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Key Words: mitral regurgitation, aortic valve, replacement, echocardiography

Discussion

Dr Ravi K. Ghanta *(Charlottesville, Va)*. Thank you. I would like to thank the association for the opportunity to present our study evaluating the natural history of coexistent MR after AVR. We have no disclosures.

We frequently identify coexistent MR in patients who have aortic stenosis. Many studies show that 50% to 75% of patients have some degree of MR at the time of AVR. I think all of us would agree that severe MR necessitates concomitant intervention of the mitral valve at the time of AVR. What to do for lesser degrees of MR, however, is unclear. It is widely assumed that MR improves after AVR. This is entirely logical because MR is at least partly exacerbated by the elevated left ventricular pressure encountered because of the elevated AVG. The AVR would relieve the AVG, and this should, logically, decrease MR.

Few studies, however, have actually evaluated whether this occurs. Dr Woo and colleagues presented at this meeting, 3 years ago, a study evaluating the short-term effects of AVR on MR. They found that MR improved only modestly after AVR. No study, however, has evaluated the long-term effects of AVR on residual MR; thus, the appropriate management of patients with moderate MR remains unclear.

The objectives of this study were to examine the evolution of residual MR following isolated AVR for aortic stenosis. We sought to identify prognostic indicators for improvement in MR after isolated AVR. We also sought to identify the effect of residual MR on survival. We evaluated consecutive patients, from 2004 to 2013, who underwent primary isolated AVR for aortic stenosis, who also had coexistent MR and at least one postoperative echocardiogram performed at the University of Virginia.

Using these criteria, we identified 423 patients. These 423 patients underwent 903 postoperative echocardiograms. The MR was graded using the American Society of Echocardiography scale, which was 0 for no MR, 0.5 for trace MR, 1 for mild, 2 for moderate, 3 for moderate/severe, and 4 for severe. These echocardiograms were obtained at varying time intervals, and the residual MR was modeled utilizing hierarchic generalized linear modeling techniques. We evaluated the relationship of AVG and change in AVG after AVR to residual MR. We divided patients into those that improved postoperatively and those that did not improve postoperatively, in terms of MR, and we compared various preoperative demographic data and hemodynamic data.

Survival data were obtained from our clinical data repository at the University of Virginia, which combines clinical data with Social Security Death Index data and data from the Commonwealth of Virginia, to determine survival. We utilized Cox proportional hazard regression analysis to assess survival in these patients.

Of the 423 patients in this study, 319 had preoperative mild MR, and 105 had preoperative moderate or greater MR. The mean age of patients in the study was 73; the mean AVG was 47.9. The majority of patients in this study had functional MR—96%. A few had rheumatic or leaflet prolapse. Comparison of the moderate to the mild MR patients preoperatively showed that the moderate patients were more likely to be female (53% vs 36%), more likely to have atrial fibrillation (40% vs 29%), more likely to have a preoperative diagnosis of heart failure (70% vs 50%), and more likely to have a higher preoperative pulmonary artery pressure (51 vs 40 mm Hg).

Figure 2 shows, on the y-axis, the median change in MR from baseline versus time, and 2 groups are shown—those that had preoperative mild MR, and those that had preoperative moderate or greater MR. The acute reduction in MR in patients who had preoperative mild MR was

0.13 degrees—so, a very small change. The acute reduction in MR in patients who had moderate MR was approximately 0.53 degrees.

At 1 year postoperatively, MR begins to worsen, and by year 4, the change in MR from baseline approaches 0, indicating that many patients return to the baseline level of MR they had prior to AVR. This figure shows the same data in a different way. The y-axis is the absolute value of the MR grade versus time, for the 2 groups—the moderate or greater MR, and the mild MR, and here you see the mild MR patients stay close to mild, and the moderate or greater MR patients initially come to a level of 1.3 and begin to worsen over time. An important finding is that 56% of patients at the conclusion of the study had the same or worse MR as they did preoperatively.

We stratified the patients, by no improvement in their MR versus improvement in their MR; 186 patients had improved MR, and 237 had no improvement or worsening of MR. The improved patients had a median improvement of 0.77 degrees. The nonimproved patients had a median increase in MR of 0.18 degrees, and residual MR was 0.56 in the patients that had improvement. There were no statistically significant differences between these 2 groups in left ventricular ejection fraction, preoperative AVG, change in AVG after AVR, or these other comorbidities.

We also performed a linearized model to look at the relationship of change in AVG to reduction of MR and found no statistically significant relationship. Figure 3 shows survival as a function of time for the 2 groups—patients who had preoperative mild MR and those that had preoperative moderate or greater MR. The 5-year survival was 71.7% versus 61.8%. This was not statistically significant. So the grade of preoperative MR did not influence 5-year survival in this study. We looked at the survival in patients that had improved MR, versus those that did not have improved MR; the 5-year survival was 74.9% versus 65.4%. This difference did not achieve statistical significance, but the P value was very close, at .06.

This is a limited study. It is a single-center study, retrospective. By the nature of that type of study, the echocardiography follow-up was irregular, and it was dependent on the practices of the cardiologists. We, of course, would expect some sampling bias, as sicker patients probably were more likely to get an echocardiogram than those who were doing well, and we did not assess the symptoms of residual MR in this study; we also did not evaluate the electrocardiograms for other factors, such as ventricular remodeling.

But from these data, we conclude that coexistent MR only modestly improves after isolated AVR for aortic stenosis, and in many patients, it eventually regresses back to baseline or worsens. Preoperative AVG, reduction of valve gradient, heart failure, and atrial fibrillation were not predictive of degree of residual MR; the degree of preoperative MR in this group of patients did not adversely affect 5-year survival. Patients with improvement in MR after AVR did demonstrate a trend toward improved survival at 5 years, and my assumption would be that if this study was further followed, the differences between the 2 groups would widen, and a statistically significant result would likely be obtained. So we would ultimately conclude that more aggressive mitral valve surgical options should be considered in select patients who have moderate or greater MR and are in need of AVR for aortic stenosis. Thank you very much. This discussion will be led by Joseph Woo.

Dr Joseph Woo *(Palo Alto, Calif)*. Thank you. So, Dr Ghanta, I congratulate you on your outstanding clinical research effort, and it is particularly reassuring to see that your MR reduction findings nearly identically mirror those reported by other groups. But your study goes further, and I commend your tracking of the longitudinal outcomes with respect to MR recurrence, as well as survival, and it is particularly notable to see that trend in difference in survival depending upon what happens to your MR. With your permission, I would like to incorporate your data on Monday morning, when we present to the National Institutes of Health Cardiothoracic Surgery Network in Bethesda a proposal to fund a multicenter, prospective, randomized trial on this topic. So I have 3 specific questions.

The first relates to anatomic criteria. So, have you looked at your echocardiograms and identified any potential structural features of the mitral valve, such as leaflet or annular calcification, that may predict a greater likelihood of not having reduction in MR after AVR?

Dr Ghanta. Excellent questions, and yes, I would be more than happy to share these data, and I do think a prospective study would be exactly what is required to evaluate this question. Although these retrospective studies have numerous limitations, primarily in sampling bias, with echocardiograms, there is a wealth of information that I think can be gained. There obviously are factors that should predict who will improve, versus who will not improve. We just have not identified them yet, and it is, I think, factors that you pointed out in terms of evaluating the mitral annulus size and dimensions, left ventricular size and dimensions, and left atrial size and dimensions—all would likely be predictive. We have not looked at the echocardiograms in for that type of analysis. It is fairly resource intensive to do that, and we would love to do that in the future.

Dr Woo. So, one of the concerns is that escalating the operation somewhat by adding a mitral intervention will increase the perioperative morbidity and mortality, and may not yield benefit long term. You have shown the impact of *not* doing something, but have you looked at any of your