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.

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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

atrial autophagy was impaired in the patients who had postoperative atrial fibrillation after coronary artery bypass grafting. These findings provide hope that pharmacologic activation of autophagy or the manipulation of key autophagic machinery-related molecules will lead to new approaches to managing heart failure related to ischemia-reperfusion.

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WHO SHOULD DECIDE MARGIN LENGTH IN PULMONARY EXCISION OF LUNG CANCER?

To the Editor:

I read with great interest the article by Dr Mohiuddin and colleagues, entitled "Relationship Between Margin Distance and Local Recurrence

FIGURE 1. Margin cytology results in cases of pulmonary wedge resection for non-small cell lung cancer according to tumor size and margin distance. Open circle represents malignant negative cytology (n = 104), and closed circle represents malignant positive cytology (n = 53).

FIGURE 2. Methods of measuring margin length.

Among Patients Undergoing Wedge Resection for Small (≤ 2 cm) Non-Small Cell Lung Cancer.” The authors stated that the distance from the margin to the tumor (margin length) of 1.5 cm was a critical point in wedge resection cases according to the rate of local recurrence and relapse-free survival.¹

I agree with their opinion because, in our experience, there are few margins revealing malignant positive cytology among patients who underwent wedge resection for peripheral non-small cell lung cancer with a margin length of 2.0 cm or greater (Figure 1). With our method, after carrying out margin cytology, the length is measured from

the cut edge of the stapled line,²⁻⁴ which may be approximately 0.5 cm or greater than in the report by Mohiuddin and colleagues.

There are different ways to measure “margin length,” as Goldstein and colleagues⁵ pointed out: (1) pleural surface-based margin distance, (2) gross cut-surface margin distance, and (3) microscopic margin distance (Figure 2). Our choice is the pleural surface-based margin distance, whereas the latter 2 may be chosen according to Mohiuddin and colleagues.¹ There may be a discrepancy of approximately 0.5 cm.

Obtaining a sufficient margin length is the most important issue