Singapore General Hospital
Singapore, Republic of Singapore
"Cardiovascular and Metabolic
Disorders

Duke–National University of
Singapore Graduate Medical School
Singapore, Republic of Singapore
"Department of Anesthesia
National University Health System
Singapore, Republic of Singapore

References

1. Ng RR, Chew ST, Liu W, Shen L, Ti LK. Identification of modifiable risk factors for acute kidney injury after coronary artery bypass graft surgery in an Asian population. *J Thorac Cardiovasc Surg*. 2014;147:1356-61.
2. Lassnigg A, Schmidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. *J Am Soc Nephrol*. 2004;15:1597-605.
3. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11:R31.

<http://dx.doi.org/10.1016/j.jtcvs.2014.03.032>

IS EARLIER AORTIC VALVE SURGERY IN REPAIR CANDIDATES JUSTIFIED?

To the Editor:

I read with great interest the report by Sharma and colleagues¹ about their experience with aortic valve (AV) repair and congratulate them on their honest presentation of the long-term data. I believe, however, that the interpretation of some aspects needs additional comments and questions. The authors stated that survival after AV repair in their population was excellent and, with 91%, 80%, and 58% survival at 5, 10, and 15 years, respectively, was indistinguishable from the healthy population. Such a survival of the healthy population with a median age of 54 years seems to be rather low, and this impression could be intensified when looking at the US Life Tables,² which revealed corresponding survival rates of 96%,

90%, and 83% for a 54-year-old population containing 76% men. The authors found (not unexpectedly, because this aspect has already been revealed after AV replacement³) that myocardial impairment (MI) was a significant predictor of mortality. They correctly noted that this is barely avoidable, because the late presentation of symptoms in some patients with aortic insufficiency does not lead to referral for surgery until the development of MI. They suggested, however, earlier surgery for patients with suitable repair anatomy. In this context, 2 questions arise: how reliable is the assessment of AV repair suitability; and are patients with MI proper candidates for AV repair? I believe AV replacement should be preferred for patients with considerable MI because such patients need a fast and safe surgery without the risk of residual or recurrent insufficiency, let alone any intraoperative revisions. The remaining aortic insufficiency, which can never be ruled out after repair, can even be considered as a potential factor that can worsen long-term survival in this special subgroup. However, the authors did not provide the rate of postoperative aortic insufficiency—neither in the entire nor in this special cohort. Thus, I am wondering whether the rate of reoperation alone would be adequate enough for assessment of clinical and, especially, functional results. Furthermore, the number of patients operated at Mayo Clinic, with an average of about 12 annually, does not indicate that a considerable share of aortic valve pathologic entities could be scheduled for the repair. By coincidence, we submitted an abstract for the same American Association for Thoracic Surgery meeting that included 137 repairs performed during a 1-year period, but it was not well received by the reviewers.

It seems that AV repairs are still limited to single centers or, even, surgeons; hence, we can hardly speak about the "expanding relevance of

AV repair." The repair rate, as presented in our abstract, was 40% for all AV surgery patients younger than 70 years or, after excluding patients with contraindications (eg, MI), even greater. Even if the suitability of repair could be assessed with a probability of about 80%, the final decision for AV repair was always performed during surgery. Thus, I am convinced that AV repair is a valuable option; however, the repair candidates must fulfill the same indication criteria as for AV replacement,³ because the need for replacement can never be ruled out.

Paul P. Urbanski, MD, PhD
Cardiovascular Clinic Bad Neustadt
Bad Neustadt, Germany

References

1. Sharma V, Suri RM, Dearani JA, Burkhart HM, Park SJ, Joyce LD, et al. Expanding relevance of aortic valve repair—is earlier operation indicated? *J Thorac Cardiovasc Surg*. 2014;147:100-8.
2. Arias E, Curtin LR, Wei R, Anderson RN. US decennial life tables for 1999-2001, United States Life Tables. *Natl Vital Stat Rep*. 2008;58:1.
3. Bonow RO, Carabello BA, Chaturjee K, de Leon AC Jr, Faxon DP, Freed MD, et al. 2008 Focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2008;52:e1-142.

<http://dx.doi.org/10.1016/j.jtcvs.2014.02.041>

COX MAZE III PROCEDURE: THE BEST ALTERNATIVE IN SURGERY FOR ATRIAL FIBRILLATION

To the Editor:

We read with particular attention the article by Stulak and colleagues.¹ After close scrutiny of this report one cannot escape the conclusion that standard cut-and-sew Cox maze III procedure, as first described by Cox and associates,² remains the criterion standard choice for the surgical treatment of any type of atrial fibrillation (AF). Of special interest is the entity of mitral valve (MV) disease with concomitant long-standing persistent

AF. Unfortunately, alternative energy sources used for the Cox maze IV have not shown consistent results.³ We had the opportunity to compare 2 groups of patients who underwent MV surgery and surgery for AF. With regard to the AF, all the cases were performed exclusively by the cut-and-sew method to guarantee total transmural lesions. One hundred patients underwent only isolation of the pulmonary veins; 20 underwent a Cox maze III procedure. All patients were operated on by the same surgeon (O.A.G.-V.). Sinus rhythm conversion rate was immensely superior for the Cox maze III group (19/20; 95%), than for the pulmonary vein isolation group (76/100; 76%) at 3 months' follow-up. The prevalence of normal sinus rhythm was higher in the Cox maze III group at 6 months' follow-up (95% vs 54%). Although our data have not yet been published, a brief analysis of them shows that the sole isolation of the pulmonary veins is not enough to eliminate long-standing persistent AF in the setting of concomitant MV disease. In addition, the Cox maze III procedure must be performed by the cut-and-sew method, because this is the only measure that will ensure transmural lesions. Moreover, a biatrial lesion set pattern is highly mandatory in the Cox maze III procedure to eliminate long-standing persistent AF.

Definitely, the standard cut-and-sew Cox-maze III procedure remains the best choice in surgery for AF, especially for patients with MV disease.

Ovidio A. Garcia-Villarreal, MD^a

Ernesto Fernández-Ceseña, MD^b

Raquel Vega-Hernández, MD^a

^aDepartment of Cardiac Surgery

^bDepartment of Cardiology

Hospital of Cardiology

Monterrey, Mexico

References

1. Stulak JM, Suri RM, Burkhart HM, Daly RC, Dearani JA, Greason KL, et al. Surgical ablation for atrial fibrillation over two decades: are the results of new techniques equivalent to the Cox maze III procedure? *J Thorac Cardiovasc Surg.* Epub 2014 Jan 18.
2. Cox J, Schuessler RB, D'Agostino HJ Jr, Stone CM, Chang BC, Cain ME, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. *J Thorac Cardiovasc Surg.* 1991;101:569-83.
3. Garcia-Villarreal OA. eComment. Alternative energy sources in surgery for atrial fibrillation. *Interact Cardiovasc Thorac Surg.* 2012;15:128.

<http://dx.doi.org/10.1016/j.jtcvs.2014.02.071>

AUTOPHAGY AND THE HUMAN HEART

To the Editor:

The noteworthy article by Singh and coworkers,¹ "Autophagy Gene Fingerprint in Human Ischemia and Reperfusion,"¹ recently published in the *Journal*, illustrates the importance of keeping surgeons informed about potentially new approaches to treating patients with heart disease. Although the process of autophagy is well known in the scientific community, few cardiothoracic surgeons are aware of its relevance to acquired heart disease, general thoracic surgery, and cardiothoracic transplantation.

This article brings to our attention the accumulating evidence from animal and human studies that cardiac autophagy is an endogenous cellular protective mechanism activated by ischemic stress. Because ischemia-reperfusion injury contributes to post-operative morbidity and mortality in a number of surgical settings, the prospect of harnessing this pathway to improve clinical outcome is highly attractive. One obstacle to overcome is the effective translation of preclinical knowledge to clinical application. The recent publication by Singh and coworkers¹ is a positive step forward. These investigators conducted a comprehensive evaluation of changes in expression of several autophagy-related genes and upstream regulators in 9 patients undergoing coronary artery bypass grafting. Key components of the autophagy pathway

were upregulated, including cysteine protease Atg4 isoforms (Atg4A, Atg4C, Atg4D), which contribute to autophagosome formation by priming LC3 for lipidation. The elevated LC3II/LC3I ratio was interpreted as an increase in cardiac autophagy. Their conclusion, that cardiac autophagy is induced in response to ischemia/reperfusion, is consistent with our 2013 observations² in 19 patients undergoing heart surgery who exhibited marked decreases in the autophagy proteins p62/SQSTM1, Beclin-1, Atg5-12, and LC3B. We concluded that ischemia-reperfusion injury was associated with a marked acceleration in autophagic flux (clearance). Of particular interest was the decrease in p62, because this bifunctional protein binds ubiquitinated targets and autophagosomal LC3. With enhanced flux, the degradation of autophagosomes and their cargo increases, as reflected by depletion of p62. We observed that decreases in both LC3-I and LC3-II correlated with a fall in p62 and that the magnitude of p62 depletion varied directly with crossclamp time and inversely with mortality and morbidity risk scores. Why our findings with respect to changes in LC3 and p62 differ from those of Singh and coworkers¹ is unclear, given our similar patient demographics. One explanation could lie with the differences in crossclamp time (118 vs 78 minutes) and cardiopulmonary bypass time (145 vs 97 minutes); they were shorter in the study of Singh and coworkers.¹ The key point is that both groups provide translational information that supports the concept that the homeostatic intracellular repair response, or adaptive autophagy, is active in the human heart. This concept is further supported by Kassiotis and colleagues,³ who reported in 2009 that left ventricular assist device unloading of the failing human heart was associated with a decrease in autophagic activity, and Garcia and associates,⁴ who reported in 2012 that