

Perioperative Myocardial Injury/Infarction in Patients with Stable or Unstable Angina Pectoris Undergoing Elective Percutaneous Coronary Intervention: The Effects of Preoperative Lipid Management

Xuefeng Chen¹, Wenlou Bai¹, Peng Qi¹, Yantao Zhang², Wenjing Yao¹, Yi Dang¹

¹Department of Cardiovascular Internal Medicine, Hebei General Hospital, Shijiazhuang, 050000, People's Republic of China; ²Department of Cardiovascular Internal Medicine, Handan Central Hospital, Handan, 056001, People's Republic of China

Correspondence: Yi Dang, Department of Cardiovascular Internal Medicine, Hebei General Hospital, 348 Shijiazhuang Heping West Road, Shijiazhuang, 050000, People's Republic of China, Tel +18603270563, Email 90030172@hebmh.edu.cn

Background: Identifying the risk factors for perioperative myocardial injury/infarction (PMI) is critical to prevent postoperative adverse cardiovascular events. However, whether reducing the preoperative LDL-C can mitigate the risk of PMI remains unclear. We therefore investigated the effect of the preoperative LDL-C level in patients with stable angina pectoris (SAP) or unstable angina pectoris (UAP) on perioperative myocardial injury/infarction (PMI) after elective percutaneous coronary intervention (PCI).

Methods: Patients with SAP or UAP who received PCI from January 2021 to June 2023 at one of the two institutions (Hebei Provincial People's Hospital, Handan Central Hospital) were reviewed. The occurrence of PMI was determined based on the elevation of cardiac troponin I (cTnI) after the operation. The preoperative low density lipoprotein cholesterol (LDL-C) level was divided into three grades: low, <1.4 mmol/L; medium, 1.4–1.8 mmol/L; high, >1.8 mmol/L. The relationship between PMI and preoperative LDL-C was analyzed.

Results: Of all 308 included patients, 226 did not have PMI and 82 experienced PMI. Positive correlation was found both between PMI and preoperative LDL-C level ($r = 0.322$, $P < 0.05$) and between PMI and preoperative LDL-C grade ($r = 0.189$, $P < 0.05$). According to the multivariate logistic regression analysis, the preoperative LDL-C grade (Medium vs Low, $OR=3.994$, $P < 0.05$; High vs Medium, $OR=6.140$, $P < 0.05$) and the number of stents implanted during PCI were independent risk factors for PMI ($OR=1.940$; $P < 0.05$).

Conclusion: For SAP and UAP patients, decreasing LDL-C to <1.4 mmol/L before elective PCI can reduce the incidence of PMI after the operation. We strongly recommend the practice of sufficiently reducing LDL-C level below 1.4 for patients with SAP or UAP who receive elective PCI.

Keywords: percutaneous coronary intervention, stable angina pectoris, unstable angina pectoris, low-density lipoprotein cholesterol, perioperative myocardial injury and infarction

Introduction

In China, percutaneous coronary intervention (PCI) has become one of the main treatment methods for coronary atherosclerotic heart disease. It is a minimally invasive procedure that improves blood flow effectively and allows a quick recovery, and the number of patients receiving the procedure is increasing each year. However, after PCI, patients can have elevated cardiac markers, especially high-sensitivity cardiac troponin. Perioperative myocardial injury is deemed to have occurred if postoperative cardiac troponin I (cTnI) exceeds $1 \times$ ULN, and PCI-related myocardial infarction is verified when the postoperative cTnI exceeds $5 \times$ ULN.^{1,2} Identifying the risk factors for perioperative

myocardial injury/infarction (PMI) is very important, as previous studies have shown that PMI is associated with postoperative adverse cardiovascular events.^{3–6}

Studies have shown that the preoperative elevation of low-density lipoprotein cholesterol (LDL-C) is associated with PMI in patients with coronary heart disease undergoing PCI, and reducing the preoperative LDL-C to below 1.8 mmol/L (70 mg/dL) significantly reduces the incidence of PMI.^{7,8} For patients at very high risk of atherosclerotic cardiovascular disease, the 2019 ESC/EAS guidelines recommend reducing LDL-C to 1.4 mmol/L (55 mg/dL) to reduce the risk of major cardiovascular events.⁹ Regarding PCI, it remains an open question whether reducing the preoperative LDL-C to below 1.4 mmol/L can mitigate the risk of PMI, thereby enhancing the prognosis of patients with stable angina pectoris (SAP) or unstable angina pectoris (UAP) who undergo elective PCI. To address this inquiry, we conducted a retrospective investigation on the impact of preoperative LDL-C levels on PMI in patients with SAP or UAP undergoing elective PCI. If a positive result is obtained, evidence for preoperative strategies aimed at intensive LDL-C lowering will be established, thereby addressing a gap in the existing literature and identifying an approach to improve the outcome of patients with SAP or UAP who receive elective PCI.

Methods

Patients and Diagnosis

This study follows the ethical principles of the Declaration of Helsinki and was approved by the Institution Review Board of Hebei General Hospital regarding research ethics (No. 2024-LW-134). Informed consent was obtained from the study participants prior to study commencement. Patients with SAP or UAP who underwent elective PCI from January 2021 to June 2023 at the Cardiovascular Department of Hebei Provincial People's Hospital or Handan Central Hospital were reviewed. The indications for PCI followed the recommendations from the American College of Cardiology and the American Heart Association. According to angiography results, the patient was diagnosed with coronary artery disease if there was substantial ($\geq 50\%$) stenosis in any coronary artery, including the left main artery, the left anterior descending artery, the left circumflex coronary artery, and the right coronary artery. The stenosis was divided into single vessel stenosis, double vessel stenosis, and triple vessel stenosis based on the number of coronary arteries involved. The severity of the target lesions was evaluated from the SYNTAX score.¹⁰

Patients were included if they (1) were 18–80 years old, (2) had normal levels of cTnI and creatine kinase MB (CK-MB) before PCI, and (3) had $< 20\%$ residual stenosis after stenting or $< 50\%$ residual stenosis after balloon dilation. Patients were excluded if (1) iatrogenic death occurred in 24 h after PCI, (2) there were coronary thrombosis, severe coronary artery calcification, or other complications such as coronary artery dissection and side branch loss, (3) they had abnormal liver or kidney functions, (4) history of previous stent implantation or (5) they experienced Class III–IV heart failure (New York Heart Association Classification) during perioperative period.

Biochemical Measurements

Fasting venous blood samples were obtained on the morning after admission to measure the lipid, liver, and renal profiles. The cTnI level was determined using an IMMULITE 1000 Immunoassay System (Siemens) both before PCI and 20–24 h after PCI. The LDL-C level was divided into three grades: low, < 1.4 mmol/L, medium, 1.4–1.8 mmol/L; high, > 1.8 mmol/L.⁹

Perioperative Interventions

Before the PCI, all patients received aspirin 100 mg daily. They also received either clopidogrel 75 mg daily or ticagrelor 90 mg twice a day. For lipid-lowering therapy, all patients were given statins and/or cholesterol absorption inhibitors. Some patients received proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors depending on their condition. All these drugs were started at least 4 days before PCI and maintained for a long time after the procedure.

Just before the PCI procedure, a bolus of unfractionated heparin (50–70 U/kg) was administered, and if the operation lasted for more than 1 h, an additional bolus (1000 U) was given. Glycoprotein IIb/IIIa receptor antagonists were used as needed intraoperatively. The procedure was performed by 2–3 experienced interventional physicians. Stent implantation

was performed in patients with >75% stenosis at the target lesions. Fractional flow reserve (FFR) or intravascular ultrasound (IVUS) were used to determine if stent implantation was required in critical lesions.

Statistical Analysis

The Shapiro–Wilk test was used to assess if the quantitative data had a normal distribution. Data were expressed as mean \pm standard deviation ($x \pm SD$) and compared using the independent samples *t*-test if they were normally distributed, and they were expressed as quartile and compared using the Mann–Whitney *U*-test if otherwise. Categorical data were expressed as [n (%)] and analyzed using the Chi-squared test or Fisher’s exact test. Kendall’s tau-b correlation was used to evaluate the correlation between cTnI and LDL-C. Factors whose difference satisfied $P < 0.15$ were considered as possible risk factors, and they were included, along with other clinically recognized common risk factors, as independent variables in the multivariate logistic regression analysis. Differences were considered statistically significant if $P < 0.05$.

Results

Clinical Characteristics

The 308 included patients were divided into two groups based on their postoperative cTnI level, ie, Group 1 (n = 82, 26.6%) with elevated cTnI after the surgery, which indicated the occurrence of PMI, and Group 0 (n = 226, 73.4%) without elevated cTnI after the surgery, which suggested the absence of PMI (Table 1). The two groups did not have any significant differences in age, sex, BMI, adverse medical history (hypertension, diabetes, and smoking), preoperative GFR, TG, and HDL-C ($P > 0.05$), but Group 1 had significantly higher preoperative LDL-C than Group 0 ($P = 0.001$). For Group 1, the incidence of PMI gradually increased with rising level of LDL-C ($P < 0.05$).

Angiographic Characteristics

No significant differences existed between the two groups in the surgical approach, number of stenosis vessels, proportion of completely occluded lesions, SYNTAX score, location of the target vessel, maximum stent release pressure, maximum stent release time, the number of stents implanted, and total stent length ($P > 0.05$) (Tables 2 and 3).

Table 1 Patient Information

| | Group 0 (n = 226) [†] | Group 1 (n = 82) [†] | P [¶] |
|-----------------------------------|--------------------------------|-------------------------------|----------------------------|
| <i>Basic information</i> | | | |
| Sex (M/F) | 176/50 (77.9%/22.1%) | 63/19 (76.8%/23.2%) | 0.846 ($\chi^2 = 0.038$) |
| Age (years) | 55.87 \pm 10.14 | 57.57 \pm 9.92 | 0.191 (t = 0.306) |
| BMI (kg/m ²) | 25.69 (24.02, 27.47) | 24.95 (23.83, 27.22) | 0.274 (Z = 8511.000) |
| <i>Conditions</i> | | | |
| Hypertension | 158 (69.9%) | 50 (61.0%) | 0.139 ($\chi^2 = 2.191$) |
| Diabetes | 45 (19.9%) | 17 (20.7%) | 0.874 ($\chi^2 = 0.025$) |
| Smoking | 116 (51.3%) | 37 (45.1%) | 0.336 ($\chi^2 = 0.927$) |
| <i>Biochemical indicators</i> | | | |
| GFR | 79.46 (67.17, 93.84) | 81.02 (66.21, 96.64) | 0.778 (Z = 9071.000) |
| TG | 1.72 (1.15, 2.34) | 1.73 (1.23, 2.24) | 0.972 (Z = 9241.500) |
| HDL-C | 1.14 \pm 0.23 | 1.20 \pm 0.29 | 0.092 (t = -1.699) |
| LDL-C | 2.37 \pm 0.71 | 2.94 \pm 0.72 | 0.001 (t = -5.477) |
| <i>Grade of LDL-C[§]</i> | | | |
| Low | 39 (17.3%) | 3 (3.7%) | 0.02 ($\chi^2 = 12.643$) |
| Medium | 58 (25.7%) | 18 (22.0%) | |
| High | 129 (57.1%) | 61 (74.4%) | |

Notes: [†]Group 0, perioperative myocardial injury/infarction (PMI) did not occur; Group 1, PMI occurred.

[¶]Marked in blue if $P < 0.15$ and in red if $P < 0.05$. [§]Low, <1.4 mmol/L; Medium, 1.4–1.8 mmol/L; High, >1.8 mmol/L.

Table 2 Summary of Angiographic Characteristics

| | Group 0 (n = 226) [†] | Group 1 (n = 82) [†] | P |
|-----------------------------|--------------------------------|-------------------------------|----------------------------|
| Transracial vascular access | 165 (73.0%) | 54 (65.9%) | 0.221 ($\chi^2 = 1.499$) |
| Number of diseased vessels | | | 0.642 ($\chi^2 = 0.886$) |
| Single lesion | 81 (35.8%) | 26 (31.7%) | |
| Double lesions | 85 (37.6%) | 30 (36.6%) | |
| Triple lesions | 60 (26.5%) | 26 (31.7%) | |
| Occlusion lesions | 28 (12.4%) | 8 (9.8%) | 0.525 ($\chi^2 = 0.404$) |
| SYNTAX score | 9.0 (6.00, 14.5) | 10.00 (7.00, 15.00) | 0.167 (U = 8312) |
| Target vessel | | | 0.154 ($\chi^2 = 0.525$) |
| RCA | 51 (22.6) | 14 (17.1%) | |
| LAD | 102 (45.1) | 35 (42.7%) | |
| LCX | 29 (12.8) | 19 (23.2%) | |
| 2 target vessels | 44 (19.5%) | 14 (17.1%) | |

Notes: [†]Group 0, perioperative myocardial injury/infarction (PMI) did not occur; Group 1, PMI occurred.

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

Table 3 Summary of Intervention Results

| | Group 0 (n = 226) [†] | Group 1 (n = 82) [†] | P [¶] |
|----------------------------|--------------------------------|-------------------------------|---------------------------|
| Stent | | | |
| Release pressure (atm) | 14.0 (12.0, 14.0) | 12.0 (12.0, 14.0) | 0.123 (U = 8281) |
| Release time (s) | 10.0 (10.0, 10.0) | 10.0 (10.0, 10.0) | 0.97 (U = 9251) |
| Total length (mm) | 18.00 (14.00, 28.00) | 22.50 (18.00, 33.75) | 0.074 (U = 8047) |
| Number of stents implanted | | | 0.19 ($\chi^2 = 4.769$) |
| 1 | 167 (73.9%) | 55 (67.1%) | |
| 2 | 50 (22.1%) | 19 (23.2%) | |
| 3 | 8 (3.5%) | 7 (7.3%) | |
| 4 | 1 (0.4%) | 2 (2.4%) | |

Notes: [†]Group 0, perioperative myocardial injury/infarction (PMI) did not occur; Group 1, PMI occurred.

[¶]Marked in blue if $P < 0.15$.

Correlation Between the Incidence of PMI and LDL-C Level

According to Kendall's tau-b correlation analysis (Table 4), the increase of postoperative cTnI, which was indicative of PMI, was positively correlated with the preoperative LDL-C concentration and LCL-C grade ($P < 0.001$).

Logistic Regression Analysis of Risk Factors for PMI

In the multivariate logistic regression analysis, the occurrence of PMI was taken as the dependent variable, and the following independent variables (marked in blue in the preceding tables if $P < 0.15$, marked in red if $P < 0.05$) were evaluated: history of hypertension, HDL-C and LDL-C concentrations, LDL-C grading, stent release pressure, total stent

Table 4 Correlation Between Preoperative LDL-C and Postoperative cTnI

| Variable | Kendall's tau [†] | P |
|--------------------------|----------------------------|-------|
| LDL-C (mmol/L) | 0.322 | 0.001 |
| LDL-C grade [§] | 0.189 | 0.001 |

Notes: [†]Correlation with postoperative cTnI as an indicator of the occurrence of perioperative myocardial injury/infarction. [§]Low, <1.4 mmol/L; medium, 1.4–1.8 mmol/L; high, >1.8 mmol/L.

Table 5 Logistic Regression Analysis of Risk Factors

| | Standard Coefficient | Standard Error | WALS | P | OR (95% CI) |
|--------------------------|----------------------|----------------|--------|-------|----------------------|
| LDL-C grade [§] | | | | | |
| Low | / | / | 9.428 | 0.009 | / |
| Medium | 1.385 | 0.663 | 4.363 | 0.037 | 3.994 (1.089–14.647) |
| High | 1.815 | 0.624 | 8.448 | 0.004 | 6.140 (1.806–20.877) |
| Number of stents | 0.663 | 0.200 | 10.982 | 0.001 | 1.940 (1.311–2.871) |

Notes: [§]Low, <1.4 mmol/L; medium, 1.4–1.8 mmol/L; high, >1.8 mmol/L.

Abbreviations: WALS, weighted-average least squares; OR, odds ratio; CI, confidence interval.

length. Age, SYNTAX score, and number of stents implanted, which are clinically recognized common risk factors, were also included in the analysis. Of these assessed variables, LDL-C grade and the number of stents implanted were independent risk factors for PMI ($P < 0.05$, Table 5).

Discussion

The exact mechanisms of PMI are only partly understood, but the risk factors can be broadly divided into patient-related factors, vessel-related factors, and procedure-related factors.¹¹ These factors involve age, sex, comorbidities, coronary artery lesion characteristics, acute branch occlusion during the surgery, target vessel spasm and dissection, slow flow or no reflow after coronary artery surgery, etc.^{12,13} Selvanayagam et al found through myocardial magnetic resonance imaging that PMI most often occurs in the adjacent part of the target vessel and its distal blood supply area, and proposed that the occlusion of minor branches and the distal thromboembolism are the main mechanisms of PMI.¹⁴ In PCI, balloon dilation can lead to plaque rupture near the target lesion, which can stimulate macrophages, activate platelets to release tissue factors and vasoconstrictor factors, initiate the coagulation cascade to produce thrombin and induce platelet aggregation, to ultimately form microthrombus. The microthrombus and the shed debris can further block the distal microcirculation and cause PMI.¹⁵ Most of the above conditions are closely related to vulnerable plaques, which are mainly characterized by thin fiber caps and large lipid cores. They are more prone to displacement, rupture, and the shedding of fragments, and are thus more likely to induce platelet aggregation and microvascular thrombosis during or after PCI. Higher LDL-C concentration has been associated with rising plaque vulnerability, and reducing LDL-C can decrease the amount of vulnerable plaques.^{16,17} In view of the above, reducing the preoperative LDL-C level may stabilize plaques and reduce the risk of PMI.¹⁸

In this study, experienced interventional cardiologists carefully read the intraoperative imaging data and excluded patients with coronary artery dissection or branch occlusion. Patients were divided into two groups based on the occurrence of PMI, and between the two groups, there were no statistically significant differences in age, sex, BMI, adverse medical history (hypertension, diabetes, smoking), GFR, TG, and HDL-C. However, the preoperative LDL-C level was an independent risk factor for PMI, and the risk of PMI was significantly lower when the preoperative LDL-C level was less than 1.4 mmol/L. There were not any statistically significant differences between the two groups in the coronary artery imaging data, including surgical approach, number of diseased vessels, proportion of completely occluded lesions, SYNTAX score, location of the target vessel, maximum dilation pressure, maximum balloon dilation time, number of implanted stents, and total stent length. Therefore, PMI was mainly caused by the debris generated by plaque rupture in this study, which formed the microthrombus that ended up blocking the distal microcirculation.

A total of 308 patients with SAP or UAP were included in this study, and their preoperative LDL-C level fell into three grades, ie, low (<1.4 mmol/L), medium (1.4–1.8 mmol/L), and high (>1.8 mmol/L). Positive correlation existed between PMI and LDL-C concentration ($r = 0.322$, $P < 0.05$) and between PMI and LDL-C grade ($r = 0.189$, $P < 0.05$). Compared to patients with low LDL-C, patients with medium or high LDL-C had a significantly higher risk of PMI ($P < 0.05$). This study provides evidence for adequate lipid management in patients with very high risk of cardiovascular disease before elective PCI. Limiting preoperative LDL-C to less than 1.4 mmol/L before PCI clearly reduced the incidence of PMI after revascularization. Sufficient evidence proves that high dose statins preloading prior to elective PCI was associated with a significant reduction of PMI.^{19,20} However, it is difficult to reduce LDL-C concentrations

below 1.4 in many cases with statins alone or in combination with cholesterol absorption inhibitors. Inclisiran and the powerful LDL-C lowering effect of PCSK9 inhibitors make this requirement possible.^{21–23} In addition, the number of intraoperative stents implanted also turned out to be an independent risk factor for PMI after adjusting for other risk factors. To reduce the risk of PMI and long-term cardiovascular adverse events, it is prudent to install fewer stents during the procedure.

The small sample size is a limitation of this work. Of the 308 patients, 42 (13.6%) had a low LDL-C level (<1.4 mmol/L) before PCI. Of the 82 patients who experienced PMI (based on elevated troponin), three (3.7%) had a low LDL-C level. In addition, this work did not include any long-term follow-up, which would be informative in evaluating if the intensive preoperative reduction of LDL-C could improve the long-term prognosis of elective PCI.

Limitations

The limitations of this experiment are manifested in the following aspects: a limited sample size, the absence of long-term follow-up, and the separate discussion of perioperative myocardial infarction and myocardial injury. If circumstances permit, we will address these issues in future in-depth investigations.

Conclusion

In summary, our results suggest that reducing preoperative LDL-C level below 1.4 mmol/L can further reduce the incidence of PMI, which is consistent with the current goal of reducing LDL-C level to less than 1.4 mmol/L in patients with super high (very high) risk of ASCVD. This suggests that the use of statins, cholesterol absorption inhibitors and even PCSK9 inhibitors before surgery to sufficiently reduce LDL-C level below 1.4 is beneficial for patients with SAP or UAP who receive elective PCI.

Abbreviations

PCI, percutaneous coronary intervention; cTnI, cardiac troponin I; PMI, perioperative myocardial injury/infarction; LDL-C, low-density lipoprotein cholesterol; SAP, stable angina pectoris; UAP, unstable angina pectoris; CK-MB, creatine kinase MB; PCSK9, proprotein convertase subtilisin/kexin type 9; FFR, Fractional flow reserve; IVUS, intravascular ultrasound; ASCVD, atherosclerotic cardiovascular disease.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no conflicts of interest in this work.

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