy in prescribing HIS ± ezetimibe therapy to improve the LDL-C goal attainment rates.

5. Conclusion

The present study revealed that patients with CAD had a lower LDL-C goal attainment rate than patients without CAD. Additionally, our results highlight that increased prescription of HIS and ezetimibe in the Lipid Clinic and the effective checklist-assisted reminding approach in electronic medical order system can facilitate the improvement of LDL-C goal attainment rates in high-risk patients.

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Competing interests

All authors have no conflicts of interest to be disclosed.

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