Mitral Regurgitation
What Causes the Leakage Is Fundamental to the Outcome of Valve Repair
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Mitrail regurgitation (MR) has become the predominant mitral valve disease as a result of the regression of rheumatic diseases and the aging of the population. The high prevalence in the elderly of degenerative and ischemic MR implies that MR is currently a public health problem. Recent data suggest that MR has severe outcome implications that are dependent on the degree of regurgitation, both for MR due to organic disease of the mitral valve and MR due to ischemic heart disease. This combination of high prevalence and relatively high risk requires careful examination of therapies applicable to MR. Unfortunately for patients with MR, therapeutic approaches for both medical and surgical treatment have not been evaluated by the state-of-the-art method—ie, by randomized clinical trials. Therefore, observational studies form the basis of our clinical decision-making process, and the quality of evidence is less than optimal. Our assessment of the improvement of outcome provided by various strategies (eg, medical treatment versus untreated observation, surgical treatment versus medical treatment of asymptomatic patients, valve repair versus valve replacement in patients who require surgery) is based on observational studies that have intrinsic limitations. The first implication of this situation is that we need (for a lack of a stronger word) appropriately designed randomized clinical trials comparing various strategies of treatment. The second implication is that it is not surprising that various observational studies, such as that presented by Thourani and colleagues in the present issue of Circulation,1 may have findings different from each other in accordance with the population examined. Consequently, it is essential to examine the current status of our knowledge and determine how to interpret data that may seem to contradict existing information.

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What does the current literature say about the potential outcome benefit of mitral valve repair for patients with MR? Valve repair, compared with valve replacement, provides a lower operative mortality rate and a better long-term survival rate.2–6 However, patients who undergo repair are often different from those who undergo valve replacement; they are usually younger, with lower prevalence of rheumatic disease and atrial fibrillation and better left ventricular function at baseline.3 Therefore, two processes have been used to examine the intrinsic benefit of the repair: (1) adjusting for differences in multivariate analysis of outcome3,4 or (2) comparing patients who have undergone valve repairs with patients who have undergone valve replacement after retrospectively matching them on the basis of selected key preoperative characteristics.6 This latter process, previously used by Craver et al,7 is rarely perfectly successful, and multivariate analysis is generally necessary to adjust for differences despite the matching. Furthermore, the matching process leaves a number of patients out, which makes the series nonconsecutive and the “matched group” quite arbitrary, particularly with regard to the degree of MR. Nevertheless, despite all these methodological issues, all studies, including that by Thourani and colleagues,1 find that repair compared with replacement is overall associated with improved rate of survival. One of the major reasons for the improved survival rate is that valve repair results in improved left ventricular function,3,8 probably because it preserves the entire native subvalvular apparatus.9 This results in a lower rate of postoperative heart failure and better functional capacity with valve repair.10,11 The improved mortality rate is also in part due to the fact that reoperation is not more frequent after valve repair than after replacement, with no late excess mortality due to reoperation.4 This result is not short-lived; Braunberger et al12 and our group4 have shown that the benefit of valve repair is sustained beyond the first 10 years of follow-up. Therefore, despite the lack of a randomized clinical trial, the only possible conclusion from all available data, including that of Thourani et al,1 is that valve repair should be the preferred mode of MR correction.

Once we have appreciated this consensus, the next question is whether this preferred approach of repairing rather than replacing mitral valves applies to all subgroups of patients with MR. Thourani et al1 answer “no” to this question. They report in the present issue that patients who are either older than 60 years or undergoing coronary bypass grafting (CABG) have no significant survival benefit from repair. Such a conclusion would be of great importance, inasmuch as these two groups represent the vast majority of patients who undergo surgery for MR (78% in our experience), and would suggest that in this majority of patients, a valve replacement without consideration of or attempt at repair would be acceptable. There would be little incentive for surgeons who at present do not routinely perform valve repair to improve their practice with this technique. This may hinder the increasing rate of mitral repair noted by the Society of
Thoracic Surgeons (from 26% in 1993 to 45% in 2001). The interpretation that older patients and those requiring CABG do not benefit from valve repair would have dramatic consequences and hinges on the generalizability of the data obtained by Thourani et al.1

First, the interpretation that valve repair is not beneficial in patients older than 60 years or in patients requiring CABG is at variance with other data. In patients with isolated, organic MR, previous reports suggest that the benefit of repair is similar whether or not CABG is performed simultaneously.2,3,5 To examine anew the generalizability of the impact of valve repair on outcome in specific subgroups, we reviewed the outcome of 1344 patients who underwent surgery for isolated (no aortic valve replacement), pure (no stenosis) MR at our institution between 1980 and 1995 (inclusive). In the 897 repairs (67%) versus 447 replacements, age (65/11006 12 years, P=0.41) and use of CABG (38% versus 38%, P=0.96) were identical, but there were differences in male sex (64% versus 55%, P<0.01) and preoperative ejection fraction (58±13% versus 55±14%, P<0.01), as previously noted. The important item of information is that after repair, a better survival rate is observed in patients either younger (at 15 years after repair: 59±8% versus 47±5%, P<0.01) or older (at 15 years after repair: 26±4% versus 16±3%, P<0.01) than 60 years (Figure 1). This result is confirmed after adjustment for age, sex, preoperative NYHA class, ejection fraction, and performance of CABG, with an adjusted risk ratio (95% CI) associated with repair of 0.65 (0.43 to 0.98) in patients younger than 60 years and of 0.79 (0.65 to 0.95) in those older than 60 years. The trend for lower benefit of repair in the older patients goes in the same direction as that of Thourani et al1 but is not significant (P=0.42). A similarly important piece of information is that after repair, a better survival rate is observed in patients without CABG (at 15 years after repair: 46±5% versus 34±3%, P<0.01) or with CABG (at 15 years after

Figure 1. Survival after surgical correction of MR in patients younger (left) and older (right) than 60 years. Graphs compare patients who had a valve repair with those who required a valve replacement. The 5-, 10-, and 15-year survival rates are indicated for each curve. In both groups, mitral valve repair is followed by a better survival rate than that seen after valve replacement.

Figure 2. Survival after surgical correction of MR in patients requiring (left) and not requiring (right) associated CABG. Graphs compare patients who had a valve repair with those who required a valve replacement. The 5-, 10-, and 15-year survival rates are indicated for each curve. In both groups, mitral valve repair is followed by a better survival rate than that seen after valve replacement.
repair: 15±5% versus 8±3%, P<0.01). This result is confirmed after adjustment for age, sex, preoperative NYHA class, and ejection fraction, with an adjusted risk ratio (95% CI) associated with repair of 0.72 (0.63 to 1.02) in those without CABG and of 0.80 (0.63 to 1.02) in those with CABG. The trend for lower benefit of repair associated with CABG goes in the same direction as that of Thourani et al but is not significant (P=0.58). Although there are some similarities between our data and that of Thourani et al, we cannot support the conclusion that repair is not beneficial in patients older than 60 years or requiring CABG. Hence, valve repair should continue to be the preferred mode of surgical correction of MR in general and specifically in these two subsets of patients. Nevertheless, an important issue is how to reconcile these divergent data.

An essential aspect of MR, previously underscored by mitral repair pioneers, is the importance of the etiology of the regurgitation in the result of repair. The profile of MR etiology in the series studied by Thourani et al is characterized by a persistently high percentage of patients with rheumatic disease (≥24%, versus 6% in our series), in which associated mitral stenosis may affect the outcome of valve repair. Another possible interference with the outcome of valve repair relates to ischemic MR. Ischemic MR is the consequence of coronary disease and is not due to an intrinsic valve disease fortuitously associated with coronary disease. The groups (older and with CABG) lacking repair benefit in the series studied by Thourani et al are those with a particularly high prevalence of ischemic MR. Indeed, in our experience, the prevalence of ischemic MR in patients younger than 60 years and not requiring CABG is only 3%, versus 24% in patients older than 60 years or requiring CABG. Although the prevalence of overt ischemic MR is low in the data of Thourani et al, the high frequency of “other” etiologies raises the possibility that age and CABG categories may be surrogates for a component of ischemic MR. Importantly, in our experience, a better survival rate is observed after mitral repair (Figure 3) in patients with nonischemic MR (P<0.01) but not with ischemic MR (P=0.48). This result is confirmed after adjustment for age, sex, preoperative NYHA class, ejection fraction, and performance of CABG, with an adjusted risk ratio (95% CI) associated with repair of 0.65 (0.53 to 0.80) in patients with nonischemic MR and of 1.08 (0.78 to 1.49) in those with ischemic MR. The higher benefit of repair in organic than in ischemic MR is highly significant (P<0.01). Our data are very similar to previous large studies, which suggested that repair is not uniformly beneficial in ischemic MR.

Whether the uncertain or weak benefit of valve repair in ischemic MR allows the reconciliation of all available data, including that of Thourani et al, remains to be verified but is essential in defining the groups that benefit most from valve repair.

What can we conclude from the currently available evidence?

- Mitral valve repair is the preferred procedure for surgical correction of MR. It is a measure of the quality of the surgical service provided, and it is a key approach to lower mortality and morbidity rates in MR.
- Subset analysis shows that mitral valve repair is beneficial in all subsets of patients with nonischemic MR. Age and associated CABG should not be a reason to deny the benefit of valve repair if the valve is repairable. Patients with nonischemic MR should be directed to surgeons proficient in reparative techniques. The increasing surgical proficiency in valve repair is encouraging and is a key component of an early surgical approach to nonischemic MR.
- Ischemic MR remains a challenge. Our data do not fully take into account the impact on outcome of annular undersizing in mitral repair, and further improvements are to be expected. Repair of ischemic MR remains a work in progress. The complex mechanism involving the valvular and subvalvular apparatus requires comprehensive reparative correction that matches these mechanistic alter-
ations, for which research is ongoing. However, currently in patients with marked subvalvular alterations and unrepairable ischemic MR, valve replacement is an acceptable option.

- The etiology and mechanism of MR are key pieces of information for the management of patients with MR, should be uniformly defined, and should be part of the data collected for surgical databases.
- New therapeutic strategies (early repair in asymptomatic patients with nonischemic MR) or devices (repair processes for ischemic MR) should be tested in appropriately designed clinical trials to minimize the uncertainties and limitations of observational databases.

References


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