- fibrillation after cardiothoracic surgery. *J Thorac Cardiovasc Surg.* 2008;135:405-11.
2. Blackstone EH. Comparing apples and oranges. *J Thorac Cardiovasc Surg.* 2002;123:8-15.
 3. Jones PH, Davidson MH, Stein EA, Bays HE, McKenney JM, Miller E, et al. Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses. *Am J Cardiol.* 2003;92:152-60.
 4. Kourliouros A, De Souza A, Roberts N, Marciniak A, Tsiouris A, Valencia O, et al. Dose-related effect of statins on atrial fibrillation after cardiac surgery. *Ann Thorac Surg.* 2008;85:1515-20.
 5. Liu T, Li L, Korantzopoulos P, Liu E, Li G. Statin use and development of atrial fibrillation: A systematic review and meta-analysis of randomized clinical trials and observational studies. *Int J Cardiol.* 2008;126:160-70.
doi:10.1016/j.ijcvs.2008.04.021

Reply to the Editor:

My coauthors and I thank Drs Kourliouros, Roberts, and Jahangiri for their interest in our recent study.¹ We do not disagree with their suggestion that different statins may exhibit varying degrees of pleiotropic effects (eg, anti-inflammatory effects), and thus believe that their hypothesis that statins may have differential abilities to prevent postcardiothoracic surgery (CTS) atrial fibrillation is not unreasonable. It is, however, important to note that the intent of our nested cohort study was to assess whether statins as a class are associated with reductions in post-CTS atrial fibrillation when used in patients who already have a high background use of β -blockers (84%) and appreciable use of prophylactic amiodarone (44%), rather than to evaluate individual statins or a dose-response relationship.¹ Our primary analysis was worthwhile, because a large proportion of patients in ARMYDA-3—the only randomized controlled trial designed to assess the effect of a statin (atorvastatin at 40 mg/d) on post-CTS atrial fibrillation as a primary end point—did not receive β -blockers (arguably the criterion standard preventative strategy), and virtually none received prophylactic amiodarone.² This treatment pattern likely explains the high incidence of post-CTS atrial fibrillation (57%) seen in the ARMYDA-3 control group.

Despite the criticism by Kourliouros, Roberts, and Jahangiri of our dose-response analysis, we believe that it provides valuable data to support the claim of a dose-response effect of statins on post-CTS atrial fibrilla-

tion. We would have liked to evaluate different statins and doses independently; however, the relatively small number of patients receiving a statin and the heterogeneous uses of different statins and doses by patients enrolled in the cohort would have resulted in an underpowered analysis.¹ That being said, we applaud the work of Kourliouros, Roberts, and Jahangiri in conducting an additional analysis to further the research in this area.³ Ultimately, as Kourliouros, Roberts, and Jahangiri suggest, all nonrandomized studies likely suffer from some degree of bias or confounding, which is why a randomized, controlled trial will be needed to determine definitively whether different statins exhibit different abilities to prevent post-CTS atrial fibrillation and whether dose-response relationships do, in fact, exist.

Craig Ian Coleman, PharmD
University of Connecticut School of Pharmacy
Storrs, Conn

References

1. Lertsburapa K, White CM, Kluger J, Faheem O, Hammond J, Coleman CI. Preoperative statins for the prevention of atrial fibrillation after cardiothoracic surgery. *J Thorac Cardiovasc Surg.* 2008;135:405-11.
2. Patti G, Chello M, Candura D, Pasceri V, D'Ambrosio A, Covino E, et al. Randomized trial of atorvastatin for reduction of postoperative atrial fibrillation in patients undergoing cardiac surgery: results of the ARMYDA-3 (Atorvastatin for Reduction of MYocardial Dysrhythmia After cardiac surgery) study. *Circulation.* 2006;114:1455-61.
3. Kourliouros A, De Souza A, Roberts N, Marciniak A, Tsiouris A, Valencia O, et al. Dose-related effect of statins on atrial fibrillation after cardiac surgery. *Ann Thorac Surg.* 2008;85:1515-20.
doi:10.1016/j.jtcvs.2008.06.009

Box lesion or not—Still unsettled question

To the Editor:

I read with interest the article by Voeller and associates¹ in the April 2008 issue of the *Journal*. This is a single center study looking at occurrences of atrial arrhythmias on follow-up in patients who had the Cox maze IV procedure with and without box lesions. Although the authors have acknowledged several limitations, I would like to point out another important limitation. Over 60% of the patients had concomitant procedures, and a significant proportion of

them had valve operations, which is a significant confounder for occurrence of postoperative atrial arrhythmias. Analysis of the lone Cox maze IV group would probably offer better insight into the benefit of the box lesion. However, the numbers seem to be so small that there may not be adequate power for this analysis. I will look forward to any follow-up data in the future from the authors.

Uma N. Srivatsa, MD
Internal Medicine/Cardiology
University of California—Davis
Sacramento, CA 95670

Reference

1. Voeller RK, Bailey MS, Zierer A, Lall SC, Sakamoto S, Aubuchon K, et al. Isolating the entire posterior left atrium improves surgical outcomes after the Cox maze procedure. *J Thorac Cardiovasc Surg.* 2008;135:870-7.
doi:10.1016/j.jtcvs.2008.04.028

Aortic valve replacement dilemma: mechanical or biological prosthesis?

To the Editor:

The selection of the appropriate prosthesis for aortic valve replacement (AVR) is still open to debate in the case of patients in the sixth and seventh decades of life. Recently Brown and colleagues,¹ from Mayo Clinic, reported in the *Journal* on an interesting retrospective study about this topic. By means of patient matching according to clinical features, they observed in their population a survival advantage after aortic valve replacement with a mechanical prosthesis relative to a bioprosthesis. Brown and colleagues¹ stated that the study was subject to selection bias and noted that despite case matching and statistical analysis, surgical bias cannot be eliminated. Also, in our opinion, it is virtually impossible to avoid all biases and confounding factors in clinical studies. Nevertheless, the recording of aortic valve replacement as associated or not with coronary artery bypass grafting simply as a binary variable could be quite misleading in drawing conclusions from data analysis. In fact, age being equal, surgeons could elect to implant a bioprosthesis rather than a mechanical valve in patients affected by more severe coronary artery disease. Both the extent—isolated single-vessel disease versus triple-vessel disease—and the

severity—proximal isolated stenoses versus multiple stenoses with distal vessel involvement—are features of coronary artery disease that strongly influence surgical strategy, complexity of the operation, and prognosis. Moreover, the quality of coronary vessels and graft availability and quality determine the completeness of the revascularization and its durability. With the matching method adopted by Brown and colleagues,¹ these data are lost to the analysis, making it impossible to evaluate any effects on the higher perioperative and long-term mortalities observed in the bioprosthesis group. Higher mortality could be related to an unfavorable preoperative status. In that case, the surgeons who performed the operations may have shown good clinical judgment, implanting bioprostheses in patients with poor prognosis. Moreover, there are no data on prosthesis sizes, effective orifice areas, and the incidence of patient–prosthesis mismatch, all of which could influence long-term results. In conclusion, Brown and colleagues deserve commendation for the insights from their interesting study. Nevertheless, extreme caution should be exercised in supporting or questioning existing clinical guidelines in response to potentially biased retrospective studies.

Aldo Cannata, MD

Claudio Francesco Russo, MD

Corrado Taglieri, MD

Angelo De Gasperis Department of Cardiac Surgery Niguarda Cà Granda Hospital Milan, Italy

Reference

1. Brown ML, Schaff HV, Lahr BD, Mullany CJ, Sundt TM, Dearani JA, et al. Aortic valve replacement in patients aged 50 to 70 years: improved outcome with mechanical versus biologic prostheses. *J Thorac Cardiovasc Surg.* 2008;135:878-84.
doi:10.1016/j.jtcvs.2008.05.025

Reply to the Editor:

Drs Cannata, Russo, and Taglieri commented on our results and the possible impact of selection bias, which is present in all observational surgical series. We matched patients and used multivariate analyses, but it is impossible to determine whether this has accounted for all possible confounders. We agree that only randomiza-

Figure 1. Survivals in mechanical aortic valve (Mech V) and bioprosthetic aortic valve (BPV) groups according to presence or absence of coronary artery disease, as indicated by coronary artery bypass grafting (CABG).

tion can distribute unmeasured covariates evenly between groups.

A question was raised regarding the extent of coronary artery disease. We used coronary artery bypass grafting as a surrogate for coronary artery disease, and the mean numbers of grafts per patient were 1.0 ± 1.3 in the mechanical aortic valve group and 1.0 ± 1.2 in the bioprosthetic aortic valve group ($P = .86$). We performed an analysis of survival of patients undergoing aortic valve replacement with and without coronary artery bypass grafting (Figure 1). The survival benefit we observed with a mechanical aortic valve appears, however, to be independent of the presence of coronary artery disease in our multivariate model, as shown in Table 5 of our original article.¹

Our finding of a survival benefit in the mechanical aortic valve group was surprising, and we have hypothesized that one possible explanation would be patient–prosthesis mismatch. We do not have the effective orifice area data available for this study group. We have, however, included information regarding body surface area and body mass index, size of prosthesis, and the incidence of aortic root enlargement in each group (see Table 1 in our original article). In general, surgeons at our clinic perform aortic root enlargement to accommodate a larger prostheses in any patient who is at risk for patient–prosthesis mismatch.²

We believe that current guidelines are generally appropriate for mechanical or bioprosthetic valve selection. Our primary

concern is with the growing trend toward placing bioprosthetic aortic valves in younger patients. All observational (retrospective or prospective) studies are unable to eliminate the potential impact of patient selection bias; however, this investigation adds equipoise.

Morgan Brown, MD

Hartzell Schaff, MD

Division of Cardiovascular Surgery, Mayo Clinic, Rochester, MN

References

1. Brown ML, Schaff HV, Lahr BD, Mullany CJ, Sundt TM, Dearani JA, et al. Aortic valve replacement in patients aged 50 to 70 years: improved outcome with mechanical versus biologic prostheses. *J Thorac Cardiovasc Surg.* 2008;135:878-84.
2. Dhareshwar J, Sundt TM 3rd, Dearani JA, Schaff HV, Cook DJ, Orszulak TA. Aortic root enlargement: what are the operative risks? *J Thorac Cardiovasc Surg.* 2007;134:916-24.
doi:10.1016/j.jtcvs.2008.06.012

Importance of stabilization of the mitral annulus in mitral valve repair

To the Editor:

We read with great interest the article of Flameng and coauthors¹ about their experiences with mitral valve repair in Barlow disease and fibroelastic deficiency. They found that not using annuloplasty ring in mitral valve repair is a risk factor for recurrent mitral valve regurgitation. We