Utjecaj rane primjene statina na unutarbolničku smrtnost te smrtnost nakon jednogodišnjeg praćenja u bolesnika s akutnim koronarnim sindromom: iskustva iz Hrvatskog ogranka registra ISACS-CT

The influence of early statin administration on in-hospital and 1-year mortality after acute coronary syndrome: experience from the Croatian branch of the ISACS-CT registry

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Uvod: Važnost primjene statina u akutnom koronarnom sindromu (AKS) dobro je definirana, no optimalan vremenski interval, posebice u prvih 24 sata nakon AKS-a, do sada nije u potpunosti istražen.[1,2] Cilj: Prikupljanje podataka o unutarbolničkoj smrtnosti i smrtnosti nakon 1-godišnjeg praćenja u Hrvatskom ogranku ISACS-CT (*International Registry of Acute Coronary Syndromes in Transitional Countries*) registra.

Bolesnici i metode: Provedena je retrospektivna opservacijska studija u razdoblju od siječnja 2012. do listopada 2017. godine, u koju je uključeno 1.898 bolesnika: 46,4% (n = 881) bolesnika s akutnim infarktom miokarda s elevacijom ST-segmenta (STEMI), 36,1% (n = 685) s akutnim infarktom miokarda bez elevacije ST-segmenta (NSTEMI) te 17,5% (n = 332) bolesnika s nestabilnom anginom pektoris (NA). Praćenje je provedeno na 33% (n = 630) uzorka, od kojih su 43,7% (n = 275) STEMI, 34,4% (n = 217) NSTEMI te 21,9% (n = 138) bolesnici s NA.

Rezultati: Ispitivanu skupinu predstavljali su bolesnici u kojih su statini primijenjeni u prvih 24 sata nakon AKS-a (n = 1.734, 93%; 24 bolesnika nedostaje), dok su bolesnici koji su liječeni statinima nakon 24h te oni koji nisu liječeni statinima tijekom hospitalizacije, predstavljali kontrolnu skupinu. Između definiranih skupina nije bilo značajne razlike u dobi, spolu, indeksu tjelesne mase, ejekcijskoj frakciji lijeve klijetke (LVEF) izmjerenoj tijekom hospitalizacije, anamnestičkim podacima o pušenju, šećernoj bolesti, arterijskoj hipertenziji ili kroničnom zatajivanju srca, tijekom unutarbolničkog i 1-godišnjeg praćenja (**tablica 1**). Ukupna unutarbolnička smrtnost iznosila je 4%, slična smrtnosti u skupini bolesnika liječenih statinima unutar prva 24h nakon AKS (3%), dok je unutarbolnička smrtnost u kontrolnoj skupini iznosila 18% (p < 0.001). Rizik za unutarbolničku smrtnost bio je značajno veći u kontrolnoj skupini bolesnika (OR 7.32, 95% CI 4.37-12.27, p < 0.001), dok se rizik za pojavu primarnog ishoda nakon 1-godine praćenja nije značajno

Background and Aim: The relevance of statin therapy in acute coronary syndrome (ACS) is well-established, but little is known about the optimal timing of statin administration, particularly within the first 24 hours following ACS.[1,2] The aim of the study was to gather data on early and late outcomes of ACS patients (pts) through the Croatian branch of the ISACS-CT (International Registry of Acute Coronary Syndromes in Transitional Countries) registry.

Patients and Methods: The data was gathered retrospectively from January 2012 to October 2017. The study population included 1898 ACS pts: 46.4% (n=881) with ST-segment elevation myocardial infarction (STEMI), 36.1% (n=685) with non-ST-segment elevation myocardial infarction (NSTEMI) and 17.5% (n=332) with unstable angina pectoris (UA). Follow-up was performed on 33% (n=630) of the cohort, 43.7% (n=275) with STEMI, 34.4% (n=217) NSTEMI and 21.9% (n=138) with UA.

Results: In the first 24 hours following ACS, statins were administered in 1734 (93%) pts (for 24 pts the data is missing), while the pts who received them later or not at all were the control group. The two groups did not differ regarding age, gender, body mass index, left ventricular ejection fraction (LVEF) during initial hospitalization, smoking status, history of diabetes, chronic heart failure or arterial hypertension at initial hospitalization nor at 1-year follow-up (**Table 1**). The overall in-hospital mortality rate was 4%, similar to that in pts treated with statins within the first 24 hours (3%), while in pts without early statin treatment, in-hospital mortality rate was 18% (p<0.001). The risk of in-hospital death was significantly higher in pts without early statin therapy (odds ratio [OR] 7.32, 95% confidence interval [CI] 4.371-12.27, p<0.001), while the risk of primary outcome at 1-year follow-up was not significantly different between groups in univariate regression analysis. Older age (OR 1.1, 95% CI 1.06-1.20, p< 0.001), higher creatinine level (OR 1.0, 95% CI 1.005-1.012, p<0.001), lower LVEF (OR

TABLE 1. Baseline characteristics and the comparison of patients with acute coronary syndrome with and without early statin therapy.

	Statin group (n=1734)	Non-statin group (n=140)	p value	Statin group 1y (n=566)	Non-statin group 1y (n=63)	p value 1y
Age (IQR)	65 (57, 75)	67 (55, 78)	0.293	65 (57, 74)	65 (52, 74)	0.402
Male sex, n (%)	1202 (69)	89 (64)	0.184	397 (70)	45 (71)	0.885
DM, n (%)	472 (27	37 (27)	0.921	161 (28)	18 (29)	0.543
HTN, n (%)	1324 (77)	103 (76)	0.912	441 (78)	51 (81)	0.240
Smoking, n (%)	809 (47)	70 (50)	0.527	274 (48)	38 (60)	0.257
CHF, n (%)	69 (4)	7 (5)	0.143	16 (3)	4 (6)	0.194
HR median (IQR)	77 (67, 90)	80 (69, 90)	0.182	-	-	-
SBP median (IQR)	138 (120, 150)	130 (118, 149)	**0.038**	-	-	-
STEMI n (%)	807 (47)	60 (43)		252 (45)	23 (37)	
NSTEMI n (%)	633(37)	44 (31)	**0.031**	196 (35)	20 (32)	0.134
UA n (%)	294 (17)	36 (26)		118 (22)	20 (32)	
Hemoglobin (IQR)	140 (129, 150)	138 (123, 150)	0.144	-	-	-
Creatinine (IQR)	94 (80, 112)	97 (78, 115)	0.819	-	-	-
hsTnT max median (IQR)	1600 (240, 5292)	1145 (242, 4245)	0.113	-	-	-
CRP median (IQR)	4 (2, 16)	10 (3, 98)	0.205	-	-	-
LVEF median (IQR)	52 (45, 60)	50 (40, 60)	0.442	47 ± 12	44 ± 16	0.708
In-hospital mortality / 1y mortality, n (%)	50 (3)	25 (18)	**<0.001**	28 (5)	6 (10)	0.238

IQR - Interquartile range; y - year; DM – Diabetes mellitus; HTN – Arterial hypertension; CHF – Chronic heart failure; HR – Heart rate; SBP – Systolic blood pressure; STEMI – ST-segment elevation myocardial infarction; NSTEMI - Non-ST-segment elevation myocardial infarction; UA – Unstable angina; hsTnT - High-sensitive troponin T; CRP – C reactive protein; LVEF – Left ventricular ejection fraction.

razlikovao između podskupina u univarijabilnoj regresijskoj analizi. Starija dob (OR 1.1, 95% CI 1.06-1.20, p < 0.001), veća razina kreatinina (OR 1.0, 95% CI 1.005-1.012, p < 0.001), niža LVEF (OR 0.90, 95% CI 0.86-0.94, p < 0.001) te izostanak rane primjene statina (OR 3.6, 95% CI 1.0-13.10, p = 0.05) povezani su sa značajno višim rizikom za unutarbolničku smrtnost u multivarijabilnom regresijskom modelu (**tablica 2**).

Zaključak: Primjena statina u prvih 24 sata nakon AKS-a značajno smanjuje rizik za unutarbolničku smrtnost, no pozitivan utjecaj rane primjene statina nije značajan nakon jedne godine praćenja.

0.90, 95%CI 0.86-0.94, p<0.001) and lack of early statin treatment (OR 3.6, 95% CI 1.0-13.10, p=0.05) were positively associated with increased odds for early primary outcome in multivariable regression model (**Table 2**).

Conclusion: Initiation of statin therapy within the first 24 hours following ACS is associated with a significant reduction in in-hospital mortality, although the positive effect of early statin therapy did not reach statistical significance at 1-year follow-up.

TABLE 2. Univariable and multivariable binary regression analysis for early statin therapy with in-hospital and 1-year death as primary outcome.

	Initial hospitalization (n=1898)			1 year follow-up (n=629)		
	HR	95% CI	p value	HR	95% CI	p value
Univariable regression	7.32	4.371-12.27	<0.001	2.02	0.80-5.09	0.135
Multivariable regression*	3.61	0.99-13.10	0.051	-	-	-

* Adjusted for age, sex, DM2, BMI, creatinine, LVEF during initial hospitalization, ACS type. DM – Diabetes mellitus; BMI – Body mass index; LVEF – Left ventricular ejection fraction; HR – Hazard ratio; CI - confidence interval.

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