Association of Preoperative Statins with Acute Kidney Injury after Cardiac Surgery: Utilization of a Consensus Definition of Acute Kidney Injury

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Introduction

Recent studies have shown the incidence of acute kidney injury (AKI) in patients undergoing cardiac surgery to be between 1.5% and 43%. The utilization of cardiopulmonary bypass has been identified as a risk for AKI in this patient population. However, little to no interventions exist for the prevention of AKI in these patients.

Studies have evaluated the association of preoperative 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors, or statins, with the incidence of AKI following cardiac surgery as a possible preventive therapy. Only one found a statistically significant reduction in the likelihood of AKI with preoperative statin use. However, these studies were limited since they only included patients undergoing one type of procedure. Also, many used broad definitions of AKI.

To address some of the limitations of previous trials our study used a consensus definition of AKI to evaluate the association of preoperative statins with the development of AKI following any cardiac surgery utilizing cardiopulmonary bypass. Our null hypothesis was that preoperative statin use is not associated with the development of AKI following cardiac surgery utilizing cardiopulmonary bypass.

Methods

This was a retrospective cohort study conducted at Mercy Hospital, a 250-bed community hospital, between April 2007 and May 2009. The study was conducted with approval from the hospital's Institutional Review Board. Inclusion criteria included patients 18 years of age or older who underwent cardiac surgery on cardiopulmonary bypass. Patients were excluded if they were receiving preoperative renal replacement therapy (RRT), had a history of stage five chronic kidney disease (CKD), or did not have a postoperative serum creatinine assessed.

The hospital's adult cardiac surgery database was used to collect all patient data. Acute kidney injury was defined as an absolute postoperative increase in serum creatinine of greater than or equal to 0.3 mg/dL from baseline or an increase of at least 1.5-times from baseline, or the need for postoperative RRT. Preoperative statin use was defined as any patient who received a statin within 24 hours prior to surgery. The primary outcome was the odds of developing AKI given the utilization of preoperative statins. Predefined secondary outcomes included the need for postoperative RRT, intensive care unit (ICU) length of stay (LOS), hospital LOS, and in-hospital mortality.

Patient demographic and perioperative data were compared between groups using the chi-square or Fisher exact test for categorical variables and the t-test for continuous variables. Development of AKI in patients taking versus those not taking preoperative statins was first assessed by univariate analysis using the chi-square test. Multivariate logistic regression was then performed with adjustment for the covariates in the Baseline and Intraoperative Characteristics of Study Population table. Finally, logistic regression was repeated in a propensity score-matched cohort. All p values were two-sided and considered significant if less than 0.05.

Results

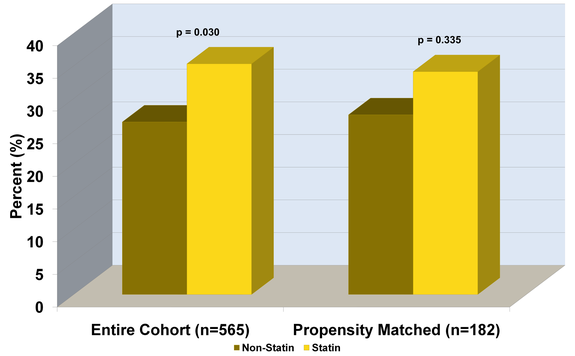
Baseline and Intraoperative Characteristics of Study Population

Characteristic	Non-Statin Group (n = 208)	Statin Group (n = 357)	p Value
	Mean ± (Standard Deviation)		
Age (years)	67 (13)	68 (11)	0.291
Body mass index (kg/m^2)	28.3 (6.0)	29.6 (6.3)	0.017
Serum creatinine (mg/dL)	1.0 (0.32)	1.1 (0.35)	0.071
Estimated creatinine clearance (mL/min)	81.8 (35.7)	84.9 (37.7)	0.345
Ejection fraction (%)[a]	52 (12)	50 (13)	0.025
Cross-clamp time (minutes)	108 (48)	103 (44)	0.232
Perfusion time (minutes)	145 (59)	138 (55)	0.117
	Number (%) of Patients		
Male	111 (53.4)	248 (69.5)	< 0.001
Diabetes mellitus	54 (26.0)	139 (38.9)	0.002
Hypertension	161 (77.4)	316 (88.5)	< 0.001
Hyperlipidemia	80 (38.5)	335 (93.8)	< 0.001
Chronic kidney disease stages III or IV	58 (27.9)	102 (28.6)	0.861
Congestive heart failure	79 (38.0)	117 (32.8)	0.210
New York Heart Association classes III or IV	50 (24.0)	84 (23.5)	0.209
Chronic pulmonary disease	52 (25.0)	85 (23.8)	0.750
Cerebrovascular disease	24 (11.5)	48 (13.4)	0.512
Peripheral artery disease	24 (11.5)	54 (15.1)	0.233
Previous cardiac surgery			
Coronary artery bypass grafting	10 (4.8)	21 (5.9)	0.588
Valve surgery	4 (1.9)	4 (1.1)	0.474
Other	3 (1.4)	6 (1.7)	1.000
Current smoker	70 (33.7)	134 (37.5)	0.354
Family history of coronary artery disease	83 (39.9)	192 (53.8)	0.001
Previous myocardial infarction	53 (25.5)	134 (37.5)	0.003
UA, NSTEMI or STEMI on admission	48 (23.1)	129 (36.1)	0.001
Preoperative ACEI or ARB	75 (36.1)	162 (45.4)	0.030
Preoperative inotrope(s)	8 (3.8)	5 (1.4)	0.080
Preoperative atrial fibrillation or flutter	48 (23.1)	44 (12.3)	0.001
Preoperative cardiogenic shock	13 (6.3)	5 (1.4)	0.002
Preoperative intra-aortic balloon pump	21 (10.1)	46 (12.9)	0.323
Preoperative resuscitation	7 (3.4)	5 (1.4)	0.137
PCA during current admission	24 (11.5)	96 (26.9)	< 0.001
Left main disease	42 (20.2)	102 (28.6)	0.028
Triple vessel disease	81 (38.9)	204 (57.1)	< 0.001
Aortic stenosis	51 (24.5)	70 (19.6)	0.170
Mitral stenosis	9 (4.3)	13 (3.6)	0.685
Aortic insufficiency	50 (24.0)	69 (19.3)	0.185
Mitral insufficiency	89 (42.8)	118 (33.1)	0.021
Nonelective surgery	102 (49.0)	185 (51.8)	0.523
Current surgery			
Coronary artery bypass grafting	124 (59.6)	98 (83.5)	< 0.001
Valve	115 (55.3)	126 (35.3)	< 0.001
Other	71 (34.1)	77 (21.6)	0.001

UA = unstable angina; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; PCA = percutaneous coronary angiography

[a] Preoperative ejection fraction was not recorded for 12 patients; six patients each in the both the non-statin and statin groups.

Incidence of Acute Kidney Injury

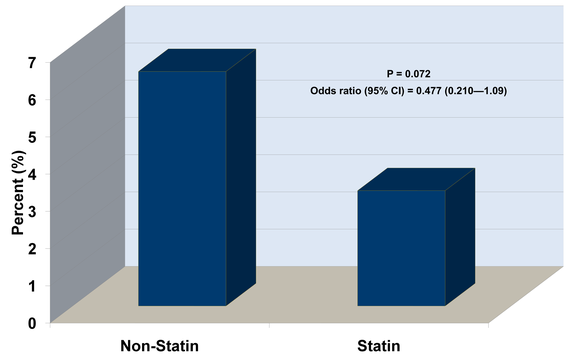


Univariate and Multivariate Analysis of Acute Kidney Injury with Statin Therapy

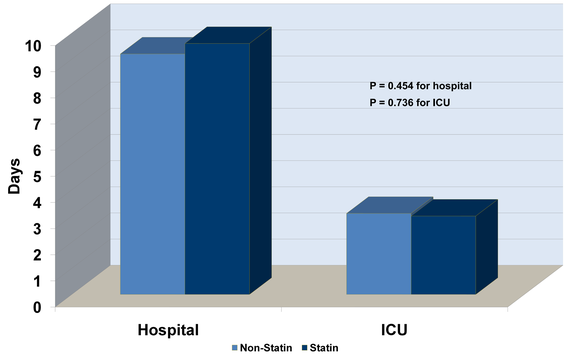
Population	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Entire Cohort (n = 565)	1.52 (1.04 – 2.21)	1.48 (0.871 – 2.53)
Propensity Matched (n = 182)	1.36 (0.725 – 2.57)	0.891 (0.384 – 2.07)[a]

[a] Result based on non-statin versus statin group.

Hospital Mortality



Length of Stay



Discussion

We found the odds of AKI in patients on preoperative statins were 1.5 times more likely than in patients not on preoperative statins. This result remained consistent after multivariate analysis and adjustment for several covariates using propensity score-matching. Although our results did not reach statistical significance they are consistent with those of other studies that investigated the effect of preoperative statins on the incidence of AKI in cardiac surgery patients.

There are several limitations to our study, the first being its retrospective design. A more important one was lack of a defined postoperative time interval in which the change in serum creatinine could occur. Other limitations included that it was a single center study, factors surrounding the use of statins by individual patients, and an inability to use postoperative urine output in our definition of AKI. The final limitation was the inability to include the use of intraoperative aprotinin as a covariate in the analysis as it was not recorded in the cardiac surgery database prior to 2008.

Conclusion

Our study found that preoperative statin use is not associated with the development of AKI following cardiac surgery utilizing cardiopulmonary bypass. To date, this association has only been investigated through retrospective studies. An adequately powered prospective trial investigating preoperative statin use on the risk of AKI following cardiac surgery is needed before more definitive conclusions can be made regarding any association.