

Asymptomatic mitral regurgitation – wait or operate?

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Goldstone *et al.* should be congratulated for presenting the first meta-analysis to assess the differences in all-cause mortality between watchful waiting versus early surgery for asymptomatic patients with severe degenerative mitral regurgitation (1). The topic is controversial and the article is timely in the context of recent changes to the American College of Cardiology/American Heart Association Guidelines (2).

Several points should be addressed regarding the statistical aspects of the study. Firstly, only three retrospective studies fulfilled the inclusion criteria for meta-analysis and thus any conclusions drawn from the results should be interpreted with caution (3-5). Two additional single-arm studies were added to evaluate the aggregate mortality rates and other secondary outcomes. Given the paucity of studies, it may also be difficult to ascertain robust findings from sensitivity analyses. The authors astutely highlighted the heterogeneous definitions of ‘early surgery’ between studies, as well as differences in the baseline patient characteristics and concomitant procedures such as coronary artery bypass graft surgery. The statistical heterogeneity identified from the meta-analyses was also duly noted by the authors.

With these limitations in mind, the meta-analysis found significantly higher long-term survival and repair rates for patients who underwent early surgery compared to watchful waiting. Admittedly, the survival outcomes were associated with significant heterogeneity ($I^2 > 50\%$), and the improved repair rates were relatively minor (RR 1.07, 95% confidence interval 1.01-1.13). Nonetheless, the authors conveyed a strong message that highlighted these two relatively ‘hard endpoints’, which suggested potential benefits of earlier surgical intervention and indicated a possible paradigm shift in the wait versus operate

management plan for asymptomatic patients with severe mitral regurgitation. Further clinical evidence to help formulate future guidelines may be derived from large, well-designed randomized controlled trials. However, a lack of clinical equipoise from surgeons and cardiologists who believe in the benefits of early intervention may preclude the completion of such trials.

From an institutional perspective, it must be emphasized that the findings of the meta-analysis were derived from highly selected patient cohorts within high-volume tertiary centers. Of the three comparative studies, the mortality rates for early surgery were 1.6%, 1.1% and 0, respectively, with repair rates of 100%, 93.0% and 94.5%, respectively (3-5). As Goldstone *et al.* emphasized in their article, these outcomes compared favorably to current national databases, and may not be applicable to all cardiothoracic units. From our own experience of 586 consecutive patients who underwent mitral valve repair for myxomatous degeneration, the mortality rate was 0.9% and the incidence of stroke was 0.7%. At the time of discharge from hospital, 99.0% of patients had at most mild regurgitation. From our experience, the key to favorable surgical outcomes is largely dependent on reproducible surgical techniques and appropriate patient selection in the setting of a collaborative multi-disciplinary approach to patient care. Asymptomatic patients with severe mitral regurgitation were often referred to our institution by physicians who recognized our clinical outcomes and felt reluctant to wait for the progression of indicators such as pulmonary hypertension, atrial fibrillation and left ventricular dysfunction. This early referral pattern relies on an understanding that perioperative outcomes may be similar or worse after surgery compared to non-surgical observation but that the benefits are evident in

long-term clinical endpoints. This was demonstrated by the large multi-institutional Mitral Regurgitation International Database that reported higher incidences of perioperative atrial fibrillation but superior 5-year mortality and heart failure outcomes for patients who underwent early surgery (4).

In brief, should an asymptomatic patient with severe mitral regurgitation undergo early surgery or watchful waiting? The answer is probably dependent on the level of expertise and surgical outcomes of the institution. Existing data suggest earlier intervention for selected patients in specialized centers, where a high standard of surgical outcomes may result in superior long-term survival.

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