

Pleiotropic Effects And Clinical Implications of Statin Therapy Post Cardiac Surgery

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Research Article

Keywords: infection, cardiac surgery, confounding, statin, prevention, prophylaxis

Posted Date: January 31st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1214451/v1>

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Abstract

Background: Perioperative statin therapy can have pleiotropic effects beyond reducing plasma cholesterol level. Whether perioperative statin therapy can reduce surgical infection after cardiac surgery remains unclear. We aimed to assess whether preoperative statin therapy is associated with a reduced risk of surgical site infections and pneumonia after cardiac surgery.

Methods: This retrospective cohort study included 1902 adult patients who had cardiac surgery between February 2015 and April 2019 at a major cardiothoracic centre in Western Australia. The primary outcomes were surgical site infections and pneumonia; secondary outcomes were inotrope requirement, duration of mechanical ventilation, intensive care unit (ICU) and hospital stay, and 30-day mortality. We used propensity-score matching to minimise confounding.

Results: Following propensity-score matching (N=1098), patients on preoperative statins (n=551) were associated with a reduced risk of postoperative wound infections (0.7% vs 13.9%, adjusted odds ratio [OR] 0.010, 95% confidence interval [CI] 0.001-0.075, P<0.001) and pneumonia (38.3% vs 52.5%, adjusted OR 0.359, 95% CI 0.278-0.464, P<0.001). The length of ICU (40.7 hrs vs 46.0 hrs, P=0.001) and hospital stay (9 days vs 10 days, P=0.016) were both also significantly shorter among those treated with preoperative statin than those without statin therapy. In the subgroup of patients who underwent non-bypass-grafting surgery, preoperative statin was associated with a reduced risk of 30-day mortality (1.5% vs 5.5%, OR 0.106, 95% CI 0.014-0.812, P=0.028).

Conclusions: Use of statin before cardiac surgery was associated with a reduced risk of postoperative surgical site infections and pneumonia.

Introduction:

By reducing plasma cholesterol level effectively, long-term statin therapy is considered a cornerstone of preventive cardiology. Whether statin can offer pleiotropic benefits - beyond its anti-cholesterol effect - especially during the perioperative period remains highly controversial. On one hand, some studies have reported that preoperative statin therapy can reduce major adverse cardiac events, including atrial fibrillation and stroke, after coronary artery bypass grafting (CABG) surgery.^(1,2) On the other hand, there are studies showing that long-term statin therapy is not useful in preventing new-onset type II diabetes mellitus;⁽³⁾ and even within the perioperative cardiac surgical setting, whether preoperative statin therapy would offer more benefits than harms is far from conclusive, including a potential risk of inducing acute kidney injury.⁽⁴⁻⁷⁾ The latest systematic review suggested that either a positive or negative effect of perioperative statin therapy on mortality could not be excluded.⁽⁷⁾

Outcomes after cardiac surgery have improved substantially in the last few decades. Nonetheless, a variety of complications - including surgical site infections (1-10%), pulmonary complications including pneumonia (10-25%), and a prolonged low cardiac output state (LCOS) - after surgery remain common.⁽⁸⁻

¹²⁾ The pathogenesis of these complications is likely multifactorial, but a substantial inflammatory and immunological response after surgery, especially with the use of cardiopulmonary bypass, could have, at least in part, contributed to the development of these complications.⁽¹³⁻¹⁶⁾ Statins

have been reported to have an immunomodulatory effect by reducing cytokines and tumour-necrosis-factor (TNF) generation and can promote wound healing.^(17,18) Our recent investigation on deep sternal wound infections after cardiac surgery showed that a history of hyperlipidaemia was a protective factor.⁽¹⁹⁾ Although the mechanistic reasons for this observation remain unclear, statin's potential immunomodulatory effect would represent a biologically plausible explanation.

We hypothesised that through its immunomodulatory effect, perioperative statin therapy could reduce risk of complications after cardiac surgery. In this cohort study, we sought to determine whether preoperative statin therapy was associated with a reduced risk of two common infections - surgical site infections and pneumonia - after cardiac surgery.

Patient And Methods:

All methods were carried out in accordance with relevant guidelines and regulations. Ethics approval was obtained from the Fiona Stanley Hospital Ethics Committee with a waiver of informed consent.

Patient population and exposure of interest

The clinical and outcome data of the adult patients who had cardiac surgery at the Fiona Stanley Hospital in Western Australia, between February 2015 and April 2019, were retrieved and analysed in this retrospective cohort study. Patients who underwent heart or lung transplantation and left ventricular assist device implantation were excluded. The exposure of interest in this cohort study was use of statin for at least two weeks before surgery. All methods were carried out in accordance with relevant guidelines and regulations.

Data sources

We used patient electronic medical records to ascertain the data on patient demographic factors and preoperative statin use and to verify the data from the Australian & New Zealand Society of Cardiac & Thoracic Surgeons (ANZSCTS) database which contains extensive information on preoperative, intraoperative and postoperative data, including postoperative complications.^(21,22)

Outcomes of interest

The primary outcomes were surgical site infections - including deep sternal wound infections (DSWI), superficial sternal wound infection (SSWI) and graft harvest site infection (GHSI) - and pneumonia at 30 days post-operative. Patients were considered to have DSWI when one of the following criteria was met : (1) positive bacterial culture from mediastinal wound swab or fluid; (2) macroscopic signs of

mediastinitis at reoperation; or (3) sternal wound discharge or positive bacterial growth in the blood culture in the presence of at least one of the following symptoms, including chest pain, sternal instability, and fever ($>38^{\circ}\text{C}$).⁽²³⁾ SSWI was defined by infection (clinical evidence of erythema, pus with or without wound dehiscence) involving only the skin, subcutaneous tissue or pectoralis fascia. For GHSI, this was defined as infection (clinical evidence of erythema, pus with or without wound dehiscence) at either the great saphenous vein or radial artery harvest site that required systemic antibiotic therapy. Pneumonia was defined by either having a positive sputum culture, and/or evidence of consolidation on the chest X-ray with raised inflammatory biomarkers.

Secondary outcomes included LCOS requiring prolonged inotrope requirement other than milrinone (≥ 4 hours), new-onset atrial fibrillation, duration of invasive mechanical ventilation, intensive care unit (ICU) and hospital stay, and 30-day mortality. The criteria we used to define the primary and secondary outcomes were the same as those used in the ANZSCTS database.²¹

Statistical analysis

Categorical variables are summarised in numbers with percentages. Continuous variables are summarised in mean with standard deviation for normally distributed data or median with interquartile range for data with skewed distributions. We used Shapiro-Wilks normality test to ascertain normality and in this study, only age met the normality criterion. Chi square, Student's t-test and Mann-Whitney tests were used to generate statistical inference for categorical, continuous variables with a normal and skewed distribution, respectively.

Because residual confounding is common in observational studies, we used propensity-score matching in our multivariable analysis. The propensity (or probability) to use preoperative statin in each study patient was generated using variables that were significantly different between statin users and non-users in the univariable analyses (**Table 1**), including age, sex, body mass index (BMI), diabetes mellitus, Canadian Cardiovascular Society (CCS) angina score, left main coronary artery disease, use of cardiopulmonary bypass and type of cardiac surgical procedures. Propensity matching was performed with a nearest-neighbour matching approach and a match tolerance of 0.005. Univariable and multivariable binary logistic regression analyses were then performed on the propensity-matched cohort. Significant covariates were further adjusted for in the subsequent multivariable analyses of the propensity-matched cohort, and no predictor was removed during the modelling process. Finally, we conducted two subgroup analyses; one on the effect of preoperative statin therapy in patients who had cardiac surgery other than CABG surgery and the other analysis was for patients who had off-pump CABG surgery. All statistical tests were two-tailed and were performed using the SPSS for Windows (IBM 26.0 software).⁽²⁴⁾ A P value <0.05 was taken as significant and not adjusted for multiple statistical testing in this study.

Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available as ethics approval does not allow for this but are available from the corresponding author on reasonable request.

Results:

Patient Characteristics:

Of the 1902 patients who met study criteria, 1119 (58.8%) were treated with preoperative statin therapy. Patient baseline characteristics are summarised in **Table 1**. Patients on preoperative statins were more likely to be older (mean age 65.4 years vs 59.9 years, $P < 0.001$), have diabetes mellitus, hypercholesterolaemia, left main coronary artery disease, a higher BMI, and higher Canadian Cardiovascular Society angina score. A total of 1098 (57.7%) patients were propensity-score matched (preoperative statins: $n = 551$ and patients not on statins: $n = 547$). The baseline characteristics of the propensity-score matched cohort are summarised in **Table 2**; all characteristics between those treated and untreated with statins, including the bypass and cross clamp time, were not significantly different. Regarding statin therapy administered (after propensity matching), 308 (55.9%) patients received atorvastatin 40mg daily, 52 (9.4%) received atorvastatin 80mg, 108 (19.6%) received rosuvastatin 20mg daily, 55 (10.0%) received rosuvastatin 40mg daily, 19 (3.4%) received pravastatin 40mg and 9 (1.6%) received simvastatin 40mg daily.

Univariable analysis of the primary outcomes:

The difference in postoperative outcomes between patients with and without preoperative statin therapy using univariable logistic regression are summarised in **Table 3** and **Figure 1**. Patients on preoperative statin therapy were associated with a significantly reduced risk of surgical site infections (0.7% vs 13.9%, OR 0.045, 95% CI 0.016-0.125, $P < 0.001$) and pneumonia (38.3% vs 52.5%, OR 0.562, 95% CI 0.442-0.716, $P < 0.001$) compared to those untreated with preoperative statin. There were no significant differences in the rates of wound infection and pneumonia when compared to the type and dose of statin therapy.

Univariable analyses of the secondary outcomes:

Preoperative statin use was associated with a significantly higher risk of prolonged (≥ 4 hours) inotrope requirement (30.3% vs 20.8%, OR 1.652, 95% CI 1.255-2.175, $P < 0.001$) and new-onset atrial fibrillation (14.2% versus 9.7%, OR 1.537, 95% CI 1.061-2.227, $P = 0.023$) after surgery than those untreated with statin (**Table 3** and **Figure 1**). Although the duration of mechanical ventilation was similar between the two groups, the length of ICU (40.7 hrs vs 46.0 hrs, $P = 0.001$) and hospital stay (9 days vs 10 days, $P = 0.016$) were both significantly shorter in patients treated with preoperative statins than those who were not treated with statin. There were no significant differences in any of the secondary outcomes when compared to the type and dose of statin therapy.

Multivariable analyses:

Preoperative statin use was associated with a reduced risk of surgical site infections (OR 0.01, 95% CI 0.001-0.075, $P < 0.001$) and pneumonia (OR 0.359, 95% CI 0.278-0.464, $P < 0.001$) after adjusting for other covariates (**Table 4**). The association between statin use and prolonged inotrope requirement remained

largely unchanged after adjusting for the significant covariates in **Table 1** (OR 2.113, 95% CI 1.612-2.770, $P < 0.001$).

Subgroup analysis of patients undergoing non-CABG surgery:

Among those who had non-CABG surgery, no patients who were treated with preoperative statins developed surgical site infections compared to 12 (6%) surgical site infections among patients who were untreated with preoperative statins. The incidence of pneumonia was also significantly lower among those treated with preoperative statins (31.9% vs 49.8%, OR=0.603, 95% CI 0.391-0.932, $P=0.017$) than those untreated with statin **Table 5** and **Figure 2**). Statin use was also associated with a reduced risk of 30-day mortality (1.5% vs 5.5%, OR=0.106, 95% CI 0.014-0.812, $P=0.028$) (**Table 5**). The duration of mechanical ventilation, and ICU and hospital stay were not significantly different between those treated and untreated with preoperative statin in patients who had non-CABG surgery.

Subgroup analysis of patients undergoing off-pump CABG surgery:

In patients undergoing off-pump CABG surgery, prolonged inotrope requirement was not significantly different between the statin (50.0% vs 37.5%, OR 1.667, 95% CI 0.854-3.253, $P=0.133$) and the non-statin groups (**Table 6**). Similarly, the risk of developing new-onset atrial fibrillation after surgery was not significantly different between the two groups (21.4% versus 11.1%, OR 2.182, 95% CI 0.860-5.534, $P=0.100$).

COMMENTS:

Although the effects of statin therapy on perioperative outcomes have been studied, its specific effect on perioperative infections has not been thoroughly investigated. Infections were reported as an outcome in seven randomised-controlled-trials assessing the benefits of perioperative statin in cardiac surgery.⁽²⁰⁾ Of these seven trials, only two (with a total of 2537 patients) were deemed to have a low risk of bias with a suggestion that statin use was associated with a statistically insignificant reduced risk of infection compared to placebo (odds ratio [OR] 0.8, 95% confidence interval [CI] 0.60-1.07; $P=0.14$). Given infection is an important cause of morbidity after cardiac surgery and short-term perioperative statin therapy is a relatively inexpensive therapy, it is paramount to establish whether preoperative statin can reduce surgical site infections and pneumonia in cardiac surgery.

This study found that preoperative statin therapy was associated with a significantly reduced risk of postoperative surgical site infections and pneumonia in adult patients undergoing cardiac surgery. The benefits remained significant after multivariable analysis on the propensity-matched cohort. In the subgroup of patients who had non-CABG cardiac surgery (i.e. valve and/or aortic procedures), preoperative statins remained significantly associated with a reduced risk of pneumonia, surgical site infections, and more importantly, also 30-day mortality. These results are clinically relevant and require careful consideration.

Previous studies have shown that diabetes mellitus, smoking, impaired left ventricular function, urgency of the procedure and type of procedure are predictors of infective complications after cardiac surgery.⁽²⁵⁻²⁷⁾ Whether preoperative statin therapy can reduce infective complications after cardiac surgery remains, however, uncertain. Current guidelines recommend that statin therapy should be continued until the day of cardiac surgery due to its cholesterol-lowering effect and long-term mortality benefits in patients with ischaemic heart disease.⁽²⁸⁾ Our results support this recommendation, and provide a possible additional explanation why continued use of statin preoperatively is important. Statins are known to modulate the inflammatory and immune responses. It is well established that cardiac surgery and the institution of cardiopulmonary bypass can provoke a vigorous inflammatory response through the activation of multiple inflammatory response modifiers, including several interleukins and tumour necrosis factor-alpha (TNF- α).⁽²⁹⁾ Excessive inflammation will induce ischaemic-reperfusion injury and production of reactive free radicals, leading to cell membrane injury, tissue damage and in severe cases, even organ failure.⁽³⁰⁾ Although statin has been shown to reduce inflammation and improve wound healing,^(17,18,31) its potential benefits on perioperative clinical outcomes after cardiac and non-cardiac surgery have been less forthcoming and certainly far from conclusive.^(4-7, 32-36) Our results add weight to support the hypothesis that statin may have some clinically-important anti-infective effects.

Although statin is inexpensive, it still has some well-documented side effects (e.g. deranged liver function test and myalgia) and also potential serious harmful effects, including inducing acute kidney injury.⁽⁴⁻⁷⁾ Our results also raise the (unexpected) concerns that statin may increase the risk of new-onset atrial fibrillation and LCOS. It is important to recognise that LCOS state was defined as prolonged inotrope requirement greater than four hours based on the ANZSCTS database. Given the variability in the management of LCOS amongst intensivists, this definition of prolonged LCOS may not reflect a true representation. Post-operative atrial fibrillation and LCOS are multifactorial processes and given the limitations of our study, our results should be interpreted with caution. As such, an adequately powered multicentre randomised controlled trial - stratified by whether the patient is undergoing CABG or non-CABG surgery - is paramount before preoperative statin is used as a prophylactic agent against infections in cardiac surgery.

Finally, we need to emphasize the limitations of this study. Although our study utilised prospectively collected data including the primary and secondary outcome endpoints, the definition of pneumonia (as defined by the ANZSCTS database) was broad and hence there was overall increased incidence of pneumonia. Furthermore, data regarding patients' plasma cholesterol levels were not available at the time of the surgery. As with any observational studies, any association between intervention and outcome should only be concluded as association and not necessarily causal in nature, and residual confounding is always possible.

In summary, our results showed that preoperative statin use was associated with a reduced risk of surgical site infections and pneumonia after cardiac surgery. In the subgroup of patients undergoing non-CABG surgery, preoperative statin use was associated with a reduced risk of 30-day mortality. Our

findings support the current guidelines in recommending continuation of statin therapy prior to cardiac surgery. An adequately-powered, double-blinded, randomised-controlled-trial with infections as the primary outcome is needed to confirm the hypothesis that statin - a relatively easy and cheap intervention – is safe and effective in reducing different types of infections after cardiac surgery.

Declarations:

This research did not receive any specific grant from funding.

Ethics approval (with a waiver of consent) was obtained from the Fiona Stanley Hospital Ethics Committee.

Funding: this study did not receive any funding

Conflicts of interest: All authors declare that they have no conflict of interests.

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Tables:

Table 1. Patient characteristics before matching

		No statin use (n=783)	Statin use (n=1119)	P value
Age, years (mean±SD)		59.9±14.7	65.4±10.6	<0.001
Gender	Female	221 (28.2%)	263 (23.5%)	0.020
	Male	562 (71.8%)	856 (76.5%)	
Indigenous		90 (11.5%)	131 (11.7%)	0.887
Body mass index, kg/m ² (median, IQR)		27.4(24.2-31.1)	29.1 (25.7-32.9)	<0.001
Type 2 diabetes mellitus		173 (22.1%)	492 (44.0%)	<0.001
Hypercholesterolaemia		5 (0.6%)	1080 (96.5%)	<0.001
Active smoking		149 (19.0%)	185 (16.5%)	0.159
COPD		102 (13.1%)	167 (14.9%)	0.252
Preoperative dialysis		21 (2.7%)	27 (2.4%)	0.713
CCS angina score	3	70 (8.9%)	151 (13.5%)	<0.001
	4	43 (5.5%)	101 (9.0%)	
NYHA class	III	143 (18.3%)	219 (19.6%)	0.116
	IV	40 (5.1%)	40 (3.6%)	
Left main coronary artery disease		132 (16.9%)	263 (23.5%)	<0.001
eGFR, ml/min/1.73m ² (median, IQR)		85.8 (61.6-109.9)	82.2 (60.2-109.5)	0.349
LVEF, % (median, IQR)		59.0 (46-63)	58.0 (48-63)	0.656
Urgency of procedure	Urgent	366 (46.7%)	507 (45.3%)	0.537
	Elective	417 (53.3%)	612 (54.7%)	
Cardiopulmonary bypass use	Off pump	85 (10.9%)	189 (16.9%)	<0.001
	On pump	698 (89.1%)	930 (83.1%)	
Procedure	Isolated CABG	286 (36.5%)	757 (67.6%)	<0.001
	Valve only	289 (36.9%)	194 (17.3%)	
	CABG + valve	77 (9.8%)	110 (9.8%)	
	Aortic procedure	99 (12.6%)	52 (4.6%)	
EuroSCORE II, % (median, IQR)		2.79 (1.68-5.13)	2.51 (1.60-4.71)	0.039

CABG indicates coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD standard deviation

Table 2: Patient characteristics after matching

		No statin use (n=547)	Statin use (n=551)	P value
Age		63.7 ±11.9	64.8 ±11.2	0.138
Gender	Female	129 (23.6%)	140 (25.4%)	0.482
	Male	418 (89.6%)	411 (74.6%)	
Indigenous		57 (10.4%)	66 (12.0%)	0.413
Body mass index, kg/m ² (median, IQR)		29.0 (25.5-32.3)	28.1 (25.0-31.9)	0.070
Type 2 diabetes mellitus		167 (30.5%)	176 (31.9%)	0.614
Active smoking		97 (17.7%)	94 (17.1%)	0.769
COPD		76 (13.9%)	83 (15.1%)	0.599
Preoperative dialysis		15 (2.7%)	13 (2.4%)	0.687
CCS	0	244 (44.6%)	230 (41.7%)	0.718
	1	108 (19.7%)	121 (22.0%)	
	2	89 (16.3%)	99 (18.0%)	
	3	69 (12.6%)	62 (11.3%)	
	4	37 (6.8%)	39 (7.1%)	
NYHA	I	271 (49.5%)	252 (45.7%)	0.545
	II	151 (27.6%)	172 (31.2%)	
	III	105 (19.2%)	105 (19.1%)	
	IV	20 (3.7%)	22 (4.0%)	
Left main coronary disease		125 (22.9%)	103 (18.7%)	0.098
eGFR, ml/min/1.73m ² (median, IQR)		86.9 (64.6-111.2)	81.6 (58.9-109.1)	0.080
LVEF, % (median, IQR)		58.0 (47.0-63.0)	59.5 (50.0-63.0)	0.506
Urgency of procedure	Urgent	258 (47.2%)	226 (41.0%)	0.080
	Elective	289 (52.8%)	325 (59.0%)	
Cardiopulmonary bypass use	Off pump	72 (13.2%)	70 (12.7%)	0.821
	On pump	475 (86.8%)	481 (87.3%)	
Procedure type	Isolated CABG	358 (65.4%)	354 (64.2%)	0.874
	Isolated valve	171 (31.3%)	179 (32.5%)	

	CABG + valve	65 (11.9%)	65 (11.8%)	
	Aortic procedure	39 (7.1%)	43 (7.8%)	
Aortic cross clamp time, mins (IQR)		54 (37-83)	56 (37-81)	0.977
Cardiopulmonary bypass time, mins (IQR)		84 (63-117)	84 (62-118)	0.708
EuroSCORE II, % (median, IQR)		2.83 (1.74-5.01)	2.79 (1.65-4.95)	0.105

CABG indicates coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; SD standard deviation

Table 3: Postoperative outcomes after propensity matching

	No statin use (n=547)	Statin use (n=551)	Odds ratio	95% CI	P value
Wound infection	76 (13.9%)	4 (0.7%)	0.045	0.016-0.125	<0.001
Pneumonia	287 (52.5%)	211 (38.3%)	0.562	0.442-0.715	<0.001
Prolonged inotrope use (>4 hrs)	114 (20.8%)	167 (30.3%)	1.652	1.255-2.175	<0.001
Post-operative atrial fibrillation	453 (9.7%)	78 (14.2%)	1.537	1.061-2.227	0.023
Ventilation time, hrs (IQR)	8.6 (5.6-17.3)	7.7 (5.3-15.7)	-	-	0.111
ICU length of stay, hrs (IQR)	46.0 (24.7-77.1)	40.7 (22.2-71.6)	-	-	0.001
Total hospital length of stay, days (IQR)	10 (7-16)	9 (6-14)	-	-	0.016
30-day mortality	18 (3.3%)	11 (2.0%)	0.599	0.280-1.280	0.186

CI indicates confidence interval; ICU intensive care unit; IQR, interquartile range

Table 4: Outcomes after multivariate analysis

	Odds ratio	95% CI	P value
Wound infection	0.010	0.001-0.075	<0.001
Pneumonia	0.359	0.278-0.464	<0.001
Prolonged inotrope use (>4 hrs)	2.113	1.612-2.770	<0.001
Post-operative atrial fibrillation	1.465	0.987-2.176	0.058

Table 5: Subgroup analysis of patients undergoing non-CABG surgery

	No statin use (n=201)	Statin use (n=204)	Odds ratio	95% CI	P value
Wound infection	12 (6%)	0 (0%)	-	-	<0.001
Pneumonia	100 (49.8%)	65 (31.9%)	0.603	0.391-0.932	0.017
Prolonged inotrope use (>4 hrs)	6 (3%)	30 (14.7%)	0.719	3.05-16.98	<0.001
Post-operative atrial fibrillation	3 (1.5%)	10 (4.9%)	3.402	0.922-12.550	0.066
Ventilation time, hrs (IQR)	8.91 (5.7-16.6)	9.3 (5.4-19.3)	-	-	0.801
ICU length of stay, hrs (IQR)	46.1 (26.9-71.8)	42.8 (23.7-93.2)	-	-	0.429
Total hospital length of stay, days (IQR)	9 (6-14)	8 (7-14)	-	-	0.641
30-day mortality	11 (5.5%)	3 (1.5%)	0.106	0.014-0.812	0.028

ICU indicates intensive care unit; IQR, interquartile range

Table 6: Subgroup analysis of patients undergoing off pump CABG surgery

	No statin use (n=72)	Statin use (n=70)	Odds ratio	95% CI	P value
Prolonged inotrope use (>4 hrs)	27 (37.5%)	35 (50.0%)	1.667	0.854-3.253	0.133
Post-operative atrial fibrillation	8 (11.1%)	15 (21.4%)	2.182	0.860-5.534	0.100

Figures

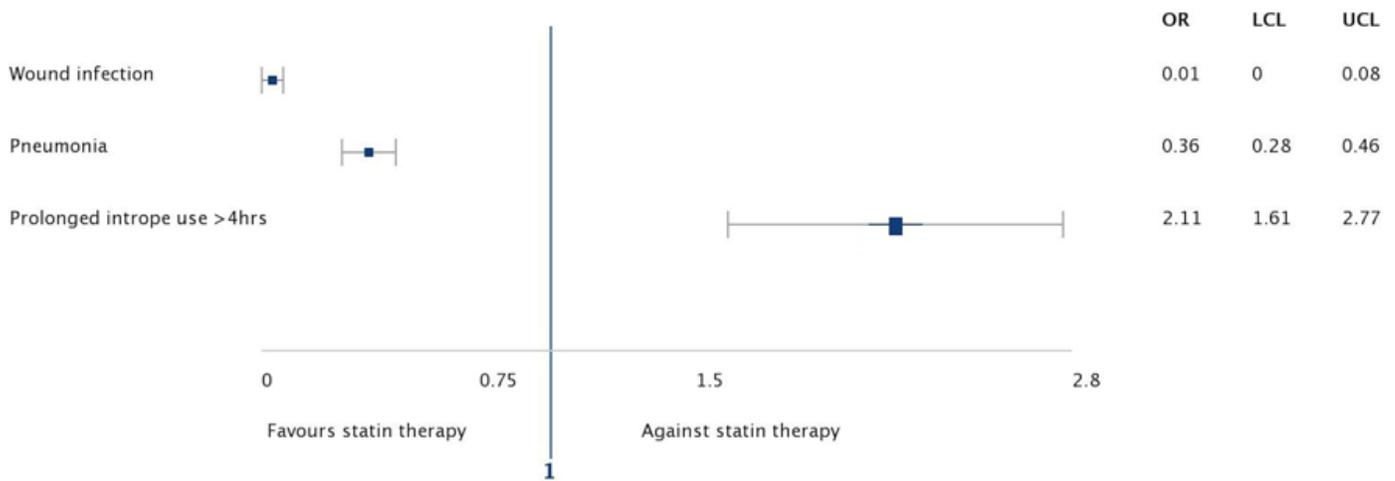


Figure 1

Forrest plot – adjusted odds ratios after propensity matching

LCL indicates lower confidence interval limit; OR odds ratio; UCL upper confidence interval limit

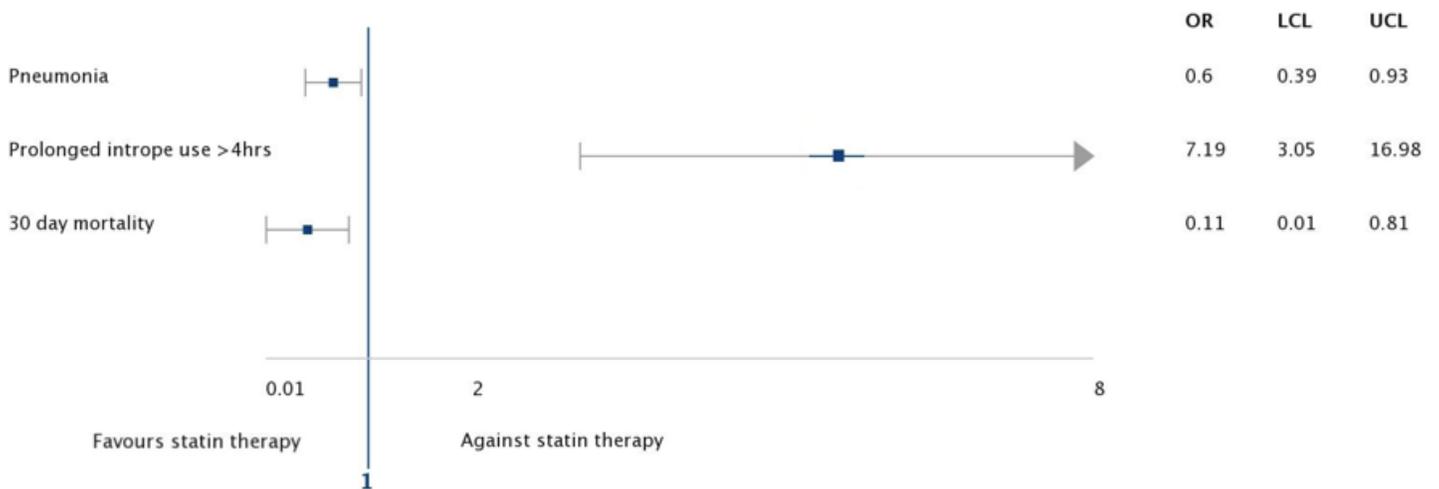


Figure 2

Forrest plot – odds ratios for patients undergoing non-CABG procedures (after propensity matching)

LCL indicates lower confidence interval limit; OR odds ratio; UCL upper confidence interval limit