Effect of previous statin use on the incidence of sustained ventricular tachycardia and ventricular fibrillation in patients presenting with acute coronary syndrome

Akut koroner sendromlu hastalarda önceden statin kullanımının sürekli ventriküler taşikardi ve ventriküler fibrilasyon gelişimi üzerine etkisi

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ABSTRACT

Objective: Recent studies suggest that statins have anti-arrhythmic effects. The aim of this study was to evaluate the effects of statins on sustained ventricular tachycardia or ventricular fibrillation (S-VT or VF) in patients presenting with acute coronary syndrome (ACS).
Methods: The population of this study consisted of consecutive patients admitted to coronary care unit. It was an observational case-controlled retrospective analysis performed on prospective cohort. From a total of 1000 patients presenting with ACS, 241 were on and 759 were not on statin. Patient demographics, clinical characteristics and previous medical treatment including statins were recorded. A S-VT or VF episode during hospitalization was accepted as endpoint. Multiple logistic regression model was performed which considered the occurrence of S-VT or VF as the response variable.
Results: Sustained VT or VF occurred in 3.3% of patients in statin group and in 9% of patients in non-statin group. Univariate positive predictors of S-VT or VF were ST elevation myocardial infarction as clinical presentation, smoking and thrombolysis; univariate negative predictors of S-VT or VF were ejection fraction, use of acetylsalicylic acid before hospitalization, use of statin before hospitalization, initiation of clopidogrel at the hospital and normal coronary arteries. In the multiple logistic regression analysis, the only independent predictor of S-VT or VF was ejection fraction (OR 0.96; 95% CI 0.93 to 0.99; p=0.005).
Conclusion: Our results indicate that, although the incidence of S-VT/VF was significantly lower in patients with ACS and previous statin use; statin use is not an independent predictor of the occurrence of S-VT or VF in patients presenting with ACS.
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Key words: Statins, acute coronary syndrome, ventricular arrhythmia, logistic regression analysis

ÖZET

Amaç: Statinlerin antiaritmik etkileri son yıllardaki çalışmalarda gösterilmiştir. Bu çalışmada, akut koroner sendromu (AKS) olan hastalarda önceden statin kullanımının sürekli ventriküler taşikardi ve ventriküler fibrilasyon (S-VT ve VF) oluşması üzerine olan etkisi değerlendirildi.
Yöntemler: Akut koroner sendrom (AKS) tanısı ile müracaat eden hastalar çalışmaya dahil edildi. Prospektif kohortta gözlemsel vaka kontrollü retrospektif analiz yapıldı. Toplam 1000 hastanın arasında 241 hasta statin kullanmakta iken, 759 hasta statin kullanmamaktaydı. Hastaların demografik, klinik özellikleri ve kullanmakta oldukları ilaçlar (statin dahil) kaydedildi. Hastanede kalış süresince, sürekli VT ve VF epizodu oluşması sonlanım noktası olarak kabul edildi. Çoklu regresyon analizinde S-VT ve VF üzerine etkili faktörler değerlendirildi.
Bulgular: Statin kullanan hastaların %3.3'ünde statin kullanmayan hastaların %9'unda S-VT ve VF epizodu saptandı. Klinik tanının ST elevasyonlu miyokart enfarktüsü olması, sigara içimi, trombolitik tedavi yapılmış olması, S-VT ve VF oluşması için pozitif tek değişkenli göstergeleri olarak tespit edilirken, önceden asetil salisilik asit ve statin kullanımı, hastanede klopidogrel başlanması, ejeksiyon fraksiyonu ve normal koroner arterler sürekli S-VT ve VF oluşması için negatif tek değişkenli göstergeleri olarak bulundu. Çok değişkenli lojistik regresyon analizinde sürekli S-VT ve VF oluşmasında, ejeksiyon fraksiyonunun tek bağımsız belirteç olduğu tespit edildi (OR 0.96; %95 güven aralığı 0.93-0.99; p=0.005).

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Sonuç: Akut koroner sendromlu hastalarda, statin alan hastalar S-VT/VF sıklığı anlamlı olarak daha düşük olsa da; statin kullanımı S-VT ve VF oluşumu için bağımsız bir belirteç değildir.
(Anadolu Kardiyol Derg 2011 1: 22-8)
Anahtar kelimeler: Statinler, akut koroner sendrom, ventriküler aritmi, lojistik regresyon analizi

Introduction

Sudden cardiac death is the most frequent cause of death in industrialized countries (1, 2). The most common cause of sudden cardiac death is coronary artery disease (CAD) and the most common arrhythmias causing sudden cardiac death are ventricular tachycardia (VT) and ventricular fibrillation (VF) (2). Previous trials have suggested that statins may decrease the incidence of sudden cardiac death in patients with CAD (3-5). This beneficial effect of statins could partly be explained with their antiarrhythmic properties (6, 7).

However, conflicting results have been obtained about the effects of statins on ventricular arrhythmias (3, 4, 6, 8-21).

The aim of the present study was to examine the effect of previous statin use on the occurrence of sustained VT (S-VT) or VF in patients presenting with acute coronary syndrome (ACS).

Methods

Patients

The population of this study consisted of 1000 consecutive patients admitted to Coronary Care Unit between January 2004 and July 2007. It was an observational case-controlled retrospective analysis performed on prospective cohort. Calculation of the number of patients needed was based on the assumption of 5% and 10% rate of S-VT or VF in statin and non-statin groups, respectively. With an alpha level of 0.05 and a power of 0.80 it was necessary to include 474 patients in each group (total 948 patients).

Exclusion criteria included hyperthyroidism, moderate to severe rheumatic valvular disease, sepsis, documented previous S-VT and/or VF, patients taking antiarrhythmic drugs for other arrhythmias such as atrial fibrillation, accelerated idioventricular rhythm and polymorphic VT. Among the screened 1020 patients, 20 were excluded due to hyperthyroidism (n=7), moderate to severe rheumatic valvular disease (n=4), accelerated idioventricular rhythm (n=8) or sepsis (n=1).

Among the statin users, 154 were on atorvastatin, 27 on fluvastatin, 10 on pravastatin, 9 on rosuvastatin and 41 on simvastatin. The mean time between initiation of statin and index ACS was 258±256 days. All ACS patients (ST elevation or non-ST elevation myocardial infarction and unstable angina) were included.

Acute myocardial infarction was diagnosed based on the presence of chest pain and/or electrocardiographic changes suggestive of infarction or ischemia, associated with the increased level of cardiac enzymes to at least twice the upper limit of the normal value. Unstable angina was diagnosed based on the presence of ischemic symptoms that were new, accelerated or occurred at rest, and dynamic ST changes other than ST elevation, but without elevation of cardiac enzymes.

A transthoracic echocardiogram was recorded in each patient (22). Modified Simpson method was used for measuring ejection fraction (23). All the patients were treated according to the latest published guidelines and clinical practice. No primary percutaneous coronary intervention is performed in our centre. Therefore, thrombolytic treatment was used as reperfusion therapy.

Follow-up for ventricular tachycardia or ventricular fibrillation

Patients were followed prospectively with continuous electrocardiogram (ECG) monitoring during coronary care unit stay and with ECG taken twice daily in the wards for the occurrence of VF or monomorphic S-VT, which was defined as sustained ventricular tachycardia (the rate >120/min) lasting >30 seconds or requiring intervention. A S-VT or VF episode during hospitalization was accepted as endpoint. Multiple logistic regression model was performed which considered the occurrence of S-VT or VF as the response variable. The mean duration of the stay in the coronary care unit was 2 days and the mean duration of entire hospitalization was 5 days.

Statistical analysis

All the analyses were performed using SPSS 9.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean±SD and categorical variables were presented as percentages. Categorical variables were compared with Chi-square test. Continuous variables were compared with unpaired Student t-test.

Predictors of S-VT or VF were determined by multiple logistic regression analysis. Strength of association between variables and occurrence of S-VT or VF was represented by odds ratios (ORs) and their accompanying 95% confidence intervals (CIs). Demographic or clinical characteristics and procedural profile shown in Tables 1 and 2 were evaluated in a univariate analysis, and those with $p<0.15$ (gender, use of statin and use of acetyl salicylic acid before hospitalization, gender, ST-elevation myocardial infarction as clinical presentation, ejection fraction, smoking, diabetes mellitus, thrombolysis, initiation of clopidogrel in the hospital and normal coronary arteries) were then entered into a multiple logistic regression analysis. The identification of the predictors was based on a forward stepwise selection method. Normality of distribution was checked with Kolmogorov-Smirnov test and non-parametric test was required for the comparison of required energy for the convertion of VT into sinus rhythm. A p value of <0.05 (2-tailed) was considered significant.

Results

Patients

From a total of 1000 patients, 241 were on and 759 were not on statin treatment. Male gender and thrombolytic treatment were more frequent in non-statin group compared with statin group (both p<0.05). Diabetes mellitus, hypertension, previous percutaneous coronary intervention (PCI), previous coronary bypass graft (CABG), beta-blocker, angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and acetyl salicylic acid use before hospitalization and clopidogrel prescription at index hospitalization were more frequently encountered in statin group compared with non-statin group (all p<0.05). Ejection fraction was higher, total cholesterol and low-density lipoprotein cholesterol levels were lower in statin group compared with non-statin group (all p<0.05). Unstable angina/non-ST elevation myocardial infarction was more frequent in statin group and ST-elevation myocardial infarction was more frequent in non-statin group (p<0.05 for both) compared with statin group. Other demographic or clinical variables were similar in the both groups (all p>0.05, Tables 1, 2).

Ventricular tachycardia or ventricular fibrillation

Sixty-eight patients in non-statin group (9%) and 8 patients in statin group (3.3%) had developed S-VT or VF (Table 3, p=0.003). All VF cases were successfully converted into sinus rhythm with defibrillation. The methods and required energy to convert VT into sinus rhythm, occurrence of S-VT or VF in different clinical presentations and their occurrence within or beyond 48 h of presentation were similar in the both groups (Table 3, both p>0.05).

Comparison of patients with and without S-VT or VF during hospitalization (Table 4)

Smoking, thrombolytic treatment and ST-elevation myocardial infarction were more frequent and ejection fraction was lower in patients with S-VT or VF compared to those without S-VT or VF (p<0.05 for all). Clopidogrel prescription at index hospitalization, unstable angina/non-ST elevation myocardial infarction and normal coronary arteries at angiography were more frequently encountered in patients without arrhythmia compared to those with S-VT or VF (p<0.05 for all). Other demographic or clinical variables were similar in the both groups (all p>0.05).

Predictors of ventricular tachycardia/ventricular fibrillation (Table 5)

Univariate positive predictors of S-VT or VF were ST elevation myocardial infarction as clinical presentation (OR 3.39; 95% CI 1.90 to 6.05; p<0.0001), smoking (OR 1.79; 95% CI 1.09 to 2.94; p=0.02) and thrombolysis (OR 1.89; 95% CI 1.41 to 2.52; p<0.001); univariate negative predictors of S-VT or VF were ejection fraction (OR 0.94; 95% CI 0.92 to 0.97; p<0.0001), use of acetylsalicylic acid before hospitalization (OR 0.61; 95% CI 0.38 to 0.99; p=0.046), use of statin before hospitalization (OR 0.34; 95% CI

Table 1. Comparison of heart rate turbulence parameters between patient and control groups

Variables	Non-statin (n=759)	Statin (n=241)	p*
Age, years	62±12	61±11	0.89
Male gender, n (%)	597 (78.7)	158 (65.6)	<0.0001
Smoking, n (%)	423 (55.7)	120 (49.8)	0.11
Diabetes mellitus, n (%)	159 (20.9)	77 (32)	0.001
Hypertension, n (%)	377 (49.7)	173 (71.8)	<0.0001
Ejection fraction, %	41±11 (20-70)	46±13 (20-75)	<0.0001
Clinical presentation, n (%)			
Unstable AP/Non ST-elevation MI	369 (48.6)	180 (74.7)	<0.0001
ST-elevation MI	390 (51.4)	61 (25.3)	
Paroxysmal atrial fibrillation, n (%)	49 (6.5)	20 (8.3)	0.31
Previous PCI, n (%)	12 (1.6)	16 (6.6)	<0.0001
Previous CABG, n (%)	21 (2.8)	18 (7.5)	0.002
Previous MI, n (%)	5 (0.7)	1 (0.4)	1
PAD, n (%)	8 (1.1)	6 (2.5)	0.11
Chronic renal failure, n (%)	4 (0.5)	1 (1.7)	0.1
Cerebrovascular accident, n (%)	11 (1.4)	-	0.07
NYHA class II heart failure, n (%)	45 (5.9)	14 (5.8)	1
Prior therapies at index hospitalization, n (%)			
B-blocker	137 (18.1)	127 (52.7)	<0.0001
ACEI or ARB	170 (22.4)	121 (50.2)	<0.0001
Acetyl salicylic acid	281 (37)	198 (82.2)	<0.0001
Clopidogrel	28 (3.6)	23 (9.5)	0.53
Spironolactone	28 (3.6)	14 (5.8)	0.19
Prescribed therapies after index event, n (%)			
B-blocker	740 (97.5)	236 (97.9)	0.81
ACEI or ARB	603 (79.4)	203 (84.2)	0.11
Acetyl salicylic acid	750 (98.8)	237 (98.3)	0.52
Heparin	759 (100)	241 (100)	1
Clopidogrel	379 (49.9)	183 (75.9)	<0.0001
Thrombolysis	295 (38.8)	48 (19.9)	<0.0001
Streptokinase	190	33	
T-pa	105	15	
Total cholesterol, mg/dl	186±41	172±46	0.03
LDL cholesterol, mg/dl	111±49	94±41	0.005
HDL cholesterol, mg/dl	39±10	40±9	0.6
Triglyceride, mg/dl	147±68	147±65	0.9

Data are presented as mean ± SD (range) or numbers (percentages)
*Chi-square and unpaired Student's t test
ACEI - angiotensin-converting enzyme inhibitor, AP - angina pectoris, ARB - angiotensin receptor blocker, CABG - coronary artery bypass surgery, HDL - high-density lipoprotein, LDL - low-density lipoprotein, MI - myocardial infarction, PAD - peripheral artery disease, PCI - percutaneous coronary intervention, T-pa - tissue plasminogen activator

Table 2. Coronary angiography profile

Variables	Non-statin (n=759)	Statin (n=241)	p*
Coronary angiography, n	673	224	-
Normal coronary arteries, n (%)	126 (18.7)	32 (14.3)	0.15
Diseased vessel, n (%)			
Single-vessel	175 (32)	72 (37.5)	0.18
Multi-vessel	372 (68)	120 (62.5)	

Data are presented as numbers (percentages)
*Chi-square test

Table 3. Follow-up findings

Variables	Non-statin (n=759)	Statin (n=241)	p*
S-VT or VF, yes, n (%)	68 (9)	8 (3.3)	0.003
Methods used to convert VT into sinus, n (%)			
Spontaneous	14 (1.8)	1 (0.4)	0.08
Pharmacological	5 (0.7)	3 (1.2)	
Lidocaine	3 (0.4)	1 (0.4)	
Amiodarone	2 (0.3)	2 (0.8)	
Electrical cardioversion	34 (4.5)	4 (1.7)	
Required energy, J	249±98	192±106	0.42
Occurrence of S-VT or VF, n (%)			
In patients with USAP	13 (4.3)	2 (1.4)	0.16
In patients with NSTEMI	3 (4.1)	2 (4.7)	1
In patients with STEMI	52 (13.3)	4 (6.5)	0.2
Within 48 h of presentation	59 (7.8)	7 (2.9)	1
After 48 h of presentation	8 (1.1)	1 (0.4)	1

Data are presented as mean ± SD or numbers (percentages)
*Chi-square and Mann-Whitney U test
NSTEMI- non-ST- elevation myocardial infarction, STEMI - ST- elevation myocardial infarction, USAP- unstable angina pectoris, VF- ventricular fibrillation, VT- ventricular tachycardia

0.17 to 0.74; p=0.006), initiation of clopidogrel at the hospital (OR 0.29; 95% CI 0.17 to 0.48; p<0.001) and normal coronary arteries (OR 0.25; 95% CI 0.08 to 0.80; p=0.02). In the stepwise logistic regression analysis, the only independent predictor of S-VT or VF was ejection fraction (OR 0.96; 95% CI 0.93 to 0.99; p=0.005).

Discussion

Main findings

Our results indicate that statin use is not an independent predictor of the occurrence of S-VT or VF in patients presenting with ACS.

Coronary artery disease and ventricular arrhythmias

Both chronic CAD and ACS may cause sudden cardiac death mostly due to ventricular arrhythmias (24-26). Most commonly chronic CAD causes reentrant arrhythmias and ACS causes non-reentrant arrhythmias (1, 2, 24-26).

Statins, coronary artery disease and ventricular arrhythmias

Statin use was associated with a reduced probability of ventricular arrhythmias in patients with CAD and implantable cardioverter defibrillator implants (6, 8, 12-15), in patients with non-ischemic cardiomyopathy (12), and in patients who underwent revascularization procedures (11). Their use has also been associated with lower rate of mortality (13, 16, 27, 28), which could partly be explained by reduced rate of ventricular arrhythmias. On the other hand, statins have been found to be ineffective in preventing ventricular arrhythmias in patients with high-risk hypertension (4), resuscitated cardiac arrest in diabetic patients (29), or in patients with chronic CAD (3, 18-20). With respect to ACS, there are four positive (9, 10, 17, 30) and one negative previous studies (21) evaluating the effects of statins on ventricular arrhythmias. Statin administration following an acute myocardial infarction was associated with low incidence of VT/VF (9, 17) and late potentials (17) and withdrawal of statins after presentation of a non-ST-segment elevation myocardial infarction was associated with higher rates of ventricular arrhythmias (10). Lorenz et al. (30) have shown that under statin therapy, non-sustained VT occurring after acute ST-elevation myocardial infarction is not associated with an adverse long-term prognosis, however; in patients not on statin treatment, the occurrence of non-sustained VT is associated with marked increase in 1-year mortality. On the other hand, MIRACL study (21) indicated that atorvastatin did not decrease the incidence of resuscitated cardiac arrest in patients with unstable angina and non-Q wave myocardial infarction. Present study is in agreement with MIRACL study and indicates that previous statin use is not associated with the occurrence of VT/VF. Endpoint was resuscitated cardiac arrest in MIRACL study; however, it was sustained VT or VF in our study.

Present study is different from those four positive studies with some respects: Kayıkçıoğlu et al. (17) prospectively evaluated the effects of a specific statin at a specific dose. However, we evaluated different statins with different doses in an observational fashion. Although other three positive studies were observational (9, 10, 30), they were very large and only patients with ST-elevation or non-ST elevation myocardial infarction were included. Patients with unstable angina were included only in our study. Not all the statins may show the same effects on ventricular arrhythmias and they may show different effects in patients with unstable angina and myocardial infarction with respect to ventricular arrhythmias. These differences and low incidence of ventricular arrhythmias (for example, incidence of ventricular arrhythmia was 3.3% vs 9% in statin and non-statin groups in the present study, however it was 26% vs 63% in the study of Kayıkçıoğlu et al., 17) may explain the negative result in the present study as opposed to previous studies (9, 10, 17, 30). In theory, statins may be more effective in modulating scar-

Table 4. Comparison of patients with and without VT/VF during hospitalization

Variables	Without VT/VF (n=924)	With VT/VF (n=76)	p*
Age, years	61±11	62±12	0.42
Male gender, n (%)	691 (74.8)	64 (84.2)	0.07
Smoking, n (%)	492 (53.2)	51 (67.1)	0.02
Diabetes mellitus, n (%)	224 (24.2)	12 (15.8)	0.12
Hypertension, n (%)	502 (54.3)	46 (60.5)	0.3
Ejection fraction, %	43±12 (20-75)	36±10 (20-60)	<0.0001
Clinical presentation, n (%)			
Unstable AP/Non ST-elevation MI	529 (57.3)	20 (26.3)	<0.0001
ST-elevation MI	395 (42.7)	56 (73.7)	
NYHA Class II Heart failure, n (%)	51 (5.5)	8 (10.5)	0.8
Previous PCI, n (%)	24 (2.6)	4 (5.3)	0.15
Previous CABG, n (%)	37 (4)	2 (2.6)	0.76
Previous MI, n (%)	6 (0.6)	0	1
Peripheral artery disease, n (%)	12 (1.3)	2 (2.6)	0.28
Chronic renal failure, n (%)	8 (0.9)	0	1
Cerebrovascular accident, n (%)	8 (0.9)	3 (3.9)	0.45
Prior therapies at index hospitalization, n (%)			
B-blocker	244 (26.4)	20 (26.3)	1
ACEI or ARB	272 (29.4)	19 (25)	0.51
Acetyl salicylic acid	451 (48.8)	28 (36.8)	0.055
Clopidogrel	48 (5.2)	3 (3.9)	1
Spironolactone	37 (4)	5 (6.5)	0.24
Prescribed therapies after index event, n (%)			
B-blocker	901 (97.5)	75 (98.7)	1
ACEI or ARB	737 (79.8)	69 (90.8)	0.22
Acetyl salicylic acid	913 (98.8)	74 (97.4)	0.25
Heparin	924 (100)	76 (100)	1
Clopidogrel	540 (58.4)	22 (28.9)	<0.0001
Thrombolysis	299 (32.4)	43 (56.6)	<0.0001
Total cholesterol	184±42	183±46	0.83
LDL cholesterol	109±50	106±40	0.52
HDL cholesterol	40±10	38±10	0.27
Triglyceride	145±65	158±83	0.28
Coronary angiography, n (%)	840 (90.9)	57 (75)	
Normal coronary arteries, n (%)	155 (16.8)	3 (3.9)	0.01
Diseased vessel, n (%)			
Single-vessel	231 (25)	16 (21.1)	0.65
Multi-vessel	454 (49.1)	38 (50)	

Data are presented as mean±SD (range) or numbers (percentages)
*Chi- square test and unpaired Student t - test
ACEI - angiotensin-converting enzyme inhibitor, AP - angina pectoris, ARB - angiotensin receptor blocker, CABG - coronary artery bypass surgery, HDL - high-density lipoprotein, LDL - low-density lipoprotein, MI - myocardial infarction, PAD - peripheral artery disease, PCI - percutaneous coronary intervention, VF - ventricular fibrillation, VT - ventricular tachycardia

Table 5. Predictors of S-VT or VF

Variables	p	OR	95% CI
Positive univariate predictors			
Smoking	0.02	1.79	1.09 to 2.94
ST-elevation MI	<0.0001	3.39	1.90 to 6.05
Thrombolysis	<0.0001	1.89	1.41 to 2.52
Negative univariate predictors			
Ejection fraction	<0.0001	0.94	0.92 to 0.97
Previous acetyl salicylic acid use	0.046	0.61	0.38 to 0.99
Previous statin use	0.006	0.35	0.17 to 0.74
Normal coronary arteries	0.02	0.25	0.08 to 0.80
Prescription of clopidogrel at the hospital	<0.0001	0.29	0.17 to 0.48
Multivariate predictors			
Ejection fraction	0.005	0.96	0.93 to 0.99

Logistic regression analysis
MI - myocardial infarction, S-VT - sustained ventricular tachycardia, VF - ventricular fibrillation

related changes in chronic CAD and as in the present study, may be less effective in ACS where electrical instability is the principal mechanism (24-26). Cardioprotective agent use such as acetyl salicylic acid, beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers before hospitalization and clopidogrel use after hospitalization was lower in non-statin group, while thrombolytic use was lower and ejection fraction was higher in statin group. These medications and ejection fraction may change the probability of the occurrence of ventricular arrhythmias making it inconclusive for statin alone reducing the arrhythmias.

Potential mechanisms of action of statins on ventricular arrhythmias

Potential mechanisms of action of statins on ventricular arrhythmias include improvement of endothelial function, reduction of oxidative stress and modulation the autonomic nervous system and also their anti-ischemic, anti-inflammatory and direct anti-arrhythmic effects (2, 31).

Study limitations

There are major differences in the patient groups with and without statins such as diabetes mellitus, hypertension, clinical presentation, prior therapies and ejection fraction, which are the limitations inherent to an observational study. Since it was not a randomized, double-blind clinical trial, other unmeasured potential factors, which are predictors of ventricular arrhythmias might also be distributed unequally between two groups and might affect the results. Although sustained VT usually causes symptoms, some patients may have suffered asymptomatic episodes. Since the ECG recording on the wards was performed only twice a day, some cases may have been missed. We did not measure C- reactive protein, which is used as an indica-

tor of the tissue inflammation. The indiscriminate inclusion of patients with a large spectrum of doses and molecules of statins is an important drawback. Many patients with ACS and ventricular arrhythmias die suddenly and do not reach the hospital. However, mortality data is lacking and the study group was selected among survived patients. One of the limitations of our study is that we calculated the sample size with the assumption of equal sized groups; however, it is appeared that percentage of patients with acute coronary syndrome with previous statin use comprised only about 25% of patents. Although, we were able to demonstrate the significant difference in the incidence of VT/VF between patients with and without statin therapy before admission, further studies on the predictive value of statin use on larger number of patients should be performed.

Conclusion

Our results indicate that, although the incidence of S-VT/VF was significantly lower in patients with ACS and previous statin use; statin use is not an independent predictor of the occurrence of S-VT or VF in patients presenting with ACS.

Conflict of interest: None declared.

References

1. Müller D, Agrawal R, Arntz HR. How sudden is sudden cardiac death? Circulation 2006; 114: 1146-50.
2. Kostapanos MS, Liberopoulos EN, Goudevenos JA, Mikhailidis DP, Elisaf MS. Do statins have an antiarrhythmic activity? Cardiovasc Res 2007; 75: 10-20.
3. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-9.
4. Sever PS, Dahlöf B, Poulter NR, Wedel H, Beevers G, Caulfield M, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomized controlled trial. Lancet 2003; 361: 1149-58.
5. LIPID Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. N Engl J Med 1998; 339: 1349-57.
6. De Sutter J, Tavernier R, De Buyzere M, Jordaens L, De Backer G. Lipid lowering drugs and recurrences of life-threatening ventricular arrhythmias in high-risk patients. J Am Coll Cardiol 2000; 36: 766-72.
7. De Sutter J, Firsovaite V, Tavernier R. Prevention of sudden death in patients with coronary artery disease: do lipid-lowering drugs play a role? Prev Cardiol 2002; 5: 177-82.
8. Riahi S, Schmidt EB, Christensen JH, Heath F, Pedersen AK, Nielsen JC, et al. Statins, ventricular arrhythmias and heart rate variability in patients with implantable cardioverter defibrillators and coronary heart disease. Cardiology 2005; 104: 210-4.
9. Fonarow GC, Wright RS, Spencer FA, Fredrick PD, Dong W, Every N, et al. Effect of statin use within the first 24 hours of admission for acute myocardial infarction on early morbidity and mortality. Am J Cardiol 2005; 96: 611-6.
10. Spencer FA, Fonarow GC, Frederick PD, Wright RS, Every N, Goldberg RJ, et al. Early withdrawal of statin therapy in patients with non-ST-segment elevation myocardial infarction: National Registry of Myocardial Infarction. Arch Intern Med 2004; 164: 2162-8.
11. Dotani MI, Elnicki DM, Jain AC, Gibson CM. Effect of preoperative statin therapy and cardiac outcomes after coronary artery bypass grafting. Am J Cardiol 2000; 86: 1128-30.
12. Chiu JH, Abdelhadi RH, Chung MK, Gurm HS, Marrouche NF, Saliba WI, et al. Effect of statin therapy on risk of ventricular arrhythmia among patients with coronary artery disease and an implantable cardioverter-defibrillator. Am J Cardiol 2005; 95: 490-1.
13. Vyas AK, Guo H, Moss AJ, Olshansky B, McNitt SA, Hall WJ, et al. Reduction in ventricular tachyarrhythmias with statins in the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II. J Am Coll Cardiol 2006; 47: 769-73.
14. De Sutter J, De Bacquer D, Jordaens L. Intensive lipid-lowering therapy and ventricular arrhythmias in patients with coronary artery disease and internal cardioverter defibrillators. Heart Rhythm Society 2006 Scientific Sessions; May 17-20 2006; Boston, MA; 2006. (Abstract)
15. Mitchell LB, Powell JL, Gillis AM, Kehl V, Hallstrom AP; AVID Investigators. Are lipid-lowering drugs also antiarrhythmic drugs? An analysis of the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. J Am Coll Cardiol 2003; 42: 81-7.
16. Goldberger JJ, Subacius H, Schaechter A, Howard A, Berger R, Shalaby A, et al. Effects of statin therapy on arrhythmic events and survival in patients with nonischemic dilated cardiomyopathy. J Am Coll Cardiol 2006; 48: 1228-33.
17. Kayıkçıoğlu M, Can L, Evrengül H, Payzin S, Kültürsay H. The effect of statin therapy on ventricular late potentials in acute myocardial infarction. Int J Cardiol 2003; 90: 63-72.
18. Pedersen TR, Faergeman O, Kastelein JJ, Olsson AG, Tikkanen MJ, Holme I, et al.; Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) Study Group. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL Study: a randomized controlled trial. JAMA 2005; 294: 2437-45.
19. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med 2005; 352: 1425-35.
20. Koren MJ, Hunninghake DB; ALLIANCE Investigators. Clinical outcomes in managed-care patients with coronary heart disease treated aggressively in lipid-lowering disease management clinics: the ALLIANCE study. J Am Coll Cardiol 2004; 44: 1772-9.
21. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomised controlled trial. JAMA 2001; 285: 1711-8.
22. Solomon SD, Glynn RJ, Greaves S, Ajani U, Rouleau JL, Menapace F, et al. Recovery of ventricular function after myocardial infarction in the reperfusion era: the healing and early afterload reducing therapy study. Ann Intern Med 2001; 134: 451-8.
23. Ilercil A, O'Grady MJ, Roman MJ, Paranicas M, Lee ET, Welty TK, et al. Reference values for echocardiographic measurements in urban and rural populations of differing ethnicity: the Strong Heart Study. J Am Soc Echocardiogr 2001;14: 601-11.

24. Mehta D, Curwin J, Gomes JA, Fuster V. Sudden death in coronary artery disease: acute ischemia versus myocardial substrate. Circulation 1997; 96: 3215-23.
25. Davies MJ. Anatomic features in victims of sudden coronary death. Coronary artery pathology. Circulation 1992; 82: 19-24.
26. Roy D, Waxman HL, Kienzle MG, Buxton AE, Marchlinski FE, Josephson ME. Clinical characteristics and long-term follow-up in 119 survivors of cardiac arrest: relation to inducibility at electrophysiologic testing. Am J Cardiol 1983; 52: 969-74.
27. Dickinson MG, Ip JH, Olshansky B, Hellkamp AS, Anderson J, Poole JE, et al. Statin use was associated with reduced mortality in both ischemic and nonischemic cardiomyopathy and in patients with implantable defibrillators: mortality data and mechanistic insights from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Am Heart J 2007; 153: 573-8.
28. Rosolova H, Cech J, Simon J, Spinar J, Jandova R, Widimsky J, et al. Short to long term mortality of patients hospitalised with heart failure in the Czech Republic-a report from the EuroHeart Failure Survey. Eur J Heart Fail 2005; 7: 780-3.
29. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomized placebo-controlled trial. Lancet 2004; 364: 685-96.
30. Lorenz H, Jünger C, Seidl K, Gitt A, Schneider S, Schiele R, et al. Do statins influence the prognostic impact of non-sustained ventricular tachycardia after ST-elevation myocardial infarction? Eur Heart J 2005; 26: 1078-85.
31. Tamargo J, Caballero R, Gomez R, Nunez L, Vaquero M, Delpon E. Lipid-lowering therapy with statins, a new approach to antiarrhythmic therapy. Pharmacol Ther 2007; 114: 107-26.