Rethinking Mitral Valve Surgery during the Golden Years

Running title: Rao et al.; Mitral valve surgery during the golden years

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Journal Subject Code: Cardiovascular (CV) surgery:[38] CV surgery: valvular disease

Key words: mitral valve regurgitation, surgery, Editorial, echocardiography, elderly
The benefit of MV surgery in elderly patients remains a major area of controversy in the treatment of mitral regurgitation. The paper by Vassileva and colleagues in this issue of Circulation examines contemporary data from the Medicare to determine how older patients fare after undergoing isolated MV surgery. This issue has important health and economic implications given the high prevalence of hemodynamically significant mitral regurgitation over the age of 75. Older studies have shown high mortality in elderly patients undergoing MV replacement in excess of 14%, and even greater than 20% in low volume centers. However, concomitant CABG is common in older patients, and prior MV surgery studies in the elderly contained a mix of patients often needing concomitant CABG or interventions on other valves. In addition, the studies included both MV repair and MV replacement patients, undoubtedly skewing the risk profile since mortality and adverse outcomes for MV replacement has consistently been shown to be higher most studies.

It is on the basis of higher mortality that the most recent ACC/AHA valve guidelines suggest that a different standard of care should be applied for elderly patients with asymptomatic or minimally symptomatic MR. The guidelines suggest a conservative, medical management approach in these patients. This recommendation is based on natural history studies and expert consensus rather than randomized trial data of surgical vs. conservative management. In contrast to asymptomatic or mildly symptomatic patients, the recommendation is for operative repair in symptomatic patients, regardless of age, when the patient is a reasonable candidate.

Over the years, increasing numbers of patients have received MV repair as opposed to replacement, with a rate of 69% in the STS database in 2007 for all surgeries for primary mitral regurgitation. Since complication rates are lower with repair for all patients, and since repair has become more common, there is a need to determine whether there are increased repair rates
and better outcomes in elderly patients undergoing mitral valve surgery.

In order to illustrate the issues facing the clinician, we will consider two patient scenarios, in which the data from this analysis may inform our decision to operate. The first is an 82 year-old small Asian woman with chronic atrial fibrillation who has minimal symptoms, no co-morbidities and moderate to severe MR with mitral valve prolapse and annular dilation. According to the STS Database calculator (http://www.sts.org), her 30-day mortality for mitral valve repair is 3.8% and for replacement is 6.8%. The second is a 78 year-old averaged sized Caucasian male with Class II heart failure symptoms and atrial fibrillation with severe MR due to mitral valve prolapse. Given a history of hypertension and diabetes, his mortality for mitral valve repair is 2.4% and for replacement, 3.9%. At a first analysis, the male patient would appear to have lower mortality than the female despite greater co-morbidities. However, are these clinical data sufficient for making the decision to operate?

In this issue of Circulation, Vassileva and colleagues examine the relative mortality (operative and late) associated with mitral valve surgery in Medicare beneficiaries, comparing mitral valve repair to mitral valve replacement. They examined a contemporary cohort of almost 184,000 patients who received surgery between 1999 and 2009. By limiting the analysis only to subjects with isolated mitral valve surgery, with the exception of tricuspid valve repair or replacement, they initially included only 31% (approximately 57,000) of the patients who underwent mitral valve replacement and repair during this period. Any patient with prior cardiac surgery or the need for other cardiovascular procedures was excluded. Further exclusions brought the ultimate sample size down to about 47,000. Nevertheless, the strengths of this study are the large number of subjects included in the analysis and that it reflects "real-world" practice. However, the use of an administrative database creates a number of important limitations, most

DOI: 10.1161/CIRCULATIONAHA.113.002574
of which they outlined in the discussion. They have controlled for a number of important baseline characteristics.

Unique to this study, Vassileva et al. demonstrate the true mortality for isolated MV surgery in the elderly. This is both a strength and detractor. It helps eliminate the confounding of outcomes that could be due to comorbidities in sicker patients such as those undergoing simultaneous CABG. However, isolated MV surgery in the elderly comprises a minority of all MV surgeries in this demographic and thus the analysis has more confined clinical applicability.

In contrast to the overall trend showing that MV repair has come to dominate replacement for primary MR, in this Medicare database of elderly patients, the trend was reversed: 64% underwent replacement. The lower rate of repair may be due to the higher prevalence of mitral annular calcification in the elderly that limits the use of ring annuloplasty, the presence of anterior or bileaflet degenerative mitral valve disease, or a higher prevalence of Carpentier class IIIb, so-called “functional” MR.

Perhaps the most dramatic and impactful finding of the study is the demonstration of very low mortality for MV repair patients, 3.9%, and only 5.1% for patients >75 years of age. This finding leads us to conclude that the occasional elderly patient with primary MR who meets current indications for MV surgery should not be denied MV repair on the basis of age alone.

Turning to the majority of patients who underwent replacement, the operative mortality was 8.9% overall and 10.6% for patients over 75 years. This mortality is high, but not as high as prior studies that did not limit inclusion to only isolated MR. What is it about MV replacement that makes mortality so much higher? This study shows that they are a sicker population with more heart failure, atrial fibrillation and other comorbidities, more likely to be female, and more likely to have non-elective surgery done in low volume centers. On a population level,
predictors of repair were male sex, younger age, elective surgery and most significantly, annual mitral procedure volume greater than 40 cases/year.

However, the study could not predict the valvular anatomic features that determine repair versus replacement. Since there is such a divergence of risk between the repair and replacement groups, pre-operative prediction of the likelihood of repair based on the echocardiographic valve appearance is of paramount importance. Such differentiation would be critical to advising elderly patients of their risk and in planning for elective intervention. The echocardiograms from the two patients described above are shown. The Asian female had minimal calcification and an increased annular measurement, making repair likely (Figure 1). The Caucasian male had significant posterior annular calcification and a small annulus, likely necessitating replacement (Figure 2). Thus, after considering the valve morphology, the predicted 30-day mortality was nearly equal for the two patients, whereas initial assessment predicted twice the mortality for the older woman. Unfortunately, even with excellent pre-operative echocardiographic images, pre-operative prediction of repair versus replacement is not always possible. 1

A delay from symptom onset to valve surgery of greater than one year was observed in this study. This finding is not surprising given the misgivings that both physicians and patients may have about risks of operating at an older age. However, in these patients, even the high risk of operative mortality for MV replacement may be an acceptable risk to potentially reduce symptoms and progression of heart failure.

It is said that in medicine we should strive to either make patients feel better or live longer, preferably both. Does MV surgery in older patients accomplish either of these aims? The durability of the repair and the long-term improvement in MR severity and most importantly, patient symptoms, could not be gleaned from this analysis of an administrative
database. And it cannot be understated how important symptom benefit (vs. survival benefit) is in the elderly population, particularly in those over 75. What remains to be determined is if the elderly gain as much symptom benefit from MV surgery as younger patients, and whether long-term symptom benefit outweighs the operative risk and recovery time. While a survival advantage can be inferred from the Kaplan-Meier it remains unproven. After the initial mortality associated with surgery, survival in the population who received mitral valve repair is equal to that of expected survival, whether they are under or over 75 years of age. For replacement, the survival is less than expected in both age groups. There is no control group of medically managed patients.

Unfortunately, data on ejection fraction and LV volumes were not available. In addition to symptoms, these variables form the basis of our current valve surgery guidelines. If there was a delay in referral for valve surgery as would be inferred from the number of patients with HF symptoms for over a year, it is possible that the MR was longstanding and irreversible LV remodeling may have occurred. If so, this may have skewed outcomes, particularly for MV replacement. The reasons for delay in surgical referral and the impact these delays had on outcomes is unknown.

Comparison to Previous Studies

A recent study linked the STS Database to longitudinal claims data from the Centers for Medicaid and Medicare Services (CMS) and examined outcomes in 14,604 patients with isolated mitral valve repair performed between 1991 and 2007. Patients with prior surgery, endocarditis and emergency operations were excluded. Operative mortality was 2.59%, lower than the repair cohort in Vassileva’s report. The mean follow-up was 5.9 years (range 1 – 18 years) with survival during follow-up at 74.9%. The 10- year event rates for mitral reoperation,
heart failure, bleeding, and stroke were 6.2%, 30.1%, 15.3%, and 16.4%, respectively. The 10-year actuarial survival of 57.4% was equivalent to the matched US population, and similar to the 53% in Vassileva’s report. Unlike the current study, data on ejection fraction were available and the mean ejection fraction for the population was 53%. This study did not compare isolated mitral valve repair to replacement and a similar analysis would be very useful based on the power of these linked databases.

A recent meta-analysis of 24 studies that examined mitral valve surgery in octogenarians and showed a much lower mortality with repair (7.3%) compared to replacement (14.2%).

Many of the included studies were not confined to isolated mitral valve surgery. However in the subset with isolated mitral valve surgery, the 5 year survival was 56%, impressive in a cohort of octogenarians.

Notably missing in all of these studies is a comparison to conservative medical management in elderly patients. However there are substantial data suggesting that mitral regurgitation, independent of mechanism, confers excess morbidity and mortality.

Since the elderly is a rapidly growing segment of the population, contemporary studies such as this are essential to challenge assumptions about negative surgical outcomes based on age alone. With a median age of 75 years including almost a quarter of the patients older than 80, this study helps guide our management of elderly patients with mitral valve regurgitation.

The major finding of this study is the very low operative mortality for isolated MV repair. Patients who are be candidates for an isolated MV repair, who are otherwise expected to have a normal life expectancy, regardless of age or severity of symptoms, should be offered repair. Unfortunately, isolated MV repair in a contemporary Medicare population still only accounts for a tenth of all MV surgeries. The patient is most likely to receive a repair if surgery is performed
under elective circumstances in center with a large volume of mitral valve surgery. However, specific patient characteristics cannot be ignored, especially those related to morphology of the valvular apparatus, such as leaflet thickening and calcification, annular dilation and calcification and the anatomy of the subvalvular apparatus. Many elderly patients have several mechanisms contributing to the valvular dysfunction and standard repair techniques with predictable durability are often not possible.  \(^{15}\)

In the United States, the only alternative is currently MV replacement, which carries greater morbidity and mortality in the elderly, although this study suggests that mortality is lower than previously shown. The benefits and risks of MV replacement in the elderly should still be carefully weighed, but not at the expense of delaying an inevitable procedure and incurring the even higher risks attendant with non-elective surgery and surgery in patients who have developed heart failure as a result of their MR. As percutaneous treatments become available for mitral regurgitation, it is hoped that high risk patients can be treated with lower morbidity and mortality.  \(^{16}\)

Should the guidelines be revised to remove the statement urging a conservative approach in asymptomatic or minimally symptomatic patients? This study, along with other recent studies, suggests that when the valvular and clinical characteristics are propitious for repair, the same criteria should be applied across all age groups. When MV replacement is likely, the outlook remains murky. The high operative risk may not be justified for an asymptomatic patient, unless it could be shown that early surgery could reduce later development of symptoms such as heart failure.

As our patients get older, and perhaps, wiser, it is imperative that our research advances. We need additional options for treating common problems such as mitral regurgitation and more
effective decision analysis for the elderly who are considering cardiac interventions. We must consider quality and quantity of life as well as interventional risk as we assist patients in making the best choices for their golden years.

Conflict of Interest Disclosures: Elyse Foster reports significant grant support from Abbott Vascular Structural Heart.

References:


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Figure Legends:

**Figure 1.** Transthoracic echocardiographic apical 4-chamber view showing severe mitral regurgitation with mild posterior leaflet prolapse, annular dilation and minimal mitral annular calcification.

**Figure 2.** Transthoracic echocardiographic long axis view showing severe mitral regurgitation with severe mitral annular calcification and minimal annular dilatation.
Figure 1
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Circulation, published online April 8, 2013;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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http://circ.ahajournals.org/content/early/2013/04/08/CIRCULATIONAHA.113.002574

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