Brief Report

Statin pretreatment and presentation patterns in patients with acute coronary syndromes

Marcelo Trivi, Ruth Henquin, Juan Costabel, Diego Conde

Cardiovascular Institute of Buenos Aires, Buenos Aires, Argentina

Correspondence to: Marcelo Trivi. Blanco Encalada 1543, Buenos Aires 1428, Argentina. Email: mstrivi@icba.com.ar.

Abstract: Statin therapy stabilizes coronary plaque, and it could be associated with less ST elevation myocardial infarction (STEMI) and acute myocardial infarction (AMI) [which includes, STEMI + non-STEMI (NSTEMI)], among patients presenting acute coronary syndromes (ACS). The aim of this study was to determine any association between prior use of statins and presentation patterns in 1,322 ACS patients admitted between 2014 and 2016: STEMI [247], NSTEMI [461] or unstable angina (UA) [614]. Coronary risk factors, history and chronic use of statins, aspirin and beta blockers were collected. Uni, multivariable and propensity score analysis were performed. About half (46%) of the patients received statins but only 14% high doses. UA patients received more statins and higher doses =335 (54%)/117 (19%) compared to NSTEMI =189 (40%)/49 (11%), and STEMI =77 (31%)/21 (9%), P<0.0001. Statin use was independently associated with a lower probability of STEMI [*vs.* NSTEMI/UA, odds ratio (OR) =0.70, 95% CI: 0.50–0.97, P=0.03] or AMI (*vs.* UA, OR=0.66, 95% CI: 0.51–0.84, P<0.01). Results were confirmed by propensity score analysis (OR=0.739, 95% CI: 0.588–0.922, P<0.01). Pretreatment with statins in ACSs was more associated with UA than with myocardial infarction. This could be a way of coronary atherosclerotic plaque's stabilization.

Keywords: Coronary artery disease; myocardial infarction; unstable angina (UA); cholesterol lowering drugs; drug therapy

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Introduction

Statins reduce cardiovascular events in patients with hypercholesterolemia (1). This benefit could be related to atherosclerotic plaque stabilization at coronary level (2).

It has recently been observed that the type of presentation of acute coronary syndromes (ACS) could be conditioned by statin therapy: patients treated with statins would be less likely to develop ST elevation myocardial infarction (STEMI, more associated with total occlusion of the culprit vessel and greater amount of myocardial necrosis) than the other forms, non-STEMI (NSTEMI) and unstable angina (UA) (3). In other words, statins may be protective of STEMI, if any ACS develops.

However, patients who present STEMI are younger and have lesser history of coronary artery disease than other forms of ACS, they receive fewer statins at lower doses. This situation must to be taken into account because it is a strong confounder. Alternatively, statins may protect not only from STEMI but also from total myocardial infarction (STEMI + NSTEMI) favoring presentation as UA (4). The aim of this study was to analyze whether there is an association between previous use of statins and the presentation of ACS, including STEMI and acute myocardial infarction (AMI).

Methods

It was analyzed a retrospective cohort of 1,322 patients hospitalized for ACS between 2014 and 2016. They were classified as STEMI [247], NSTEMI [461] or AU [614] according to the 3rd universal definition of myocardial

Table 1 Clinical characteristics and presentation of ACS

Variable	STEMI [247]	NSTEMI [461]	UA [614]	P
Age	64±11	68±13	68±11	0.0001
Female	48 (20%)	105 (23%)	168 (27%)	0.0032
Hypertension	142 (57%)	297 (64%)	439 (71%)	0.0001
Hypercholesterolemia	161 (64%)	369 (80%)	475 (77%)	<0.0001#
Smoking	172 (69%)	278 (60%)	394 (64%)	0.054
Diabetes	41 (16%)	105 (22%)	141 (22%)	0.06
Familiar history	52 (20%)	89 (19%)	162 (26%)	0.018
Prior AMI	41 (16%)	111 (24%)	185 (30%)	0.014#
Prior PCI	36 (14%)	124 (27%)	249 (40%)	<0.0001#
Prior coronary surgery	11 (4%)	47 (10%)	82 (13%)	0.001/0.06#
Statins	77 (31%)	189 (40%)	335 (54%)	<0.0001#
High dose statins	21 (9%)	49 (11%)	117 (19%)	<0.0001#
Aspirin	86 (35%)	206 (46%)	358 (59%)	<0.0001#
Beta blockers	63 (26%)	181 (40%)	289 (48%)	0.005#

Multiple chi square. #, chi square trend. ACS, acute coronary syndrome; STEMI, ST elevation myocardial infarction; NSTEMI, non-STEMI; UA, unstable angina; AMI, acute myocardial infarction.

infarction (5) using high-sensitive cardiac T troponin with upper reference limit =14 ng/L representing the 99th percentile for this technique. Information of coronary risk factors, prior history of myocardial infarction or previous revascularization, chronic angina, and use of statins prior to admission (considering high doses when receiving at least atorvastatin 40 mg or rosuvastatin 20 mg), and other drugs that might condition the presentation of ACS, such as aspirin and beta-blockers, were collected. The protocol was approved by the institutional ethics committee

Statistical analysis

Values are expressed as mean ± standard deviation or median and interquartile range and they were compared by parametric tests or Kruskal Wallis as appropriate. Categorical variables were compared with the simple chi square test with Yates correction, chi square trend or multiple chi-square. To assess the effect of previous statins on the presentation of ACS, logistic regression analysis and propensity score (weighting) were performed. The program used (STATA/SE 11.2 for Windows) rejected the variable "previous angioplasty" among the variables of the propensity score model by collinearity (all patients with previous angioplasty received statins).

Results

The mean age was 67±12 years and 1,001 subjects (76%) were male. Clinical characteristics in the three types of ACS were compared in *Table 1*.

Patients with UA were older, more women and they had more coronary risk factors and cardiovascular history than the others.

There was a clear trend towards greater use of statins, aspirin and beta blockers in UA patients, followed by NSTEMI and STEMI (*Figure 1*).

On the other hand, patients receiving statins (45%) had more coronary risk factors and cardiovascular events too, but less STEMI, NSTEMI and AMI compared with those statins naive (*Table 2* and *Figure 1*).

In logistic regression analysis (*Table 3*), pre-treatment with statins was statistically associated with a lower incidence of STEMI and AMI and higher incidence of UA as a form of presentation of ACS. The same was seen with pre-treatment with aspirin but not with beta-blockers to predict AMI.

In order to analyze the effect of statins in such different

Table 2 Clinical characteristics and use of statins prior to admission

Variable	Statins [601]	Statins naive [721]	P
Age	68±11	66±12	<0.05
Female	127 (21%)	195 (27%)	<0.05
Hypercholesterolemia	530 (88%)	401 (56%)	<0.001
Hypertension	462 (77%)	479 (39%)	<0.001
Diabetes	125 (25%)	142 (20%)	<0.02
Prior AMI	211 (35%)	126 (17%)	<0.001
Prior PCI	283 (47%)	126 (17%)	<0.001
Prior coronary surgery	94 (16%)	46 (6%)	<0.001
Chronic angina	53 (9%)	34 (5%)	<0.05
ACS type			
AMI	267 (44%)	442 (61%)	<0.001
STEMI	78 (13%)	170 (23%)	<0.001
NSTEMI	189 (31%)	273 (38%)	<0.02
UA	335 (56%)	280 (39%)	<0.001

AMI, acute myocardial infarction; STEMI, ST elevation myocardial infarction; NSTEMI, non-STEMI; UA, unstable angina.

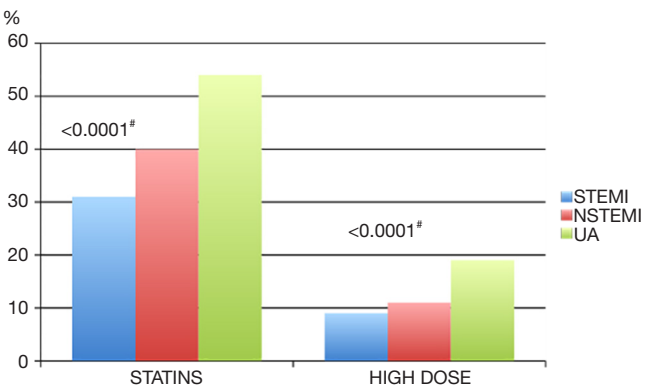

Figure 1 Previous statins use and type of ACS. #, Chi square trends between groups. ACS, acute coronary syndrome; STEMI, ST elevation myocardial infarction; NSTEMI, non-STEMI; UA, unstable angina.

samples, the propensity score was used in order to obtain more comparable samples. After adjustment by propensity score, statin therapy continued to be independently associated with a lower incidence of AMI: propensity score weighting (IPTW) [odds ratio (OR) =0.739, 95% CI: 0.588–0.922, P<0.01].

Discussion

ACS usually occurs as a result of a rupture of an atherosclerotic plaque in the coronary arteries. Cholesterol plays an important role in the genesis and frailty of this plaque.

Several studies suggest that pretreatment with statins reduces the likelihood of presenting as STEMI in the event of an ACS, probably because of a pleiotropic effect on plaque stabilization (6). However, as evidenced in our study and in previous ones, patients pretreated with statins are different from others, which hinder the comparison between groups.

Statin therapy is more frequently used for secondary prevention (after a cardiovascular event) than for primary prevention. It is not surprising that patients with prior myocardial infarction or coronary revascularization receive more statins than those at lower risk (7).

In our population, we observed more use of previous statins in UA, followed by NSTEMI and STEMI respectively. These may be related to prior cardiovascular events, because the same pattern was observed with other protective drugs, as aspirin or beta-blockers.

We hypothesized that previous use of statins could protect not only STEMI but also the whole AMI (STEMI and NSTEMI), and this was the basis of our analysis.

It is already stated in introduction, since this was a retrospective analysis we needed a special statistical treatment for the groups to be comparable. Logistic regression is aimed to get a better balance of the variables, logistic regression controls the confounder effect of several variables, but it not makes comparable samples.

The propensity score is so the right method to control sample difference bias. However, one important variable as prior coronary angioplasty could not be taken into account due to high collinearity between use of statins and angioplasty. So, the propensity score did not take this variable to make more comparable the samples. Anyway, among UA patients without previous angioplasty, chronic statin use was significant more frequent than the others.

In our study, the use of statins was independently associated with less AMI and UA as presentation pattern of ACS, both by multiple logistic regression and by propensity score analysis. Moreover, prior aspirin use followed the same pattern, but not the prior use of beta-blockers.

Gottlieb *et al.* (3) analyzed data from the ACSs survey in large population in Israel and they found similar results using propensity score too: STEMI had lesser previous

Table 3 Multivariable predictors for STEMI and AMI

Parameter	STEMI			AMI		
	Odds ratio	95% CI	P (>|Z|)	Odds ratio	95% CI	P (>|Z|)
Age	0.986	0.973–0.999	0.0364	1.002	0.992–1.013	0.627
Gender (male)	1.515	1.055–2.176	0.0246	1.617	1.234–2.120	0.0005
Hypertension	0.672	0.486–0.927	0.0156	0.764	0.578–1.010	0.0583
Hypercholesterolemia	0.852	0.612–1.185	0.3417	0.810	0.613–1.069	0.1371
Smoking	1.474	1.079–2.015	0.0149	1.035	0.814–1.315	0.7785
Diabetes mellitus	0.860	0.581–1.273	0.4525	1.002	0.756–1.328	0.9901
Family history	0.818	0.572–1.171	0.2729	0.743	0.565–0.978	0.0342
Prior MI	0.921	0.612–1.385	0.6914	1.032	0.775–1.375	0.8283
Prior angioplasty	0.487	0.317–0.746	0.001	0.567	0.426–0.754	<0.0001
Prior coronary surgery	0.579	0.299–1.121	0.1051	0.785	0.533–1.154	0.2187
Chronic angina	0.099	0.020–0.482	0.0042	–	–	–
Prior statins	0.701	0.500–0.981	0.0385	0.729	0.561–0.947	0.0195
Prior aspirin	–	–	–	0.730	0.559–0.952	0.0203
Prior beta blockers	–	–	–	0.924	0.712–1.198	0.5495

STEMI, ST elevation myocardial infarction; AMI, acute myocardial infarction.

statins than NSTEMI and UA, but they did not analyze total AMI. Even more, statin use was better correlated with type of ACS than cholesterol level at admission. Ndrepepa *et al.* (4) observed at cath lab less ACS among patients receiving chronic statins. Statin intolerance has recently been observed to be associated with a poor prognosis (8) and this may be related to lack of benefits of these drugs. Patients pretreated with statins before STEMI would have a better outcome (9) and lower in-hospital and out-of-hospital mortality rate (10,11).

Limitations

the main weak of the study is, as common is this type of studies, to have non-comparable samples, which introduce a bias. Although bias could not be deal with statistics, propensity score technic helps with it. The low percentage of STEMI and high doses of statins prevented a more specific analysis in these subgroups. Another problem is the impossibility to score by previous coronary angioplasty.

Conclusions

Pretreatment with statins was associated with a more benign presentation in ACSs, more like UA (without elevation of biomarkers) than with AMI. This could be a way of coronary atherosclerotic plaque's stabilization.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jxym.2017.08.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Chou R, Dana T, Blazina I, et al. Statins for Prevention of Cardiovascular Disease in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2016;316:2008-24.
2. Takata K, Imaizumi S, Zhang B, et al. Stabilization of high-risk plaques. Cardiovasc Diagn Ther 2016;6:304-21.
3. Gottlieb S, Kolker S, Shlomo N, et al. Association between statin treatment and LDL-cholesterol levels on the rate of ST-elevation myocardial infarction among patients with acute coronary syndromes: ACS Israeli Survey (ACSIS) 2002-2010. Int J Cardiol 2016;210:133-8.
4. Ndrepepa G, Fusaro M, King L, et al. Statin pretreatment and presentation patterns in patients with coronary artery disease. Cardiol J 2013;20:52-8.
5. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. J Am Coll Cardiol 2012;60:1581-98.
6. Otsuka F, Hibi K, Kusama I, et al. Impact of statin pretreatment on the incidence of plaque rupture in ST-elevation acute myocardial infarction. Atherosclerosis 2010;213:505-11.
7. Moran L, Fugate T, Xiang Y, et al. Statin pretreatment is protective despite an association with greater coronary artery disease burden in patients presenting with a first ST-elevation myocardial infarction. Prev Cardiol 2008;11:21-5.
8. Serban MC, Colantonio LD, Manthripragada AD, et al. Statin Intolerance and Risk of Coronary Heart Events and All-Cause Mortality Following Myocardial Infarction. J Am Coll Cardiol 2017;69:1386-95.
9. Mytas D, Zairis M, Karanasos A, et al. Effect of statin pretreatment on the outcome of ST-segment elevation myocardial infarction in patients without prior history of coronary artery disease. Hellenic J Cardiol 2013;54:422-8.
10. Lev EI, Kornowski R, Vaknin-Assa H, et al. Effect of previous treatment with statins on outcome of patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention. Am J Cardiol 2009;103:165-9.
11. Oduncu V, Erkol A, Kurt M, et al. The prognostic value of very low admission LDL-cholesterol levels in ST-segment elevation myocardial infarction compared in statin-pretreated and statin-naive patients

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