Clinical Investigations

Current Statin Usage for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: Multicenter Survey in Korea

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ABSTRACT

Background: Although high-dose statin therapy has been reported to improve outcomes in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI), patterns of statin usage for such patients have not been reported in real-world clinical practice.

Hypothesis: Some clinical factors would affect the pattern of statin usage in patients with ACS.

Methods: In the multicenter prospective registry, 3362 patients with ACS who underwent PCI were analyzed. High-dose statin treatment was defined as atorvastatin $\geq$40 mg or rosuvastatin $\geq$20 mg per day. The patterns of statin usage were investigated for 30 days after the index PCI.

Results: High-dose statins were administered prior to PCI to 13.7% and 19.6% of patients with unstable angina/non–ST-elevated myocardial infarction (UA/NSTEMI) and ST-elevated myocardial infarction (STEMI), respectively ($P < 0.001$). After PCI, 476 (14.2%) patients were maintained on high-dose statins, and 550 (16.4%) patients received no statins. Independent factors associated with high-dose statin usage after PCI were STEMI (odds ratio [OR]: 1.704, 95% confidence interval [CI]: 1.321–2.197, $P < 0.001$), high total cholesterol level (OR: 1.445, 95% CI: 1.136–1.837, $P = 0.003$), and current smoker (OR: 1.556, 95% CI: 1.206–2.008, $P < 0.011$). The absence of hypercholesterolemia was an independent factor determining the nonuse of statins (OR: 0.229, 95% CI: 0.148–0.353, $P < 0.001$).

Conclusions: In real-world clinical practice, high-dose statin treatment is being underused despite extensive evidence for patients with ACS undergoing PCI, particularly in UA/NSTEMI. Efforts are needed to ensure that clinical practice complies with evidence-based guidelines.

Introduction

Although the primary goal of statin treatment in acute coronary syndrome (ACS) is to lower the blood low-density lipoprotein cholesterol (LDL-C) level to <70 mg/dL, the benefits beyond LDL-C reduction have been addressed in many recent reports. Intensive statin treatment in the hyperacute stage of ACS could improve endothelial function, coronary flow, and clinical outcomes.[1–4] The efficacies of statins in patients with ACS undergoing percutaneous coronary intervention (PCI) are now reflected in the latest American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) guidelines, which recommend administration of high-dose statins before PCI as a reasonable treatment (class IIa) to reduce the risk of periprocedural myocardial infarction (MI).[5] The goal of this study was to investigate the status of statin usage and the factors affecting prescription for patients with ACS undergoing PCI in real-world clinical practice.

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Methods

Study Design and Population

We designed a Korean multicenter survey of health-status outcomes after percutaneous coronary angioplasty in patients with ACS (MUSTANG) to survey basic clinical data about ACS patients treated with PCI in daily practice. Between September 2009 and July 2010, consecutive patients were enrolled prospectively from 48 hospitals with PCI case volumes of ≥75 per year. Patients were considered eligible if they presented with unstable angina (UA), non–ST-elevated myocardial infarction (NSTEMI), or ST-elevated myocardial infarction (STEMI) and underwent PCI. Exclusion criteria were delayed treatment in patients with STEMI (PCI done ≥12 h after onset of symptoms), inability to answer the questionnaire to assess functional status, or unwillingness to provide written informed consent. Patients were followed up for 30 days after the index PCI. Major adverse clinical events were defined as ≥1 of the following: cardiovascular or noncardiovascular death, nonfatal MI, nonfatal stroke, recurrent significant angina, and target-lesion revascularization.

Acute coronary syndrome was diagnosed by characteristic clinical presentation, electrocardiogram, and increase in cardiac enzymes.[6–8] Decision for PCI referral and other further medical treatment were at the discretion of the attending physicians. Among the study definitions, the volume of hospital was indicated by the total number of available beds. Hypercholesterolemia was defined as the fasting serum total cholesterol ≥200 mg/dL (5.1 mmol/L). High-dose statin was defined as atorvastatin ≥40 mg or rosuvastatin ≥20 mg per day. All lesser dosages used were defined as low-dose.

To investigate the pattern of statin usage after PCI, the patients who had been treated with a fixed statin dosage throughout 30 days after index PCI were analyzed. The study population was classified into 3 groups depending on the maintenance statin dosage during the post-PCI period, regardless of the pre-PCI statin treatment. No-statin treatment was defined as the absence of any statin treatment during the study period (group 1). A high-dose statin treatment was defined as maintenance of high-dose statin treatment for 30 days after PCI (group 3). Non–high-dose statin treatment was defined as maintenance of low-dose statin treatment for 30 days after index PCI (group 2). The factors affecting the usage of statins after PCI were analyzed according to these classifications.

The functional status of the patients was assessed by 2 health-related quality-of-life (HRQOL) tools, the Seattle Angina Questionnaire (SAQ) and the Euro Quality of Life 5-Dimensional Classification (EQ-5D), using standardized written questionnaires.[9,10] The HRQOL data were acquired directly from the patients within 24 hours after PCI through an in-depth interview by trained personnel. The scores of each subscale of SAQ tools ranged from 0 to 100, where higher scores indicated better health status. The EQ-5D is a 5-item questionnaire that quantifies 5 domains of general health status. The scores of each domain were converted to a summary index ranging from 0 (the worst possible health state or death) to 1 (the best possible health state).

Each local institutional review board at the individual hospitals approved the study protocol, and all the patients offered written informed consent. The data were collected by investigators at each site and analyzed by an independent statistician. The authors were solely responsible for the design and conduct of the study.

Statistical Analysis

Differences among groups were compared using the 1-way ANOVA test for the continuous data and the χ^2 test for the frequency data. The changes in each subscale of HRQOL from baseline to 30 days were compared using the paired t test. Logistic regression analysis was used to determine the independent factors influencing the statin usage patterns. Multivariate models for both pre-PCI and post-PCI statin usage pattern were constructed with the baseline clinical characteristics and HRQOL status. Two-sided P values of <0.05 were considered statistically significant. All analyses were performed by using SPSS for Windows software, version 17.0 (SPSS Inc., Chicago, IL).

Results

A total of 3362 patients (mean age, 63.7 ± 11.0 y) were eligible for the analysis. Among the overall study population, 359 patients (19.7%) were treated at hospitals with <500 beds, 1232 (36.6%) at hospitals with 500 to 800 beds, 1167 (34.7%) at hospitals with 800 to 1000 beds, and 604 (18.0%) at hospitals with >1000 beds. The number of patients with UA/NSTEMI was 2516 (74.8%), of which 1495 patients (59.4%) underwent PCI within 12 hours. The median hospital stay was 5.0 (range, 3.0–7.0) days. The major adverse events that occurred in 52 (1.5%) patients at the 30-day follow-up after index PCI were as follows: cardiovascular deaths in 14, noncardiovascular deaths in 4, nonfatal MIs in 9, nonfatal strokes in 3, and recurrent anginas in 15. The target-lesion revascularization procedures (PCI or coronary artery bypass surgery) were performed in 10 patients within 30 days.

Pre-PCI statin treatment was administered in 1673 patients (49.8%). Among these, 511 patients received high-dose statins. Pre-PCI high-dose statin was administered in 13.7% and 19.6% of the patients with UA/NSTEMI and STEMI, respectively ($P < 0.001$; Figure 1). Independent factors influencing pre-PCI high-dose statin loading were STEMI (odds ratio [OR]: 1.717, 95% confidence interval [CI]: 1.343–2.195, $P < 0.001$) and current smoker (OR: 1.457, 95% CI: 1.136–1.870, $P = 0.003$, Figure 2). At day 30 post-PCI, 2814 patients (83.7%) received statin treatment. Among these, high-dose statins were administered in 12.2% and 20.1% of patients with UA/NSTEMI and STEMI, respectively ($P < 0.001$). The usage of low-dose statin sharply increased after PCI compared with pre-PCI, but that of high-dose remained similar between the pre-PCI and post-PCI period (Figure 1).

There were significant differences in the pre-PCI high-dose statin usage depending on the hospital volume from which the patients were treated (Figure 3). The rate of pre-PCI high-dose statin treatment was significantly higher in hospitals with <500 beds and in hospitals with 500 to 800 beds compared with hospitals with >800 beds ($P < 0.001$). The rate of post-PCI high-dose statin treatment was also higher in the smaller hospitals ($P < 0.001$) than larger ones.

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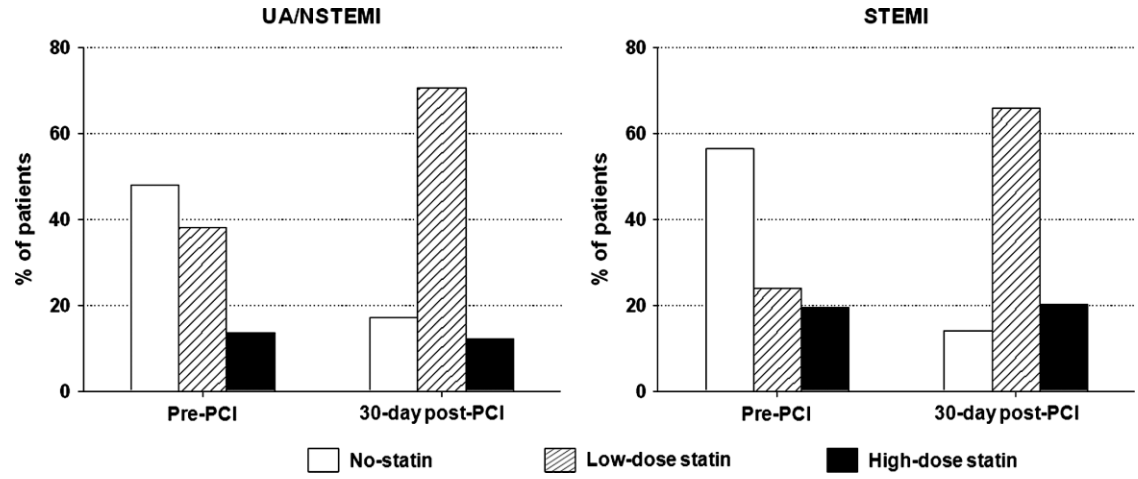

Figure 1. Statin dosage used in pre-PCI and post-PCI period in patients with UA/NSTEMI and STEMI. Abbreviations: NSTEMI, non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

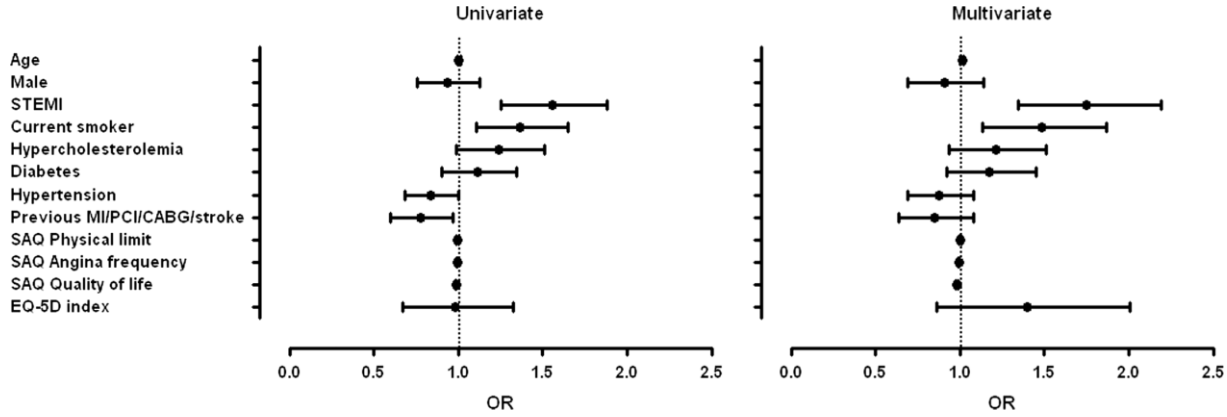

Figure 2. Impact of baseline characteristics and HRQOL status on the pre-PCI high-dose statin therapy. Abbreviations: CABG, coronary artery bypass grafting; EQ-5D, Euro Quality of Life 5-Dimensional Classification; HRQOL, health-related quality of life; MI, myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; SAQ, Seattle Angina Questionnaire; STEMI, ST-segment elevated myocardial infarction.

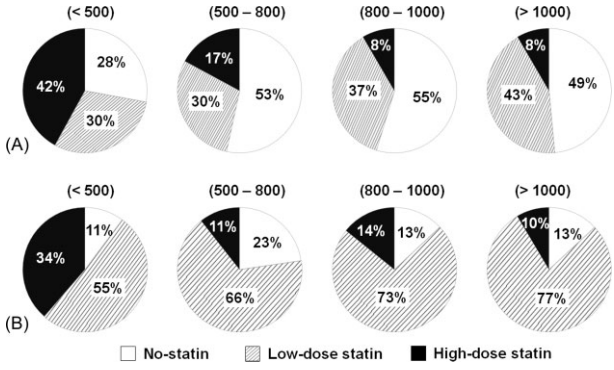

Figure 3. Statin dosage used at pre-PCI (A) and 30-day post-PCI (B) according to the size of participating hospitals. Abbreviations: PCI, percutaneous coronary intervention.

Patterns for statin usage after PCI were analyzed for the 2782 patients who had been treated with a fixed statin dosage throughout 30 days after index PCI. Three subgroups of the prespecified statin treatment patterns were evident according to the post-PCI dosage (Table 1). Group 3 patients were significantly younger and showed a higher frequency of STEMI, current smoking, and hypercholesterolemia. The functional status assessed by the angina-specific HRQOL tool was best in group 1, intermediate in group 2, and worst in group 3. All 3 groups showed similar general health status measured by the EQ-5D index. Significant differences were also observed in the usage of medications other than statins. When surveyed at 30 days after the index PCI, the prescription rates of aspirin, thienopyridine, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, and β-blockers were highest in group 3. Among the 402 patients who had received post-PCI high-dose statin treatment, 231 (57.5%) had also been treated with high-dose statin during the pre-PCI period. In multivariate analysis, high-dose statin treatment after PCI was more frequently done for patients with STEMI (OR: 1.704, 95% CI: 1.321–2.197, $P < 0.001$), who are current smokers (OR: 1.556, 95% CI: 1.206–2.008, $P < 0.011$), and have hypercholesterolemia (OR: 1.445, 95% CI: 1.136–1.837, $P = 0.003$; Figure 4A). The factor that determined the

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Table 1. Baseline Characteristics According to the Pattern of Statin Usage After PCI

	Group 1: No Statin (n = 354)	Group 2: Non–High Dose (n = 2026)	Group 3: High-Dose (n = 402)	*P* Value
Age, mean ± SD, y	65.3 ± 11.7	63.7 ± 10.8	61.7 ± 11.7	<0.001
Male sex, n (%)	249 (70.1)	1378 (68.0)	289 (71.9)	0.252
STEMI, n (%)	73 (20.6)	459 (22.7)	142 (35.3)	<0.001
Current smoker, n (%)	95 (26.8)	555 (27.4)	162 (40.3)	<0.001
DM, n (%)	125 (35.3)	659 (32.5)	116 (28.9)	0.149
Hypertension, n (%)	201 (56.8)	1202 (59.3)	211 (52.5)	0.034
Hypercholesterolemia, n (%)	31 (8.8)	558 (27.5)	135 (33.6)	<0.001
Previous MI, n (%)	21 (5.9)	128 (6.3)	19 (4.7)	0.481
Previous PCI, n (%)	57 (16.1)	319 (15.7)	49 (12.2)	0.194
Previous CABG, n (%)	5 (1.4)	24 (1.2)	5 (1.2)	0.944
Previous stroke, n (%)	17 (4.8)	118 (5.8)	21 (5.2)	0.678
HRQOL, mean ± SD				
SAQ physical limitation	80.2 ± 19.8	76.6 ± 23.1	77.9 ± 22.9	0.025
SAQ angina frequency	73.5 ± 23.3	70.5 ± 26.1	66.5 ± 28.5	0.001
SAQ QOL	52.9 ± 21.4	45.4 ± 18.9	43.6 ± 20.3	<0.001
EQ-5D index	0.79 ± 0.27	0.77 ± 0.28	0.81 ± 0.24	0.041
Concurrent medications				
Aspirin	291 (82.2)	2010 (99.2)	402 (100)	<0.001
Thienopyridine	311 (87.9)	1810 (89.3)	373 (92.8)	0.058
ACEI or ARB	241 (67.0)	1544 (76.2)	309 (76.9)	0.003
BB, n (%)	202 (57.1)	1435 (70.8)	325 (80.8)	<0.001
CCB, n (%)	76 (21.5)	462 (22.8)	86 (21.4)	0.741
Nitrate, n (%)	152 (42.9)	739 (36.5)	170 (42.3)	0.012

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BB, β-blocker; CABG, coronary artery bypass grafting; CCB, calcium channel blocker; DM, diabetes mellitus; EQ-5D, Euro Quality of Life 5-Dimensional Classification; HRQOL, health-related quality of life; MI, myocardial infarction; NSTEMI, non–ST-segment elevated myocardial infarction; PCI, percutaneous coronary intervention; QOL, quality of life; SAQ, Seattle Angina Questionnaire; SD, standard deviation; STEMI, ST-segment elevated myocardial infarction.

nonuse of statins was the absence of hypercholesterolemia (OR: 0.229, 95% CI: 0.148–0.353, $P < 0.001$; Figure 4B). Patients with lower SAQ quality-of-life subscale but high general health status tended to use high-dose statins; however, they failed to reach the statistical significance.

Discussion

This study reports the current status of statin usage in real clinical practice for patients with ACS undergoing PCI. First, we found that blood cholesterol levels influence the physicians' decision to prescribe statins and the dosage for use in ACS. Statins were not used in up to 16.4% of the study population. Second, high-dose statin treatment is used more frequently in patients with STEMI. Third, physicians tend to make the decision whether to prescribe high-dose statins before PCI, based on the patients' baseline characteristics.

Usually one hardly has enough time to administer medications prior to PCI in patients with ACS, particularly in cases with STEMI. A low-dose statin is often used after PCI. The usage of high dosage, however, was similar between the pre-PCI and the post-PCI period, which might be caused by a specific intent of the physician. In some patients, high dosages were loaded during the pre-PCI period, and then maintained with a lower dosage. The blood cholesterol levels seem to determine the change in dosage.

Most of the favorable evidence about high-dose statin therapy has been acquired from UA/NSTEMI. High-dose atorvastatin therapy reduced recurrent ischemic events of non-STE ACS.[11] The effects of early-stage therapy were observed for up to 24 months.1 Even the high-dose pre-PCI loading reduced adverse clinical events in 30 days.3 Few studies have reported on whether or not these beneficial effects can be extended in cases of

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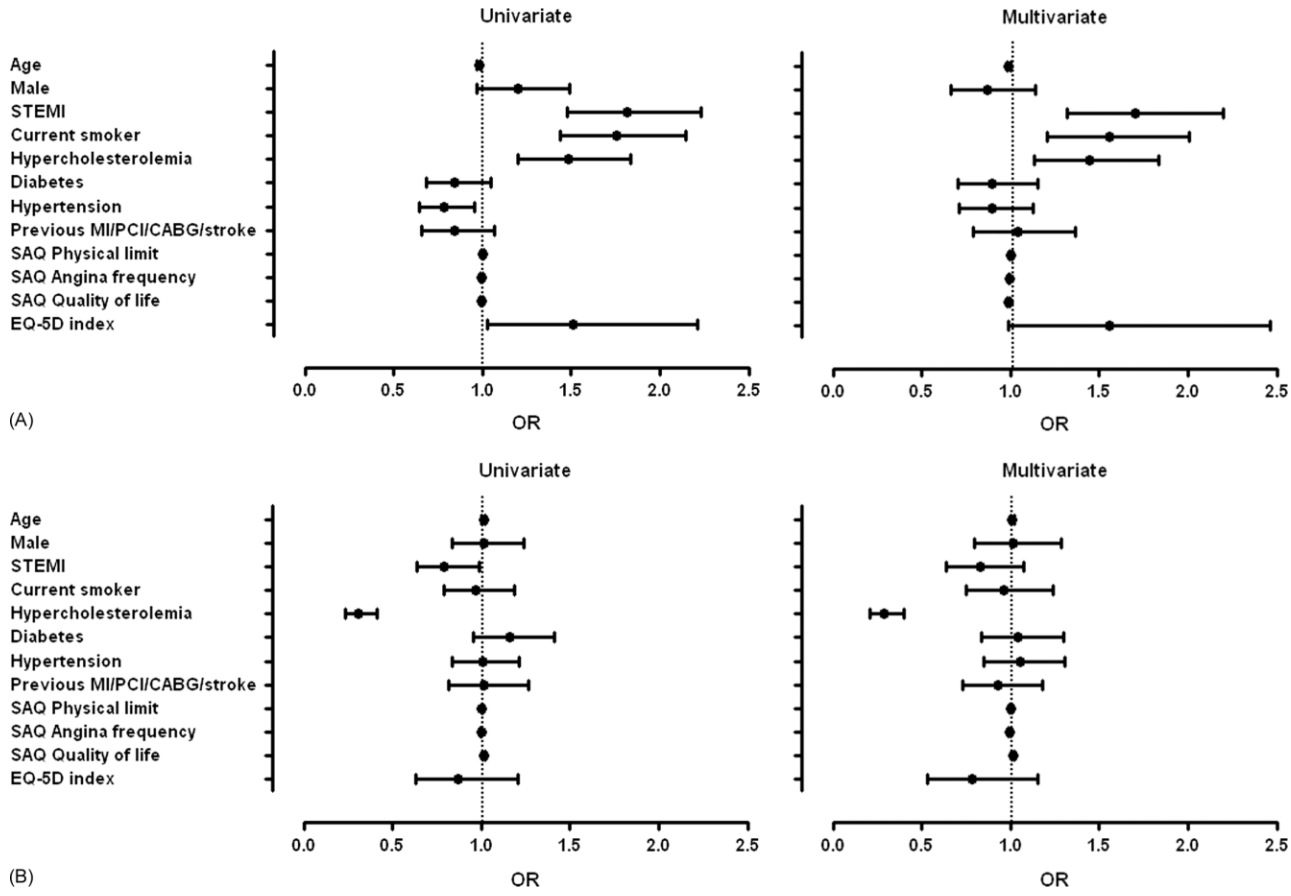

Figure 4. Impact of baseline characteristics and HRQOL status on the pattern of statin usage after PCI. Results for high-dose statin treatment (A) and no-statin treatment (B). Abbreviations: CABG, coronary artery bypass grafting; EQ-5D, Euro Quality of Life 5-Dimensional Classification; HRQOL, health-related quality of life; MI, myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; SAQ, Seattle Angina Questionnaire; STEMI, ST-segment elevated myocardial infarction.

STEMI. In the Efficacy of High-Dose Atorvastatin Loading Before Primary Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction (STATIN STEMI) trial, which studied the effects of 80 mg atorvastatin before PCI in STEMI, high-dose statin therapy failed to reduce 30-day adverse clinical events.[2] Physicians might have believed without concrete evidence that patients with STEMI would benefit more from intensive statin treatments than those with UA/NSTEMI. The rates of medications, other than statins, that are known to reduce mortality in ACS, such as aspirin, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, and β-blockers, were higher in patients who were treated with high-dose statin. Complex factors, including the severity of the patient's condition, propensity of the physician, and the medical service system, combined to set the final statin usage pattern.

Statins are an essential component of ACS management for reducing vascular events and death.[1,11,12] The current guidelines recommend administration of statins for patients with ACS regardless of the baseline LDL-C level.[13] Although intensive statin therapy based on the blood lipid level to rapidly reduce LDL-C level is mentioned in the current guidelines, numerous benefits beyond lipid-lowering have been reported for acute-stage ACS management. As such benefits are dependent on the timing and dose of statin administration, it can be augmented with a loading of maximal dosage in the hyperacute stage of ACS.[14] High-dose statin therapy prior to PCI is acknowledged as a beneficial treatment for patients with ACS undergoing PCI. However, our results revealed that intensive statin therapy is not prevalent in real-world clinical practice. High-dose statins were maintained for only 14.2% of the patients after PCI. Compared with the pre-PCI data, only hypercholesterolemia was added as an independent factor for the high-dose statin usage after PCI. The determinant factor for the nonuse of statins was the absence of hypercholesterolemia. This indicates that blood cholesterol level can be used as a major factor in determining statin usage in patients with ACS.

It is unclear why the usage of high-dose statin treatment was more frequent in smaller hospitals. In fact, this contradicts previous studies that reported better quality of care in higher-volume medical centers. One possible explanation is that the same interventional cardiologist may be more involved in the primary care for patients and the decision-making process in a small hospital. In a high-volume hospital, in contrast, a larger team of other

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healthcare personnel, such as house staff, general practitioners, and noninterventional cardiologists, may be involved in the management of patient care. This may cause treatment gaps leading to differences in quality of care across a variety of medical personnel in a larger hospital. Another explanation is that our study focuses on the medication dosage instead of the seriousness of the clinical outcomes, which has been the subject of other studies investigating the relationship between the hospital volume and the quality of practice.[15–17]

Although no statistical significance was demonstrated by multivariate analysis, patients with better general health status tended more frequently to receive high-dose statin after PCI. This is consistent with other recent reports that more-serious patients tended to receive less-optimal medical treatment. In a report by Lee et al, the rates of optimal medical treatment were higher in patients with STEMI, higher ejection fraction, and younger age, and in patients without heart failure.[18] A Canadian group also showed that patients who received in-hospital statin treatment had better clinical profiles than those who did not.[19]

Several limitations of this study have been considered. First, our definition for high-dose statin was arbitrary and was lower than the reference dose used in international papers. Dosage modification was necessary in our study because 80 mg of atorvastatin or 40 mg of rosuvastatin is not allowed as the initial dosage in Korea due to insurance reasons. Second, our results were acquired only from PCI-treated patients. Patients with ACS who had been treated with medical strategy were not included in the present study. Third, only the patients who were capable of answering the HRQOL questionnaire were included. Therefore, the results could not be applied to critically ill patients. Fourth, whether the clinical signs of heart failure or the echocardiographic/angiographic findings affected the statin usage patterns was not investigated. Finally, 30 days is not enough time to obtain complete information about the medication usage. However, this time frame may be sufficient to grasp the physician's intent of whether or not to prescribe statin.

In conclusion, high-dose statin treatment is being underused in real clinical practice despite extensive evidence for patients with ACS undergoing PCI, particularly in UA/NSTEMI. Efforts must be made to ensure that clinical practice complies with evidence-based guidelines.

Appendix

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