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Commentary: Missing the trees for the forest: Transcatheter versus surgical approaches to secondary mitral regurgitation

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The optimal treatment of secondary mitral regurgitation (MR) remains controversial in the era of transcatheter mitral valve repair (TMVr). Patients with severe secondary MR are undoubtedly a challenging population. Perhaps 20% or more of patients with chronic heart failure have MR, which increases their risk of death by at least 2-fold.¹ Surgery, specifically chordal-sparing mitral valve replacement, has been shown to reduce significant postoperative MR, heart failure–related adverse events, and admissions for this population, but has not been demonstrated to improve survival.² In this issue of the *Journal*, Okuno and colleagues² attempt a comparison of surgical mitral valve repair (SMVr) with a ring annuloplasty versus edge-to-edge TMVr. They attempt to control for significant differences in patients receiving either treatment using propensity scoring and create 101 pairs out of more than 400 patients. The authors find no difference in 2-year mortality among matched pairs, although surgical repair appears associated with improvements in residual MR, left ventricular ejection fraction, and symptoms.

The article by Okuno and colleagues² is a reasonable attempt at addressing an important and difficult area of clinical uncertainty, but the work has methodological limitations that must be noted. To begin with, there are clear

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Although survival differences between treatment strategies for secondary MR may be similar, secondary end points may favor surgical therapies.

difficulties in matching these 2 retrospective patient cohorts. It is impossible to confirm that patients in each propensity-matched treatment arm were truly candidates for both procedures. In fact, this is highly likely not to be the case, raising into question the propensity scoring methodology's appropriateness. The European System for Cardiac Operative Risk Evaluation was significantly higher in the TMVr cohort, and one imagines that some of these patients may have been considered inoperable. Barring this objection, standardized mean differences between the 2 groups are large (>0.1) for 5 covariates, suggesting the groups are not especially well matched. The unmatched histogram of Figure S2 highlights the heterogeneous nature of these 2 treatment groups, which makes matching predictably challenging. Particularly puzzling is the observation that twice as many patients undergoing TMVr had prior percutaneous coronary intervention as did patients undergoing SMVr. Accordingly, the authors appropriately made an attempt to confirm the finding of no difference in survival at 2 years using Cox models by creating additional Cox models including covariates exhibiting imbalance. No differences were found for the primary outcome, although the large 95% confidence intervals in these adjustment models point to the low event rates observed. Indeed, no power calculation was included in the "Materials and Methods" section, and 2 groups of approximately 100 patients would be insufficient to detect small differences in mortality rates.

Moreover, it is plausible that the secondary outcomes in this patient cohort study are just as important as the primary mortality outcome or that the trees are just as important as their forest. The finding of no difference in survival at

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2 years in this limited sample of patients receiving 2 strikingly different treatments is unsurprising. Mortality was approximately 23% at 2 years between matched groups, consistent with prior surgical and transcatheter studies addressing secondary MR.^{3,4} Although recent data have shown in 1 of 2 randomized trials to have a benefit of edge-to-edge TMVr over medical therapy in secondary MR, no good studies have been performed comparing surgery with medical therapy.^{4,5} However, one must not miss the trees for this particular forest. In the present study of Okuno and colleagues,² the secondary end points among the matched groups merit consideration. Approximately 40% of patients undergoing TMVr had moderate or greater residual MR versus 15% of patients undergoing SMVr. Ejection fractions were unchanged for patients undergoing TMVr, but improved 10% in surgical patients. New York Heart Association class III/IV status was present in 30% of patients undergoing TMVr compared with 13% of patients undergoing SMVr. The secondary end points suggest that surgery (even repair, which some consider inferior to chordal-sparing mitral valve replacement) can better

improve MR, ventricular function, and, most important, symptoms. These and other data comparing transcatheter and surgical mitral therapies for secondary MR may be unlikely to demonstrate survival advantages in the short-to-medium term given data already accumulated. However, within the forest of underpowered survival analyses, the “trees” or secondary end points must not be overlooked.

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