Achievement of LDL-Cholesterol Goal with Statins after an ST Segment Elevation Myocardial Infarction

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Background: In patients with very high cardiovascular risk, low-density lipoprotein cholesterol (LDL-C) less than 70 mg/dL or at least 50% reduction of LDL-C are recommended targets. High-dose atorvastatin has been shown to reduce death and ischemic events among patients with acute coronary syndrome.

Objective: To evaluate the proportion of STEMI patients that achieve LDL-C goal after hospital discharge from a real-world setting in Thailand. To determine if the formulation of statin prescribed affected the LDL-C goal achievement.

Material and Method: The authors analyzed data from a cohort of patients with STEMI enrolled from June 1, 2008 through May 31, 2011. Patients who survived, were prescribed a statin on discharge and had LDL-C data at follow-up were analyzed. The formulation of statin was categorized as simvastatin or other statins (atorvastatin or rosuvastatin) group.

Results: Ninety-seven percent (n = 265 of 272) of patients were prescribed a statin at discharge. Of these, 216 patients had LDL-C data during a 3-month follow-up period, 75% were men, the mean age was 60.5 ± 12.2 years old and the mean baseline LDL-C was 118.1 ± 41.2 mg/dL. 73% (n = 157) of patients received simvastatin and 27% (n = 59) received other statins. At discharge, the median daily dose of simvastatin, atorvastatin and rosuvastatin were 20, 20 and 10 mg respectively. At follow-up, target LDL-C <70 mg/dL or LDL-C reduction $\geq 50\%$ was achieved in 30.1% (n = 65) of patients, 27.4% (n = 43) on simvastatin and 37.3% (n = 22) on other statins, (p = 0.158, simvastatin versus other statins). When stratified by the dose intensity of statin, a significantly greater proportion of patients on moderate to high intensity statin attained LDL-C goals than those on low intensity statin: (36.3% versus 24.3%, p = 0.038).

Conclusion: Most patients with STEMI are prescribed statin therapy at discharge. Despite this, the target LDL-C is attained in a minority of the patients due to suboptimal statin dosing. The formulation of statin did not affect LDL-C goal attainment. High-dose statin therapy is underused in real-world clinical practice. These findings emphasize the opportunities to improve outcomes of STEMI patients with evidence-based therapies.

Keywords: Acute coronary syndrome, ST-segment elevation myocardial infarction, Statin, LDL-C

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Major clinical trials with stain therapy have shown that lowering low-density lipoprotein cholesterol (LDL-C) reduces cardiovascular events in patients stabilized after acute coronary syndrome (ACS) including ST-segment elevation myocardial infarction (STEMI)^(1,2). The 2013 American College of Cardiology/ American Heart Association (ACC/AHA) guidelines for the management of STEMI give a level IB recommendation for starting statin, specifically highdose atorvastatin, in all STEMI patients without contraindications before hospital discharge⁽³⁾. The current European Society of Cardiology (ESC) guidelines for the management of dyslipidemia and the management of STEMI consider ACS patients at

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very high cardiovascular risk and recommend a goal to reduce LDL-C to <70 mg/dL and/or at least 50% reduction of LDL-C^(4,5).

Patients with ACS in Thailand confer a high mortality when compared to those of the western world⁽⁶⁻⁸⁾. Thus, it is critical that physicians caring for ACS patients provide guideline-supported, evidence-based therapies, which are comprised of statins, to achieve recommended LDL-C targets.

Despite the dissemination of international guidelines, numerous studies have shown that in a real-world setting most patients do not achieve their recommended LDL-C goal. Previous studies in the US⁽⁹⁾ have described the actual practice of lipid lowering therapy in ACS patients that LDL-C goal of <100 mg/dL was achieved in 71% of patients but the optional LDL-C goal \leq 70 mg/dL was achieved in only 31%. The LTAP-II study in Thailand⁽¹⁰⁾ reported that in patients with stable coronary heart disease (CHD)

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or CHD equivalents only one-third of the patients achieved the LDL-C target of <100 mg/dL. More recent data from a Thai population of stable CHD patients⁽¹¹⁾, reported up to 74% of patients achieved their LDL-L goal of <100 mg/dL.

There is a lack of data on the attainment of LDL-C goal after STEMI in local Thai practice. The authors describe the LDL-C achievement post-hospital discharge and prescribing practices related to the formulation and dose of statin therapy after STEMI from a single center.

Objective

To evaluate the proportion of STEMI patients that achieve LDL-C goal after hospital discharge from a real-world setting in Thailand and determine if the formulation of statin prescribed affected the LDL-C goal achievement.

Material and Method

This observational study was conducted at a large tertiary care academic hospital in Bangkok, Thailand. The authors analyzed data from a cohort of patients with STEMI who were prospectively enrolled from June 1, 2008 through May 31, 2011. STEMI was diagnosed by having EKG changes demonstration either ST-segment elevation ≥ 1 mm or new left bundle branch block. All patients who were admitted to the hospital with STEMI, survived until discharge, were prescribed a statin on discharge and who had LDL-C data at 3-6 month follow-up were analyzed.

Data collection

Patient's data on baseline characteristics, clinical presentation, initial laboratory data and inhospital management were collected by cardiac nurses and/or cardiologists. Data were transcribed onto standard case record forms and entered onto a webbased database. Demographic variables included gender and age. Dyslipidemia, diabetes, hypertension, current tobacco use and family history were used to characterize risk factors. Diabetes was diagnosed when the patient's fasting plasma glucose was 126 mg/dl or higher on at least two occasions or there was a history of diabetes treated either through dietary control or antidiabetic medication. Hypertension was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg or a previous diagnosis of hypertension. Dyslipidemia was diagnosed when total cholesterol was >200 mg/dl, LDL cholesterol >130 mg/dl, high-density lipoprotein (HDL) cholesterol

<40 mg/dl or if there was a previous diagnosis of dyslipidemia and/or when currently being treated with a lipid-lowering agent. Current tobacco use was defined by the habitual use of tobacco within 1 month of index hospital admission. Initial laboratory data on creatinine and lipid profile, including total cholesterol, triglyceride, HDL-C and LDL-C, were recorded.

Data on the formulation of statin, categorized as simvastatin or other statins (atorvastatin or rosuvastatin), and the statin dose were collected. The patients were further stratified by the intensity of statin dose. Simvastatin 10-20 mg was characterized as low-intensity statin and the remainder of statin therapies as moderate to high-intensity statin. The LDL-C value at 3 months follow-up was obtained through chart abstraction.

The protocol was approved by the hospital ethics committee and was in accordance with the Declaration of Helsinki. Informed consent was obtained from every patient.

Statistical analysis

Patient characteristics, lipid values, medication use and LDL-C goal attainment were compared between patients on simvastatin and those who were on other statins. In addition, the authors compared LDL-C goal attainment for those on low-intensity statin compared to those on moderate to high intensity statin. Categorical data are presented as frequencies and percentage. Continuous variables are reported as mean \pm standard deviation or median and 25th and 75th percentile when there was skewed distribution. Categorical data were compared using the Chi-square or Fisher's exact test and continuous data were compared with the Student's t-test (normality) or Mann-Whitney U test (non-normality). The statistical test was performed at the alpha level of 0.05, 2-tailed. Multiple logistic regression analysis was used to estimate independent predictors of achieving LDL-C goal at follow-up and presented as odds ratio and 95% confidence interval. Data were analyzed with PASW Statistics V.18.0 (IBM Corporation, New York, USA).

Results

During the 3-year period, 309 consecutive patients with STEMI were prospectively enrolled (Fig. 1). Patients who died during the index admission, who were not prescribed with statin at discharge or had missing LDL-C data at follow-up were not analyzed. There were 97% (n = 265 of 272) of patients with STEMI who were prescribed a statin at discharge.



Fig. 1 Scheme of statin therapy in patients admitted with STEMI.

The reason for seven patients not being given statins included two patients who had abnormal liver function test and unknown in the remainder of the patients. Two hundred sixteen patients had LDL-C data during follow-up, 75% were men, the mean age was 60.5 years old and the mean baseline LDL-C was 118.1 mg/dL. 73% (n = 157) of patients received simvastatin and 27% (n = 59) received other statins. Simvastatin and other statins treatment groups were well matched with respect to baseline characteristics (Table 1), baseline laboratory data (Table 2) and discharge medication (Table 3). There were significant differences in the patient's insurance status between the two groups. Among patients who were under universal coverage, almost all received simvastatin whereas almost all patients that were prescribed other statins were civil servant reimbursement patients.

At discharge, the median dose of simvastatin, atorvastatin and rosuvastatin were 20, 20, 10 mg, respectively. At a median follow-up time of 3 months, target LDL-C <70 mg/dL or LDL-C reduction \geq 50% was achieved in 30.1% (n = 65) of patients (Fig. 2),

Table 1. Baseline characteristics categorized by formulation of statin

Variable	Overall $(n = 216)$	Simvastatin ($n = 157$)	Other statins $(n = 59)$	<i>p</i> -value	
Age (years), mean ± SD	60.5±12.2	59.9±12.3	62.0±11.8	0.292	
Female, n (%)	53 (24.5)	43 (27.4)	10 (16.9)	0.112	
BMI (kg/m ²), mean \pm SD	24.6±3.3	24.4±3.4	25.2±3.0	0.214	
Insurance status, n (%) Universal coverage Social insurance Civil servant Self paid	84 (38.6) 14 (6.5) 113 (52.6) 5 (2.3)	82 (52.2) 14 (8.9) 57 (36.3) 4 (2.5)	2 (3.4) 0 (0) 56 (94.9) 1 (1.7)	<0.001	
Diabetes mellitus, n (%)	68 (31.5)	52 (33.1)	16 (27.1)	0.397	
Hypertension, n (%)	137 (63.4)	97 (61.8)	40 (67.8)	0.414	
Dyslipidemia, n (%)	121 (56.0)	85 (54.1)	36 (61.0)	0.364	
Current smoking, n (%)	89 (41.2)	69 (43.9)	20 (33.9)	0.181	
Prior myocardial infarction, n (%)	21 (9.7)	13 (8.3)	8 (13.6)	0.243	
Prior PCI, n (%)	17 (7.9)	11 (7.1)	6 (10.2)	0.443	
Prior CABG, n (%)	4 (1.9)	2 (1.3)	2 (3.4)	0.309	

BMI = body mass index; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft surgery

Table 2. Baseline laboratory data by formulation of statin

Variable	Overall $(n = 216)$	Simvastatin ($n = 157$)	Other statins $(n = 59)$	<i>p</i> -value
Creatinine (mg/dL), median (P25, P75)	1 (0.8, 1.2)	1 (0.8, 1.2)	1 (0.9, 1.2)	0.990
Total cholesterol (mg/dL), mean \pm SD	188.0±45.0	189.6±41.1	183.9±53.9	0.411
Triglyceride (mg/dL), median (P25, P75)	115 (89, 172)	115 (90.5, 175.5)	114.5 (87, 165)	0.695
HDL-C (mg/dL), mean \pm SD	42.7±12.1	42.9±12.7	41.3±10.5	0.410
LDL-C (mg/dL), mean \pm SD	118.1±41.2	118.9±38.0	116.1±48.8	0.659

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol



Fig. 2 Proportion of patients that achieved LDL-C goals at follow-up.

27.4% (n = 43) on simvastatin and 37.3% (n = 22) on other statins, (p = 0.158, simvastatin versus other statins) (Fig. 3). Multiple logistic regression analysis used to evaluate independent predictors of achieving LDL-C goal (Table 4) revealed that the formulation of statin was not an independent predictor.

The distribution of each statin formulary and its dose intensity is depicted in Fig. 4. When stratified by the dose intensity of statins a significantly greater proportion of patients on moderate to high intensity statin attained LDL-C goals than those on low intensity statin (36.3% versus 24.3%, p = 0.038).



Fig. 3 Proportion of patients that achieved LDL-C goals at follow-up: categorized by formulation of statin.



Fig. 4 Distribution of statin dosage in overall patients.

Table 3.	Discharge	medications	categorized	by	formul	ation	of statin

Medication	Overall $(n = 216)$	Simvastatin ($n = 157$)	Other statins $(n = 59)$	<i>p</i> -value
Aspirin, n (%)	213 (98.6)	154 (98.1)	59 (100.0)	0.286
Clopidogrel, n (%)	196 (90.7)	142 (90.4)	54 (91.5)	0.807
Beta-blocker, n (%)	182 (84.3)	128 (81.5)	54 (91.5)	0.072
ACE inhibitor, n (%)	160 (74.1)	118 (75.2)	42 (71.2)	0.553
ARB, n (%)	6 (2.8)	4 (2.5)	2 (3.4)	0.748

ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker

Table 4.	Multivariate analysis: ind	lependent predictor	s of achieving LDL-C	$<70 \text{ mg/dL or} \ge 50\%$	6 LDL-C reduction

Factors	Univariate analysis		Multivariate analysis		
	Crude OR (95% CI)	<i>p</i> -value	Adjusted OR (95% CI)	<i>p</i> -value	
Other statins	0.8 (0.4, 1.6)	0.158	0.8 (0.4, 1.6)	0.551	
Age	1.0 (1.0, 1.0)	0.194	1.0 (1.0, 1.0)	0.142	
Current smoking	1.5 (0.8, 2.9)	0.081	1.2 (0.6, 2.4)	0.561	
Systolic blood pressure	1.0 (1.0, 1.0)	0.061	1.0 (1.0, 1.0)	0.930	
Diastolic blood pressure	1.0 (1.0, 1.0)	0.109	1.0 (1.0, 1.0)	0.671	
Heart rate	1.0 (1.0, 1.0)	0.172	1.0 (1.0, 1.0)	0.623	
Creatinine	0.8 (0.6, 1.0)	0.143	0.8 (0.6, 1.1)	0.217	
In hospital heart failure	0.4 (0.2, 0.8)	0.023	0.5 (0.2, 1.1)	0.077	

Discussion

The present study reports the current status of statin usage in real clinical practice for patients admitted with STEMI. The LDL-C goal <70 mg/dL or LDL-C reduction \geq 50% was achieved after hospital discharge in only 30% of patients after STEMI. There was a trend towards a higher proportion of patients to attain the target LDL-C with atorvastatin/rosuvastatin compared to simvastatin. However, the difference was not statistically significant. Moderate to high intensity statin resulted in up to 36% of the patients attaining target LDL-C and was statistically superior to low-intensity statin.

The relationship between LDL-C lowering with statins and the reduction of cardiovascular events has been well established^(1,2,12-15). Statin pleiotropic effects have been postulated to confer additional benefits in preventing recurrent events beyond lipid lowering⁽¹⁶⁾. These robust data have led to a dramatic increase in statin prescriptions in real-world practice⁽⁸⁻¹⁰⁾. In the present study, most patients (97%) were discharged home on a statin, exemplifying excellent adherence to guidelines.

The 2013 ACC/AHA guideline for the management of STEMI recommend starting a statin, specifically high-dose atorvastatin, in all STEMI patients without contraindications before hospital discharge⁽³⁾. The current ESC guidelines for the management of dyslipidemia and the management of STEMI consider ACS patients at very high cardiovascular risk and recommend a goal to reduce LDL-C to <70 mg/dL and/or at least 50% reduction of LDL-C^(4,5). Despite the adoption of international guidelines, studies have shown that most patients in a real-world setting do not achieve their recommended LDL-C goal. The LTAP-II study in Thailand⁽¹⁰⁾ reported that in patients with stable coronary heart disease (CHD) and CHD equivalents only one-third of the patients achieved the LDL-C target of <100 mg/dL. More recent data from a Thai population of stable CHD patients⁽¹¹⁾, reported up to 74% of patients achieved their LDL-L goal of <100 mg/dL. The MAINTAIN registry from the US⁽⁹⁾ showed that the actual practice of lipid lowering therapy in ACS patients resulted in the LDL-C goal of <100 mg/dL in 71% of patients but the optional LDL-C goal \leq 70 mg/dL was achieved on only 31%. These findings are nearly identical with the present study. In the present study, the formulation of statin did not affect LDL-C target attainment. The two most commonly used statins were simvastatin and atorvastatin and the

choice was likely driven by the patient's insurance status as almost all patients who were under universal coverage received simvastatin. Several studies have demonstrated that atorvastatin and rosuvastatin have higher LDL-C lowering efficacy compared to simvastatin^(17,18). However, the median doses of simvastatin and atorvastatin used were both 20 mg/day, which was most likely suboptimal. Incremental dosage of atorvastatin results in greater efficacy from 35.7% to 52.2% LDL-C reduction with atorvastatin 10 and 80 mg/day, respectively⁽¹⁹⁾. A high-intensity statin regimen would most likely improve the treatment targets. Hence, the present study supports the recommendation that a more intensive dose of statins should be started at hospital discharge to attain the LDL-C target of <70 mg/dL^(4,5). This is further reinforced by the most recent ACC/AHA guidelines on the management of high cholesterol that recommends high-intensity statin that provides a 50% LDL-C reduction should be given to all patients with known atherosclerotic cardiovascular disease⁽²⁰⁾. Provocatively, the guidelines state that a target LDL-C is no longer recommended which has created considerable controversy in the medical community^(21,22).

Some possible explanations for the limitation of LDL-C goal achievement are as follows. First, financial constraints, as the more potent statin formulations are generally more costly and patients may not be reimbursed for their prescription. Second, physicians may defer optimization of medication until the outpatient setting. Third, in the acute phase of acute coronary syndrome the acute inflammatory reaction may alter lipid values to be lower than the baseline value⁽²³⁾. Lastly, physician inertia in applying evidence-based therapies into practice.

Conclusion

From this observational cohort study, most patients with STEMI are prescribed statin therapy at discharge. Despite this, the target LDL-C is attained in only one-third of the patients due to suboptimal statin dosing. The type of statin did not affect LDL-C goal attainment. High-dose statin therapy is underused in real-world clinical practice. These findings emphasize the opportunities to improve outcomes of STEMI patients with evidence-based therapies.

Limitations

The major limitation of the present study is that it is based on data derived from an observational

cohort study. The study is based on a patient population of STEMI that was treated at a single center, tertiary care academic hospital in Thailand which may not be representative of all Thais. Our study included only patients that had LDL-C data 3 months after hospital discharge, resulting in 18% of the patients being excluded from the analysis. Hence, the results on goal attainment may be higher than the usual practice in Thailand. Very few patients were prescribed highintensity statin; therefore, patients on moderate to high-intensity statin were combined and compared to those on a low intensity dose. There is lack of information on the patient's compliance, being switched from one statin to another and the effect of dietary control or exercise.

What is already know on this topic?

Most patients do not achieve the recommended LDL-C goal.

What this study adds?

The target LDL-C is attained in only one-third of patients after sustaining an ST segment elevation myocardial infarction due to suboptimal statin dosing.

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Potential conflicts of interest

None.

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การรักษาล่า LDL-cholesterol บรรลุตามเป้าหมายหลังภาวะหัวใจขาดเลือดเฉียบพลันชนิด ST ยก

วิวรรณ ทั้งสุบุตร, บัณฑิตา พงษ์ตัณฑกุล

ภูมิหลัง: ในผู้ป่วยที่มีความเสี่ยงต่อโรคหลอดเลือดหัวใจสูงมาก เป้าหมายการรักษาควรลดค่าไขมัน LDL-C ให้น้อยกว่า 70 มก./ดล. หรือลดลงอย่างน้อยร้อยละ 50 สำหรับผู้ป่วยโรคหลอดเลือดหัวใจขาดเลือดเฉียบพลันนั้นมีข้อมูลของยา atorvastatin ในขนาดสูง ว่าสามารถลดอัตราเสียชีวิตและอัตราการเกิดหัวใจขาดเลือด

วัตถุประสงค์: เพื่อศึกษาผู้ป่วยที่เป็นโรคหัวใจขาดเลือดเฉียบพลันชนิด ST ยก ในประเทศไทย เมื่อออกจากโรงพยาบาลว่าสามารถ ลดค่า LDL-C ได้บรรลุตามเป้าหมายเพียงใด และประเมินว่าชนิดของยาลดไขมัน statin มีผลต่อการบรรลุเป้าหมายหรือไม่

วัสดุและวิธีการ: ได้นำผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST ยก ที่อยู่ในการศึกษาแบบติดตาม ตั้งแต่ วันที่ 1 มิถุนายน พ.ศ. 2551 ถึง 31 พฤษภาคม พ.ศ. 2554 มาวิเคราะห์ โดยผู้ป่วยด้องไม่เสียชีวิตในโรงพยาบาลได้รับยา statin เมื่อออกจาก โรงพยาบาล และมีข้อมูลค่า LDL-C ในระยะติดตามผู้ป่วย ชนิดของยา statin แบ่งเป็นยา simvastatin หรือ ยา statin อื่น ๆ (ได้แก่ atorvastatin หรือ rosuvastatin)

ผลการสึกษา: ผู้ป่วยร้อยละ 97 (265 ใน 272 ราย) ได้รับยา statin เมื่อออกจากโรงพยาบาล เมื่อติดตามผู้ป่วยที่เวลา 3 เดือน มีจำนวนผู้ป่วย 216 ราย ที่มีค่า LDL-C ร้อยละ 75 เป็นเพศชาย อายุเฉลี่ย 60.5±12.2 ปี และค่าเฉลี่ยของ LDL-C 118.1±41.2 มก./ดล. ผู้ป่วยร้อยละ 73 (157 ราย) ได้รับยา simvastatin และร้อยละ 27 (59 ราย) ได้รับยา statin อื่น ๆ ค่ามัธยฐานของขนาดยาที่ผู้ป่วยได้รับดังนี้ simvastatin 20 มก. atorvastatin 20 มก. และ rosuvastatin 10 มก. ที่ระยะเวลา ดิดตามสามารถลดค่า LDL-C ตามเป้าหมาย LDL-C <70 มก./ดล. หรือ ลดลงมากกว่าหรือเท่ากับร้อยละ 50 ดังนี้ ร้อยละ 30.1 (65 ราย) ของผู้ป่วยทั้งหมด ร้อยละ 27.4 (43 ราย) ในผู้ป่วยที่ได้รับยา simvastatin และร้อยละ 37.3 (22 ราย) ที่ได้รับยา statin อื่น ๆ (p = 0.158 ยา simvastatin เทียบกับยา statin อื่น ๆ) เมื่อแบ่งผู้ป่วยตามขนาดของยา statin ผู้ป่วยที่ได้รับยา statin ขนาดปานกลางถึงขนาดสูง สามารถบรรลุค่า LDL-C ตามเป้าหมายได้มากกว่าผู้ป่วยที่ได้รับยา statin ในขนาดต่ำ (ร้อยละ 36.3 เทียบกับ ร้อยละ 24.3, p = 0.038)

สรุป: ผู้ป่วยโรคหัวใจขาดเลือดเฉียบพลันชนิด ST ยก ส่วนใหญ่ได้รับยา statin เมื่อออกจากโรงพยาบาล แต่สามารถลดค่า LDL-C บรรลุตามเป้าหมายได้เพียงหนึ่งในสามของผู้ป่วย น่าจะเนื่องจากใช้ขนาดยาที่ต่ำ ชนิดของยา statin ไม่มีผลต่อการบรรลุเป้าหมาย LDL-C การใช้ยา statin ในเวชปฏิบัตินั้นใช้ในขนาดไม่สูงพอ การศึกษานี้แสดงถึงโอกาสพัฒนาการดูแลรักษาผู้ป่วยโรคหัวใจ ชนิดขาดเลือดเฉียบพลันชนิด ST ยก