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ST segment elevation myocardial infarction (STEMI) patients are more likely to achieve lipid-lowering treatment goals

A retrospective analysis of patients presenting with first acute coronary syndromes

Ünal Güntekin, MD[a], Veysel Tosun, MD[b,*], Ali Yaşar Kılınç, MD[a], Gündüzalp Saydam, MD[a], Necmettin Korucuk, MD[c], Mehmet Nuri Bozdemir, MD[d]

Abstract

Statin nonadherence or discontinuation is associated with increased cardiovascular events. Many factors related to the physicians or the patients are influential in this. We aimed to compare the compliance with statin therapy between the patients who first presented with ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UA) based on the target achievement according to the current dyslipidemia guidelines.

We retrospectively acquired all the information about demographic characteristics, in-hospital revascularization procedures, prescribed treatments, and index and up to 6-month follow-up laboratory results of the first acute coronary syndrome patients. Acute coronary syndrome patients were divided into 3 groups as STEMI, NSTEMI, and UA.

The STEMI group consisted of 260 patients, NSTEMI group consisted of 560 patients, and UA group consisted of 206 patients. Seventy-six percent of patients underwent percutaneous coronary interventions, 18.3% were managed medically, and 5.7% were referred for coronary artery bypass grafting. There was a significant decrease in low-density lipoprotein-cholesterol (LDL-C) values with the statin treatment at the follow-up in all 3 groups (for all $P < .001$). In the STEMI group, the percentage of those achieving the target LDL-C level was significantly higher than those who did not achieve the target according to both The American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology dyslipidemia guidelines. The LDL-C target achievement rates were also higher in the STEMI group than in the NSTEMI and UA groups.

Our study concluded that statin treatment goals were more attained in STEMI patients than NSTEMI and UA. All physicians should encourage lifelong intensive statin treatment in UA and NSTEMI patients such as STEMI patients.

Abbreviations: ACC/AHA = The American College of Cardiology/American Heart Association, ACS = acute coronary syndrome, ALT = alanine aminotransferase, AST = aspartate aminotransferase, CABG = coronary arteries bypass grafting, CAD = coronary artery disease, DM = diabetes mellitus, ESC = European Society of Cardiology/European Atherosclerosis Society, HDL-C = high-density lipoprotein-cholesterol, HT = hypertension, LDL-C = low-density lipoprotein-cholesterol, NSTEMI = non-ST-elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction, TG = triglycerides, UA = unstable angina pectoris.

Keywords: angina pectoris, dyslipidemia, LDL, lipoproteins, non-ST elevation myocardial infarction, ST elevation myocardial infarction

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[a] Department of Cardiology, Akdeniz University Faculty of Medicine, Antalya, [b] Department of Cardiology, Şanlıurfa Education and Research Hospital, Şanlıurfa, [c] Department of Cardiology, Private Medical Park Hospital, [d] Department of Emergency Medicine, Antalya Education and Research Hospital, Antalya, Turkey.

[*] Correspondence: Veysel Tosun, Department of Cardiology, Şanlıurfa Education and Research Hospital, Yenice Boulevard, Şanlıurfa 63200, Turkey (e-mail: veyseltosun8810@gmail.com).

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1. Introduction

Dyslipidemia is a major risk factor for coronary artery disease (CAD) such as hypertension (HT), diabetes mellitus (DM), smoking, and familial disposition. Dyslipidemia is a modifiable risk factor and statins have been used safely as lipid-lowering therapy for primary and secondary prevention for decades. Long-term HMG-COA (5-hydroxy-3-methylglutaryl-coenzyme A) reductase inhibitor (statin) therapy reduces the risk of CAD, peripheral artery disease, stroke, and myocardial infarction.[1–3] Although benefit has been demonstrated even with short-term use, maximal benefit requires persistent use of the drugs and extended studies indicate that benefit increases the longer the drug is taken.[4,5] The full benefit of statins is generally not realized as a result of poor patient adherence.[6] Statin non-adherence and discontinuation was associated with increased cardiovascular events.[7–9] Factors such as disregarding physicians' instructions, miscommunication with patients, levels of education of the patients, financial constraints, and lack of

follow-up after the first prescription are reasons for poor statin therapy adherence.

The concept of acute coronary syndromes (ACS) encompasses ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UA). STEMI patients should undergo rapid revascularization therapy within 90 to 120 minutes according to the door-to-balloon time and followed up in coronary intensive care units, while STEMI and UA patients may undergo coronary revascularization within 24 to 36 hours.[10,11]

Adherence to statin drugs in the real world is known to be very poor between different ACS types. We aimed to compare the frequency of compliance with statin therapy between STEMI, NSTEMI, and UA patients based on the target achievement according to the current ACC/AHA (The American College of Cardiology/American Heart Association) and ESC (European Society of Cardiology/European Atherosclerosis Society) guidelines.[12,13]

2. Methods

2.1. Source of data

We obtained all information from our university database. Hospital discharge abstracts pertaining to index admission, demographic characteristics, in-hospital revascularization procedures, index, and follow-up laboratory results were compiled from database. Statin use was determined using the electronical prescription claims database, which contains information on in-hospital and outpatient prescription drug use. The cohort consisted of patients aged between 31 and 82 years old getting diagnosis of STEMI, NSTEMI, and UA between February 2014 and December 2016 who were survived at least 6 months and followed-up in outpatient clinic after hospitalization. The patients who had been prescribed atorvastatin and rosuvastatin were used for analysis, because the rates of other statins (pravastatin, simvastatin, atorvastatin 10 mg, and rosuvastatin 10 mg) being prescribed were very low for statistical analysis. First laboratory results were obtained from initial hospitalization before first statin intake; second laboratory results were obtained from follow-up visit outpatient laboratory results 3 to 6 months after initial hospitalization. The protocol design was approved by the local institutional Research Ethics Committees of our faculty of medicine.

2.2. Patient population and definitions

ACS was diagnosed in compliance with the guidelines, in cases where along with typical symptoms presented by patients. The following syndromes were observed:

(1) Preserved ST segment elevation in specific adjacent ECG leads was grouped as STEMI.[10] These patients had undergone coronary angiography within 90 minutes according to the door-to-balloon time.
(2) Nonpreserved ST segment elevation in ECG but with increasing myocardial ischemia marker levels in laboratory tests was grouped as NSTEMI.[11] These patients had undergone coronary angiography within 24 to 36 hours.
(3) Nonpreserved ST segment elevation in ECG with no increasing myocardial ischemia marker levels in laboratory tests was grouped as UA.[11] These patients had also undergone coronary angiography within 24 to 36 hours.

All the patients had undergone cardiac coronary catheterization and revascularization was performed with percutaneous coronary intervention (PCI) or coronary arteries bypass grafting (CABG). In addition, all the patients were very high risk group according to the actual ESC and ACC/AHA guidelines. Patients whose laboratory and prescription data were not within the specified period, ACS patients followed with medical therapy without coronary angiography, patients undergoing elective coronary angiography, patients having severe comorbid diseases such as severe liver or renal dysfunction, and patients having a history of previous CAD or ACS or previous statin usage were not included in the study.

Cholesterol measurements were obtained by venous blood analysis with a fasting more than 10 hours. Low-density lipoprotein-cholesterol (LDL-C) was calculated by Friedewald method and direct LDL-C measurements were performed when triglycerides (TGs) values were >400 mg/dL.[14] Target levels of all lipid fractions in pharmacologically treated patients were set in line with the ESC and ACC/AHA guidelines. Treating targets were LDL-C <70 mg/dL based on the ESC guideline or as a therapeutic response with approximately ≥50% reduction in LDL-C based on the ACC/AHA guideline with high-intensity statin treatment.

2.3. Statistical analysis

Basic parameters of descriptive statistics for the analyzed continuous variables were presented as mean ± standard deviation (SD) for normal distributions, or median with interquartile range for non-normal distributions. Qualitative variables were presented as numeric and percentage values. Normality of distribution was verified using the Shapiro–Wilks normality test. The comparison between groups regarding dependent variables were verified using the paired samples *t* test (for normally distributed variables) or the Wilcoxon Signed Rank test (for non-normally distributed variables). The 1-way analysis of variance (ANOVA) and Kruskal–Wallis tests were performed after assessment of distributions for more than 2 independent groups. The Pearson Chi-squared test was used for comparison of categorical variables. All *P* values were 2-sided and considered statistically significant when they were <.05. All tests were performed in the 22.0 SPSS for Windows (SPSS Inc., Chicago, IL).

3. Results

The basic characteristics and laboratory findings of analyzed groups are presented in Table 1. HT and DM frequencies were not different between all groups regardless of whether the target has been achieved or not (for all $P > .05$). Smoking rates were higher in the STEMI group than in NSTEMI and UA group ($P = .001$). NSTEMI and UA patients were older than STEMI patients ($P < .001$). Male sex percentage was higher in the STEMI group than in the other groups ($P = .009$). The majority of patients (76%) underwent PCIs, 18.3% were managed medically, and 5.7% were referred for coronary artery bypass grafting.

As it is summarized in Table 2, there was a decrease in LDL-C with the statin treatment in all 3 groups regardless of whether the target has been achieved or not (for all $P < .001$). No statistically significant changes were observed in high-density lipoprotein-cholesterol (HDL-C) and TG with the statin treatment within all 3 groups (for all $P > .05$). There was no significant change in alanine aminotransferase (ALT) in the STEMI and NSTEMI groups (for both $P > .05$). There was a significant increase in ALT

Table 1

Demographic and clinical characteristics of acute coronary syndrome groups.

Variables	STEMI (n = 260)	NSTEMI (n = 560)	UA (n = 206)	*P*
Age, y	58.1 ± 12.2	63.9 ± 11.9	61.7 ± 10.2	**< .001**[*] **.031**[†] .097[‡]
Male n (%)	203 (78.1)	418 (74.6)	135 (65.5)	.642[*] .086[†] **.009**[‡]
DM n (%)	66 (25.4%)	170 (30.3%)	65 (31.6%)	.355[*] .985[†] .375[‡]
HT n (%)	63 (24.2%)	144 (25.7%)	49 (23.8%)	.956[*] .927[†] .999[‡]
Smoking n (%)	88 (33.8%)	118 (21.1%)	42 (20.4%)	**.003**[*] .996[†] **.001**[‡]

Bold data indicate statistical significance.

DM = diabetes mellitus, HT = hypertension, NSTEMI = non-ST segment elevation myocardial infarction, STEMI = ST segment elevation myocardial infarction, UA = unstable angina pectoris.

[*] *P* value between STEMI and NSTEMI.

[†] *P* value between NSTEMI and UA.

[‡] *P* value between STEMI and UA.

in the UA group ($P = .009$). In STEMI and NSTEMI groups, there was a significant reduction in aspartate aminotransferase (AST) ($P < .001$, $P = .003$, respectively) (Table 2).

In the STEMI group, according to the ACC/AHA dyslipidemia guidelines, the percentage of those achieving the target LDL-C level was significantly higher than those who did not achieve the target. However, in the NSTEMI and UA groups, the percentage of those achieving the target was significantly lower than those who did not achieve the target (41.1% vs 22%; 43.3% vs 57%; 15.6% vs 21%, respectively; $P < .001$). According to the ESC guidelines, in the STEMI group, the percentage of those achieving the target was significantly higher than those who did not achieve the target, too. Conversely, in the NSTEMI and UA groups, the percentage of those achieving the target was significantly lower than those who did not achieve the target (29.2% vs 22.6%; 53.5% vs 55.3%; 17.2% vs 22.1%, respectively; $P = .024$). When we compared between groups by the post hoc analysis according to the ESC guidelines, the target achievement rates were higher in the STEMI group than in the UA group ($P = .022$). There was no significant difference between the NSTEMI and the UA group in terms of LDL-C target achievement ($P = .480$). When we compared between groups by the post hoc analysis according to the ACC/AHA guidelines, the LDL-C target achievement rates were higher in the STEMI group than in the NSTEMI and UA groups (for both $P < .001$). In addition, the LDL-C target achievement rates were higher in the NSTEMI group than in the UA group ($P < .001$) (Table 3).

In terms of whether there is a difference between gender in LDL-C target achievement, there were no any differences between male and female according to both ACC/AHA and ESC dyslipidemia guidelines ($P = .119$; $P = .095$, respectively) (Table 4). In terms of whether there is a difference between type of statin in LDL-C target achievement, there were not any differences between type of statin according to both ACC/AHA and ESC dyslipidemia guidelines ($P = .662$; $P = .599$, respectively) (Table 5).

4. Discussion

This retrospective database analysis demonstrated that the rates of target LDL-C level achievement of statin treatment were higher in STEMI group patients than in NSTEMI and UA patients according to the both ACC/AHA and ESC guidelines. There was no relationship between sex and target achievement of statin treatment. In addition, there were no differences between type of statin and target achievement according to the both ACC/AHA and ESC guidelines.

Table 2

In-hospital and outpatient follow-up laboratory findings between acute coronary syndrome groups.

	STEMI (n = 260)			NSTEMI (n = 560)			UA (n = 206)		
Variables	Pre-statin	Post-statin	*P*	Pre-statin	Post-statin	*P*	Pre-statin	Post-statin	*P*
LDL-C, mg/dL	126.6 ± 33.8	80.73 ± 25.8	**< .001**	122.1 ± 37.8	85.4 ± 28.9	**< .001**	116.8 ± 39.8	87.0 ± 25.0	**< .001**
HDL-C, mg/dL	39.6 ± 11.5	40.1 ± 12.2	.429	40.1 ± 11.8	40.9 ± 12.2	.380	41.8 ± 14.7	40.3 ± 11.6	.079
TG, mg/dL	167.4 (96.0–188.0)	150.5 (94.2–190.0)	.437	168.4 (87.5–201.0)	161.8 (98.0–209.0)	.305	176.6 (100.0–217.0)	184.2 (106.0–241.0)	.356
ALT, U/L	30.8 (16.0–31.0)	25.8 (16.0–32.2)	.097	23.5 (14.0–27.0)	24.0 (15.0–26.0)	.514	21.1 (14.0–22.2)	23.9 (16.0–27.0)	**.009**
AST, U/L	45.3 (20.0–42.0)	26.5 (18.0–28.2)	**< .001**	30.9 (19.0–33.0)	24.8 (18.0–26.0)	**< .003**	22.9 (17.0–26.0)	23.5 (18.0–25.2)	.051
Creatinine, mg/dL	1.1 ± 0.5	1.2 ± 0.4	.672	1.2 ± 0.5	1.1 ± 0.6	.574	1.0 ± 0.5	0.9 ± 0.4	.342

Bold data indicate statistical significance.

ALT = alanine aminotransferase, AST = aspartate aminotransferase, DM = diabetes mellitus, HDL-C = high-density lipoprotein cholesterol, HT = hypertension, LDL-C = low-density lipoprotein cholesterol, NSTEMI = non-ST segment elevation myocardial infarction, STEMI = ST segment elevation myocardial infarction, TG = triglyceride, UA = unstable angina pectoris.

Table 3

Comparison of target achievement percentages between acute coronary syndrome groups according to the ACC/AHA and ESC dyslipidemia guidelines.

			Acute coronary syndrome type			
			STEMI	Non-STEMI	UA	Total
Target (ACC/AHA guidelines)	No	N (%)	186 (22)	482 (57)	178 (21)	846 (100)
	Yes	N (%)	74 (41.1)	78 (43.3)	28 (15.6)	180 (100)
Total		N (%)	260 (25.3)	560 (54.6)	206 (20.1)	1026 (100)
Target (ESC guidelines)	No	N (%)	136 (22.6)	333 (55.3)	133 (22.1)	602 (100)
	Yes	N (%)	124 (29.2)	227 (53.5)	73 (17.2)	424 (100)
Total		N (%)	260 (25.3)	560 (54.6)	206 (20.1)	1026 (100)

For ACC/AHA guidelines: χ^2 (2, N = 1026) = 28.70, $P < .001$.
For ESC guidelines: χ^2 (2, N = 1026) = 7.43, $P = .024$.
ACC/AHA = The American College of Cardiology/American Heart Association, ESC = European Society of Cardiology/European Atherosclerosis Society guidelines, NSTEMI = non-ST segment elevation myocardial infarction, STEMI = ST segment elevation myocardial infarction, UA = unstable angina pectoris.

Table 4

Comparison of target achievement percentages between male and female patients according to the ACC/AHA and ESC dyslipidemia guidelines.

			ACC/AHA			ESC		
			No	Yes	Total	No	Yes	Total
Sex	Male	N (%)	615 (81.3)	141 (18.7)	756 (100)	432 (57.1)	324 (42.9)	756 (100)
	Female	N (%)	231 (%)	39 (14.4)	270 (100)	170 (63)	100 (37)	270 (100)
Total		N (%)	846 (82.5)	180 (17.5)	1026 (100)	602 (58.7)	424 (41.3)	1026 (100)

For ACC/AHA guidelines: χ^2 (1, N = 1026) = 2.43, $P = .119$.
For ESC guidelines: χ^2 (1, N = 1026) = 2.78, $P = .095$.
ACC/AHA = The American College of Cardiology/American Heart Association, ESC = European Society of Cardiology/European Atherosclerosis Society guidelines.

HMG-COA reductase inhibitors (statins) are the most effective and inexpensive lipid-lowering treatment with a low risk of side effects in primary and secondary prevention of cardiovascular events.[15–18] A significant mortality reduction has been demonstrated in numerous randomized controlled trials, many observational studies, and meta-analyses. Currently, the European and American dyslipidemia guidelines suggest statins after ACS.[12,13] A reduction of LDL-C levels by 1 mmol/L results in a decrease in cardiovascular mortality and in the occurrence of the nonfatal myocardial infarction by 20% to 25%.[19]

Statins are being prescribed approximately 95% to 98.3% of patients after ACS.[20,21] Among with cardiovascular disease patients taking statins, 43% of the European patients and 64% of United States patients do not reach their target LDL-C levels.[12,13] Fifteen to 40% of patients with a diagnosed CAD stop taking medicine during the first year of treatment, 20–64% during the second or third year of treatment, and after 5 years less than 45% of patients regularly take statins. Among patients not diagnosed with cardiovascular disease, these numbers are even more pessimistic.[22] According to a previous study, physicians' decision to stop the treatment is the most common cited reason of discontinuation. Side effects, perception that medication was unnecessary, and medication costs are the other uncommon reported reasons of discontinuation.[21] In addition, older patients compared with younger, and married patients compared with nonmarried were more likely to discontinue statin. No significant differences were found according to the educational status in this study.[21] In another study, increasing age, psychiatric illnesses, and increasing numbers of recurrent admissions within the year following ACS remained as independent determinants of poorer statin continuation.[3] We aimed to investigate whether there is any difference in the statin continuity between the MI groups unlike these factors, because a comparison was made in only 1 previous study between the

Table 5

Comparison of target achievement percentages between statin groups according to the ACC/AHA and ESC dyslipidemia guidelines.

			ACC/AHA			ESC		
			No	Yes	Total	No	Yes	Total
Statin	Atorvastatin 20	N (%)	145 (60.7)	94 (39.3)	239 (100)	199 (83.3)	40 (16.7)	239 (100)
	Atorvastatin 40	N (%)	175 (60.3)	115 (39.7)	290 (100)	240 (82.8)	50 (12.7)	290 (100)
	Atorvastatin 80	N (%)	115 (54.8)	95 (45.2)	210 (100)	174 (82.9)	36 (17.1)	210 (100)
	Rosuvastatin 20	N (%)	96 (56.8)	73 (43.2)	169 (100)	142 (84)	27 (16)	169 (100)
	Rosuvastatin 40	N (%)	71 (60.2)	47 (39.8)	118 (100)	91 (77.1)	27 (22.9)	118 (100)
Total		N (%)	602 (58.7)	424 (41.3)	1026 (100)	846 (82.5)	180 (17.5)	1026 (100)

For ACC/AHA guidelines: χ^2 (4, N = 1026) = 2.40, $P = .662$.
For ESC guidelines: χ^2 (4, N = 1026) = 2.76, $P = .599$.
ACC/AHA = The American College of Cardiology/American Heart Association, ESC = European Society of Cardiology/European Atherosclerosis Society guidelines.

other evaluations with the backward bias and no significant results were observed. We found that STEMI patients are better to adapt to statin therapy and reach current guidelines goals. In addition, no significant relation was observed between the sex of the patients and the type of statin and achieving the treatment targets like other studies.[23,24]

ACS patients (especially STEMI) often report feelings of fear, vulnerability, loss of control, and worry about their risk of death.[25] About 12% of ACS patients had a positive post-traumatic stress disease (PTSD) related to their cardiac event.[25] From 15% to 20% of patients who have experienced myocardial infarction have a major depressive episode within a few days of the acute events, and about 25% develop minor depression or depressive mood.[26] Acute chest pain activates acute cardiac autonomic control and results in mental stress and anxiety. Those with more frequent pain episodes and those with higher pain scores have higher distress and fear of dying.[27] This stress anxiety and fear of death might cause patients to greater adaptation to the physicians' recommendations, lifestyle changes, and the continuity of drug treatment.

There was no significant change in ALT value in the STEMI and NSTEMI groups. Only a significant increase in ALT was observed in the UA group in the follow-up. There was a significant decrease in AST in the STEMI and NSTEMI groups. It is estimated that index AST elevation foreground may be secondary to the damage seen in myocardial infarction as other myocardial damage biomarkers. It is wrong to be associated with statin therapy. If LDH values were also found, supporting findings could be obtained. On the contrary, it may be thought that as global stress during UA may be less, the increase in ALT may be associated with statin treatment.

Our study has some limitations. The most important one is that our study was a retrospective study. Additional clinical variables such as echocardiographic parameters, patients' ethnicity, socioeconomic levels, and clinical presentations (risk scores, arrhythmia episodes, cardiogenic shock, etc) data were not evaluated in the study. The psychological and psychiatric illnesses of patients were unknown. In addition, we had no information on other actual lifestyle behaviors (smoking cessation, diet, and physical activity). These factors might play a role for drug continuation and target achievement. The longer follow-up (up to 3 years) of the patients could able to make our study stronger.

In conclusion, we found that statin treatment goals were more attained in STEMI patients than NSTEMI and UA. According to NSTEMI and UA in STEMI patients, the attainment of treatment goals may be due to the more serious approach of the physicians and the patients' fear of death. All physicians need to comply with the current guidelines and encourage lifelong intensive statin treatment in UA and NSTEMI patients like STEMI patients. It would be beneficial to support this topic with prospective studies.

Author contributions

Conceptualization: veysel tosun.
Data curation: veysel tosun, Ali Yaşar Kılınç, Gündüzalp Saydam.
Formal analysis: veysel tosun.
Investigation: veysel tosun, Gündüzalp Saydam.
Methodology: Ünal Güntekin, veysel tosun, Ali Yaşar Kılınç, Gündüzalp Saydam, Necmettin Korucuk.
Project administration: Ünal Güntekin, veysel tosun, Ali Yaşar Kılınç, Gündüzalp Saydam.
Resources: Ünal Güntekin, veysel tosun, Ali Yaşar Kılınç, Gündüzalp Saydam.
Software: veysel tosun, Ali Yaşar Kılınç, Gündüzalp Saydam.
Supervision: Ünal Güntekin, Necmettin Korucuk, Mehmet Nuri Bozdemir.
Validation: Necmettin Korucuk.
Visualization: Ünal Güntekin, Necmettin Korucuk.
Writing – original draft: veysel tosun, Necmettin Korucuk.
Writing – review & editing: veysel tosun, Necmettin Korucuk, Mehmet Nuri Bozdemir.

veysel tosun orcid: 0000-0001-7629-2108

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