Preoperative statin therapy reduces postoperative all-cause mortality in cardiac surgery: A meta-analysis of controlled studies

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Two recent meta-analyses[1,2] demonstrated that postoperative mortality was significantly lower in patients undergoing cardiac surgery who received preoperative statin therapy than in those who did not. The meta-analysis by Kapoor and associates,[1] however, included merely 4 published articles, and that by Hindler and colleagues[2] cited 4 published articles and 3 scientific abstracts. Therefore, the appropriate role of preoperative statin therapy in cardiac surgery remains unclear. Furthermore, several controlled studies of preoperative statin therapy in cardiac surgery have been published to date since the 2 meta-analyses were conducted. Herein, we performed a meta-analysis of controlled studies of preoperative statin therapy for prevention of postoperative all-cause mortality in cardiac surgery.

MATERIALS AND METHODS

All controlled studies (English-language full-text journal publications excluding scientific abstracts) of preoperative statin therapy in cardiac surgery were identified by a 2-level search strategy. First, a public domain database (MEDLINE) was searched using a Web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources including references of initially identified articles and a search of reviews and commentaries. The MEDLINE database was searched from January 1966 to December 2007. MeSH keywords included ''Hydroxymethylglutaryl-CoA Reductase Inhibitors'' and ''Cardiac Surgical Procedures.'' Studies considered for inclusion met the following criteria: the design was a controlled study of preoperative statin therapy; the study population was patients undergoing cardiac surgery; and main outcomes included postoperative all-cause mortality. Data regarding detailed inclusion criteria and mortality were abstracted (as available) from each individual study. For each study, data regarding mortality in both the statin and control (placebo or no statin) groups were used to generate crude odds ratios (ORs) and 95% confidence intervals (CIs). We also abstracted adjusted ORs and 95% CIs for mortality if reported. Study-specific estimates were combined using inverse variance-weighted averages of logarithmic ORs in a random-effects model. Between-study heterogeneity was analyzed by means of standard χ^2 tests. Publication bias was assessed mathematically using an adjusted rank-correlation test.

RESULTS

Our search identified 13 controlled studies of preoperative statin therapy in cardiac surgery, the majority of which was coronary artery bypass graft surgery (Table 1). These included 3 randomized controlled trials,[3-5] 3 prospective cohort studies, and 7 retrospective cohort studies. Pooled analysis of crude ORs from all 13 studies (representing 19,542 patients) demonstrated a statistically significant 45% reduction in postoperative all-cause mortality with preoperative statin therapy relative to control (pooled crude OR, 0.55; 95% CI, 0.46–0.66; $P < .01$). There was neither study heterogeneity of results ($P = .64$) nor evidence of significant publication bias ($P = .74$). Six of the 10 observational studies reported adjusted ORs for mortality by multivariate analysis or propensity score matching. When adjusted ORs from these 6 observational studies and ORs from the 3 randomized controlled trials[3-5] were pooled (representing 18,637 patients), preoperative statin therapy was associated with a 25% reduction in mortality relative to control that remained statistically significant (pooled adjusted OR, 0.76; 95% CI, 0.64–0.90; $P < .01$). There was neither study heterogeneity of results ($P = .60$) nor evidence of significant publication bias ($P = .53$). Pooled analysis of ORs and adjusted Ors, respectively, from 2 randomized controlled trials[3,4] and 3 observational studies that enrolled patients undergoing coronary artery bypass graft surgery exclusively (representing 7205 patients) demonstrated a statistically significant 41% reduction in mortality with preoperative statin therapy relative to control (adjusted OR, 0.59; 95% CI, 0.36–0.97; $P = .04$). There was neither study heterogeneity of results ($P = .57$) nor evidence of significant publication bias ($P = .62$).

DISCUSSION

The present meta-analysis of 13 controlled studies demonstrated that preoperative statin therapy reduced postoperative all-cause mortality in cardiac surgery. The analysis, however, included 10 observational studies but merely 3 small randomized controlled trials (sample size: 40, 77, and 200).[3-5] In an attempt to correct for and minimize selection bias, which exists in observational studies, related to statin use, we pooled adjusted instead of crude ORs from the observational studies and ORs from the randomized controlled trials, resulting in a statistically significant benefit of preoperative statin therapy for mortality in cardiac surgery or exclusive coronary artery bypass graft surgery. Nevertheless, larger randomized controlled trials are needed to confirm our results. Until sufficient numbers of events will be accumulated by evidence from randomized controlled trials to provide a definitive answer,

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Received for publication Jan 22, 2008; accepted for publication Feb 24, 2008.

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J Thorac Cardiovasc Surg 2009;137:e52-3
0022-5223/$36.00

doi:10.1016/j.jtcvs.2008.02.045

TABLE 1. Characteristics and outcomes of included studies

Author	Publication	Design	Sample size	Type of operation	OR (95% CI) for mortality	
					Crude	Adjusted
Ali and Buth	*Int J Cardiol*. 2005;103:12-8	Retrospective cohort	5,469	Cardiac surgery (Isolated CABG 80%)	0.50 (0.38–0.67)	0.87 (0.61-1.25)*
Chello et al[4]	*Crit Care Med*. 2006;34:660-7	Randomized controlled	40	Elective isolated CABG	1.00 (0.02–52.85)	
Christenson[3]	*Eur J Cardiothorac Surg*. 1999;15:394-400	Randomized controlled	77	Elective isolated CABG	0.93 (0.02–47.85)	
Clark et al	*J Thorac Cardiovasc Surg*. 2006;131: 679-85	Retrospective cohort	3,829	Elective cardiac surgery (any CABG 81%)	0.43 (0.28–0.66)	0.51 (0.27-0.94)*
Coleman et al	*Curr Med Res Opin*. 2007;23:1783-90.	Retrospective cohort	1,934	Cardiac surgery (isolated CABG 63%)	0.68 (0.45–1.03)	0.80 (0.64-0.99)†
Collard et al	*J Thorac Cardiovasc Surg*. 2006;132: 392-400	Prospective cohort	2,666	Elective primary isolated CABG	0.79 (0.47–1.33)	0.04 (0.08-0.93)†
Dotani et al	*Am J Cardiol*. 2000;86:1128-30, A6	Retrospective cohort	323	Elective isolated CABG	0.12 (0.01–2.08)	NR
Liakopoulos et al	*Thorac Cardiovasc Surg*. 2006;54:250-4	Prospective cohort	36	Elective isolated CABG	1.00 (0.02–53.12)	NR
Mariscalco et al	*Ann Thorac Surg*. 2007;84:1158-64	Retrospective cohort	405	Elective primary isolated CABG	0.28 (0.01–7.03)	NR
Pan et al	*Circulation*. 2004;110(11 Suppl 1):II45-9	Retrospective cohort	1,663	Primary isolated CABG	0.47 (0.25–0.87)	0.58 (0.31–1.09)*
Pascual et al	*Ann Thorac Surg*. 2006;81:78-83	Prospective cohort	141	Elective isolated CABG	0.16 (0.03–0.79)	NR
Patti et al[5]	*Circulation*. 2006;114:1455-61	Randomized controlled	200	Elective cardiac surgery (isolated CABG 79%)	0.98 (0.14–7.10)	
Thielmann et al	*J Thorac Cardiovasc Surg*. 2007;134: 1143-9	Retrospective cohort	2,759	Elective primary isolated CABG	1.08 (0.39–3.00)	1.18 (0.36–3.87)*
Total			19,542		0.55 (0.46–0.66)‡	0.76 (0.64–0.90)‡

OR, Odds ratio; *CI,* confidence interval; *CABG,* coronary artery bypass graft surgery; *NR,* not reported. *Propensity score matching. †Multivariate analysis. ‡Pooled estimate using a random-effects model.

advocating routine preoperative statin therapy in cardiac surgery is premature.

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