ORIGINAL ARTICLE

Impact of Achieving LDL-C Level Target and Major Adverse Cardiovascular Events in Patients Undergoing Percutaneous Coronary Intervention

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Background: Serum low-density lipoprotein cholesterol (LDL-C) levels are associated with cardiovascular diseases. Elevated LDL-C levels increase the risk of cardiovascular diseases and are associated with high mortality rates. Patients with established cardiovascular diseases, particularly those undergoing percutaneous coronary intervention (PCI), are at high risk.

Objective: The present study aimed to assess the impact of achieving the target LDL-C level (LDL-C <70 mg/dL) on the incidence of major adverse cardiovascular events (MACE).

Materials and Methods: This retrospective cohort study was conducted using medical records of patients who underwent PCI at Vajira Hospital, Bangkok, Thailand. Data were collected between January 1, 2016, and December 31, 2020. Following PCI, patients were classified into two groups: those who achieved the LDL-C target (serum LDL-C level below 70 mg/dL at 3 months after PCI) and those who did not (serum LDL-C level equal to or more than 70 mg/dL at 3 months after PCI). Follow-up was performed for 1 year or until the first occurrence of composite cardiovascular outcomes (nonfatal myocardial infarction, nonfatal stroke, congestive heart failure, and cardiovascular death).

Results: Among the 205 patients who underwent PCI within the specified period, 63% were male, with a mean age of 64 years and a baseline LDL-C level of 114.92±46.46 mg/dL. Only 39.5% of patients achieved the target LDL-C level. After 1-year follow-up, MACE occurred in 18 patients who did not achieve the target LDL-C level (14.5%) and in one patient who achieved the target LDL-C level (1.2%). The multivariable Cox proportional hazard model showed that achieving the target LDL-C level significantly lowered the MACE rate (HR=0.08, 95% CI 0.011 to 0.599, p=0.01).

Conclusion: Within 1 year of follow-up after PCI, achieving an LDL-C level of less than 70 mg/dL 3 months after stent implantation considerably reduced the occurrence of severe cardiovascular events.

Keywords: Low-density lipoprotein cholesterol (LDL-C); Major adverse cardiac event; Myocardial infarction; Percutaneous coronary intervention (PCI)

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Cardiovascular diseases (CVDs) are a leading cause of mortality worldwide[1], including in Thailand. According to statistics from the Ministry of Public Health in 2019, cerebrovascular disease ranked second and coronary heart disease ranked fourth among noncommunicable disease-related deaths in Thailand[2]. The incidence of CVDs continues to rise annually, posing a considerable public health challenge globally and in Thailand.

Low-density lipoprotein cholesterol (LDL-C) is a key risk factor for atherosclerosis and the underlying cause of most cardiovascular events[3]. The mechanism involves oxidative stress-induced damage to the endothelial lining of blood vessels, causing endothelial dysfunction and LDL-C infiltration into the vessel wall. This process generates lipid-laden foam cells and fatty streaks in the vessel wall, initiating a cascade of events that culminate in the formation of a fibrous cap. The rupture of this fibrous cap leads to thrombosis and subsequent cardiovascular events[4], such as myocardial infarction and ischemic stroke, potentially resulting in death or disability.

In Thailand, the use of percutaneous coronary intervention (PCI) to treat patients with coronary artery disease continues to increase steadily, with an estimated annual increase of over 10,000 cases. However, approximately 4.69% of Thai patients experience recurrent stenosis after PCI[5]. Furthermore, a correlation has been

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observed between recurrent coronary events and LDL-C levels[6]. Current treatment guidelines from the European Society of Cardiology[7] and the 2016 The Royal College of Physicians of Thailand Clinical Practice Guideline on Pharmacologic Therapy of Dyslipidemia for Atherosclerotic Cardiovascular Disease Prevention[8] recommend targeting LDL-C levels below 70 mg/dL to reduce the incidence of cardiovascular events. However, studies on achieving target LDL-C levels in Thailand are still lacking.

The present study was designed to compare the incidence of major adverse cardiovascular events (MACE) between post-PCI patients who achieved target LDL-C levels and those who did not achieve target LDL-C levels in real-life practice.

Materials and Methods

Study design

This retrospective cohort study included patients with coronary artery disease treated with PCI and stent placement at Vajira Hospital, Bangkok, Thailand, from January 1, 2016, to December 31, 2020. Baseline demographics, clinical data, medical history, medications, and laboratory results (including LDL-C levels) were obtained from electronic medical records. Exclusion criteria were patients under 18 years of age, those without follow-up data, those who died before post-PCI LDL-C testing, those who underwent CABG within 1 year after PCI, those with history of post-CABG, those with PCI-related complications, those who underwent staged PCI, and those with advanced chronic liver disease, end-stage kidney disease, advanced cancers, or pregnancy. According to the 2019 European Society of Cardiology lipid management guidelines, the target LDL-C level was defined as <70 mg/dL, typically measured 3 months after PCI or from the closest available blood test within 3 months. A detailed study flow is provided in Figure 1.

Data and statistical analyses

Clinical outcomes were compared between patients who achieved the target LDL-C level (LDL-C <70 mg/dL) and those who did not achieve the target LDL-C level (LDL-C >70 mg/dL) 3 months after PCI. The primary outcome was MACE, which was defined as a composite endpoint of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, and congestive heart failure. The secondary outcome included the data on LDL-C level management in patients post PCI.

Categorical variables such as gender, comorbidities, medications used, types of lipid-lowering drugs, types of antiplatelet drugs, and types of stents were compared using Chi-square or Fisher's exact tests, depending on data suitability. The results were presented as frequency distributions and percentages. Continuous variables such as age, weight, height, blood pressure, and laboratory test results were analyzed using independent Student's t-test. Data were presented as mean ± standard deviation. For the comparison of the incidence rates of MACE between the two groups, frequency distributions and percentages

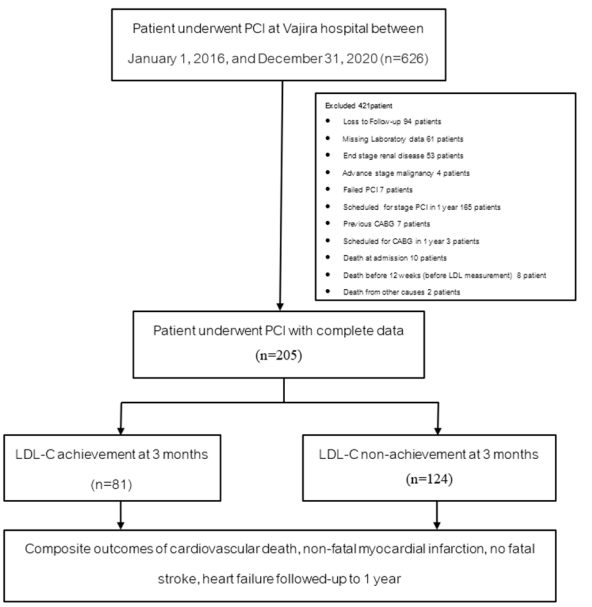

Figure 1. Study flow.

(incidence rates) were reported with a 95% confidence interval. Differences between groups were assessed using the Cox proportional hazards model. Survival analysis was performed using Kaplan–Meier curves, and the log-rank test was applied to compare survival rates between the two groups. Multivariate analysis using Cox proportional hazards was conducted to analyze the relationship between LDL-C levels and MACE incidence. The results were reported as hazard ratios with a 95% confidence interval, and statistical significance was set at α=0.05. All data analyses were performed using the STATA/BE software version 17.0 (Stata Corp, College Station, TX, USA).

Ethical approval

This study was conducted in accordance with the international guidelines for human research protection as Declaration of Helsinki, The Belmont Report, CIOMS Guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP). The study protocol was reviewed and approved by the Institutional Review Board of the Faculty of Medicine Vajira Hospital (COA 019/2565).

Results

Study population

A total of 205 patients diagnosed with coronary artery disease and treated with coronary artery stenting at the Faculty of Medicine, Vajira Hospital, were included in the present study. Among them, 129 were male (63%) with an average age of 63.9±11.29 years and an average weight of 67.53±14.15 kilograms. Additionally, 104 patients (51%) were statin naïve, and 32 (15.6%) were current smokers. Regarding PCI, 127 patients (62%) underwent PCI due to acute coronary syndrome (ACS) in the admission and 78 (38%) had elective PCI. The baseline LDL-C level upon admission was 114.92±46.46 mg/dL. Comorbidities included diabetes mellitus in 105 patients (51.2%), hypertension in 161 patients (78.5%), stage III or higher chronic kidney disease in 37 patients (18%). Regarding home medications after PCI, 201 patients (98%) received aspirin, 39 patients (19%) received clopidogrel, 147 patients (71.1%) received ticagrelor, and 19 patients (9.3%) received prasugrel. High-intensity statin therapy was prescribed to 186 patients (90.7%), intermediate intensity to 14 patients (6.8%), and low intensity to three patients (1.5%). Finally, 81 patients (39.5%) achieved the target LDL-C level, while 124 patients (60.48%) did not, as shown in Table 1.

Clinical outcomes

At 1-year follow-up, 19 patients experienced MACE, including 18 in the nonachieving group (14.5%) and 1 in the achieving group (1.2%) (HR=0.08, 95% CI 0.011 to 0.599, p=0.01). Specifically, nonfatal myocardial infarction occurred in nine patients in the non-achieving group and one patient in the achieving group. Heart failure and ischemic stroke occurred in five and three patients in the nonachieving group, respectively. One case of mortality was recorded in the nonachieving group, as shown in Table 2.

The multivariable Cox proportional hazards model showed that achieving the target LDL-C level significantly lowered the MACE rate by 13.28% (absolute risk reduction=13.27%, number needed to treat=8) (HR=0.08, 95% CI 0.011 to 0.599, p=0.014). The survival analysis graph is shown in Figure 2.

Discussion

The present study is the first to evaluate the impact of early LDL target achievement at 12 weeks in post-PCI patients, categorized as very high-risk, on mortality and MACE outcomes in Thailand. Our findings demonstrate that achieving the LDL target within 12 weeks post-PCI significantly reduced the composite endpoint of cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, and heart failure. These results are consistent with previous studies[9-11], such as the research by Sudd M, which showed that achieving the LDL target at 6 months post-PCI significantly reduced adverse cardiovascular events[12]. Similarly, Phattararuethai S et al. reported that early achievement of an LDL-C level <70 mg/dL within 3 months of acute coronary syndrome onset significantly reduced cardiovascular events[13]. These findings support the notion that early achievement of the LDL target in very high-risk cardiovascular patients is beneficial for reducing MACE.

However, managing LDL levels in cardiovascular disease patients remains a global challenge. A real-world study by Nishant P, et al. found that over 60% of patients with atherosclerotic cardiovascular disease had uncontrolled LDL levels (>70 mg/dL)[14], which aligns with our findings. In our study, more than 60% of post-PCI patients did not reach the LDL target. Other studies in Thailand have shown that most cardiovascular patients also fail to achieve the target[13,15,16]. Therefore, achieving LDL targets remains a key challenge in reducing future MACE.

According to the PLATO trial[17], Ticagrelor significantly reduces MACE in Acute Coronary Syndrome patients compared to clopidogrel. In our study, while the non-LDL Achieve group received more clopidogrel than the LDL Achieve group, this difference was statistically significant. However, subgroup analysis showed no significant differences between patients who received clopidogrel and those who did not. Since our study included both Acute Coronary Syndrome and Chronic Coronary Syndrome patients who underwent PCI, this may explain the differing results compared to previous studies.

Table 1. Baseline patient characteristics

	All patient, (n=205)	LDL achieved, (n=81)	LDL non-achieved, (n=124)	p-value
Age (yrs)	63.9±11.29	64.63±10.53	63.42±11.78	0.45
Female gender	76 (37.1%)	31 (38.3%)	45 (36.3%)	0.77
Body weight (Kg)	67.53±14.15	66.19±12.72	68.4±14.99	0.27
Current smoke	32 (15.6%)	7 (21.9%)	25 (20.2%)	0.02
Statin naïve	104 (51%)	39 (48.1%)	65 (52.8%)	0.51
Type of PCI				0.21
Elective	78 (38%)	35 (43.2%)	43 (34.7%)	
ACS	127 (62%)	46 (56.8%)	81 (65.3%)	
Comorbidities				
Diabetes mellitus	105 (51.2%)	45 (55.6%)	60 (48.4%)	0.31
Hypertension	161 (78.5%)	60 (74.1%)	101 (81.5%)	0.20
Dyslipidemia	116 (56.6%)	47 (58%)	69 (55.6%)	0.73
CKD III or higher	37 (18%)	14 (17.3%)	23 (18.5%)	0.81
CHF	14 (6.8%)	6 (7.4%)	8 (6.5%)	0.79
Laboratory				
Creatinine (mg/dl)	1.09±0.73	1.1±0.4	1.09±0.88	0.92
eGFR	73.77±24.58	70.64±24.93	75.81±24.23	0.141
HbA1C (%)	9.41±20.38	10.4±23.85	8.77±17.9	0.58
Total cholesterol (mg/dL)	190.68±88.94	197.74±127.37	186.24±52.21	0.40
HDL (mg/dl)	47.14±13.22	46.92±12.99	46.92±12.99	0.78
Triglyceride (mg/dl)	135.14±92.66	117.66±73.97	146.75±101.89	0.03
LDL (mg/dl)	114.92±46.46	107.79±46.87	119.59±45.78	0.07
Medication at discharge				
Antiplatelet				
Aspirin	201 (98%)	78 (96.3%)	123 (99.2%)	0.14
Clopidogrel	39 (19%)	10 (12.3%)	29 (23.4%)	0.04
Ticagrelor	147 (71.1%)	62 (76.5%)	85 (68.5%)	0.21
Prasugrel	19 (9.3%)	9 (11.1%)	10 (8.1%)	0.46
Anticoagulant	25 (12.1%)	12 (14.8%)	13 (10.4%)	0.51
Ezetimibe	40 (19.5%)	21 (25.9%)	19 (15.3%)	0.06
Beta blocker	170 (82.9%)	65 (80.2%)	105 (84.7%)	0.41
ACEI/ARB	141 (68.8%)	54 (66.7%)	87 (70.2%)	0.59
Hydralazine	10 (4.9%)	5 (6.2%)	5 (4%)	0.48
Nitrate	51 (24.9%)	25 (30.9%)	26 (21%)	0.10
Furosemide	46 (22.4%)	23 (28.4%)	23 (18.5%)	0.09
MRA	38 (18.5%)	20 (24.7%)	18 (14.5%)	0.06
SGLT2 inhibitor	11 (5.4%)	6 (7.4%)	5 (4%)	0.29

Values are mean ± SD or n (%).

PCI=percutaneous coronary; CKD=chronic kidney disease; CHF=Congestive heart failure; HDL=High-density lipoprotein; LDL=Low-density lipoprotein; ACEI=Angiotensin-converting enzyme inhibitor; ARBs=Angiotensin II receptor blockers; MRA=Mineralocorticoid receptor antagonist; SGLT2=Sodium-glucose cotransporter-2; ACS=Acute coronary syndrome (STEMI, NSTEMI)

The strength of this study lies in its focus on a high-risk population of patients with coronary artery disease who underwent PCI. Additionally, clear target groups were defined, with exclusion criteria including patients with chronic kidney disease, chronic liver disease, and advanced-stage cancer. However, the present study has some limitations. The first is the small sample size. Initially, the authors included 626 participants, but after applying the exclusion criteria, only 205 remained. Despite this, statistical analysis revealed significant differences between the two groups, so no additional data were collected. Nevertheless, further data collection may uncover additional results. Second, the present study was conducted at a single site in Thailand; including multiple sites could provide more diversity. Third, as a retrospective cohort study, it may have residual confounding bias.

Table 2. Multivariate cox proportional hazard analysis shown the effect of achieved LDL and MACE in post PCI patient

	LDL achieved, (n=81)	LDL non-achieved, (n=124)	HR (95% CI)	p-value
MACE	1 (1.23%)	18 (14.5%)	0.08 (0.011 to 0.599)	0.01
Myocardial infarction (non-fatal)	1 (1.23%)	9 (7.2%)		
Cerebrovascular events (non-fatal)	0	3 (2.4%)		
Congestive heart failure	0	5 (4.0%)		
Cardiovascular death	0	1 (0.8%)		

Values are n (%).

MACE=Major adverse cardiovascular events

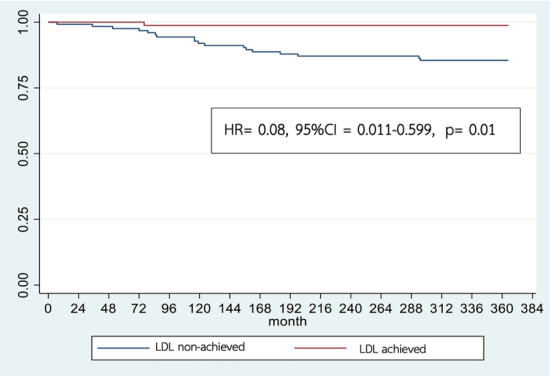

Figure 2. Comparison of cumulative survival between LDL achieved and non-achieved.

Conclusion

Post-PCI patients are at a very high risk for cardiovascular events. Achieving an LDL-C level of less than 70 mg/dL within 3 months after stent implantation is crucial during the first year of follow-up, as it significantly reduces the occurrence of severe cardiovascular events.

What is already known on this topic?

LDL-C levels are a critical factor in the development of cardiovascular disease. According to the Thai guidelines for dyslipidemia 2016, it is recommended to set a target LDL-C level of <70 mg/dL for patients with a history of cardiovascular disease to effectively reduce the risk of recurrent cardiovascular events.

What this study adds?

Early achieving the target level of LDL-C within 3 months is highly beneficial in reducing the incidence of MACE within 1 year in Thai patients with coronary artery disease who have undergone PCI with stent.

Conflicts of interest

The authors declare no conflict of interest.

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