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Aortic stenosis and mitral regurgitation: implications for transcatheter valve treatment

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KEYWORDS

- aortic stenosis
- mitral regurgitation
- transcatheter aortic valve implantation

Abstract

Moderate or severe mitral regurgitation (MR) is a common finding in patients with severe aortic stenosis (AS). The combination may be a relative indication for double valve surgery, particularly when MR is severe, degenerative, associated with left atrial dilation, chronic atrial fibrillation, or mitral annular calcium. However, in patients for whom open surgery is not desirable, TAVI may provide a reasonable therapeutic strategy with an expectation in selected patients that MR may improve, be better tolerated, or be amenable to staged transcatheter mitral interventions. In this paper, we briefly review the surgical experience with concomitant AS and MR and discuss the potential implications of transcatheter-based heart valve techniques in this patient group.

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Introduction

Mitral regurgitation (MR) is a common finding in patients with aortic stenosis (AS)[1]. At the time of aortic valve replacement (AVR), up to two thirds of patients with AS have varying degrees of MR[1]. The aetiology of concomitant MR can be considered as degenerative or functional. Degenerative MR can result from rheumatic or myxomatous processes or, particularly in the elderly, calcification of the mitral apparatus. Functional MR, on the other hand, is usually caused by the increased left ventricular (LV) afterload and/or LV remodelling. There is a general consensus that severe MR associated with AS should be corrected at the time of AVR, particularly if the aetiology is degenerative[2,3]. However, the surgical management of mild to moderate MR in the setting of severe AS remains controversial.

Most published studies on valvular heart disease have focused on either regurgitant or stenotic single valve disease. Data on multivalve disease are scarce. As a result, North American and European guidelines offer limited insight with respect to the management of multivalve disease[2,3]. Those recommendations that are made are largely based on small studies or on expert consensus opinion (Grade C). Here we review briefly the surgical experience with concomitant AS and MR and discuss the potential implications of transcatheter-based heart valve techniques in this patient group.

Outcomes of combined surgical aortic and mitral valve intervention

Best management of moderate to severe MR in the setting of severe AS is often debated because of the increased risks associated with combined aortic and mitral valve replacement and because improvement of functional MR often occurs after isolated AVR. Operative mortality for double valve surgery may be twice that of isolated AVR[1,4-10]. In the Euro Heart Survey operative risk ranged from 0.9% to 3.9% for single valve interventions, but rose to 6.5% with multiple valves[1]. In the Society of Thoracic Surgeons (STS) National Database mortality was 4.3% and 6.4% for isolated aortic and mitral valve replacement, respectively, increasing to 9.6% for double valve replacement[10]. Multiple factors contribute to this increased procedural mortality[8]. In addition, late valve-related mortality and morbidity following combined aortic and mitral valve surgery remain considerable[4,5,7-9]. On the other hand, the risk of combined aortic and mitral valve surgery has to be balanced with the odds of reintervention on the mitral valve in a patient who has a surgically implanted aortic prosthesis.

Impact of preoperative MR on outcomes after isolated AVR

An important issue is the prognostic significance of moderate to severe MR in patients undergoing isolated AVR. The majority[11-15] of the evidence tends to support the concept that moderate or severe MR is associated with higher mortality, congestive heart failure and subsequent mitral valve surgery, particularly in patients with a high preoperative transaortic gradient, dilated left atrium, or atrial fibrillation[12]. In contrast, Coutinho et al[16] found that late (10-year) survival after isolated AVR was similar in patients with or without concomitant mitral valve surgery. However, patients undergoing concomitant mitral valve surgery experienced less heart failure at follow-up and more pronounced reverse LV remodelling. However, it has to be pointed out that, in this latter study, all patients had baseline moderate secondary MR. The heterogeneity of mechanism and severity of MR across all these studies are the explanation of these contrasting results.

MR change after isolated AVR

A decrease in MR severity is common following isolated AVR[12,13,17-23]. Early improvement might result from acute reverse LV remodelling, including a reduction in LV end-diastolic volume and a decrease in mitral tethering forces[19,20]. Additional benefit may be achieved over time with a further regression of LV hypertrophy and resolution of volume overload.

Not surprisingly, some recommend a conservative approach to concomitant MR, particularly functional MR. Others advocate a more aggressive approach to operating on the mitral valve, citing evidence that concomitant moderate to severe MR may not improve in up to one half of patients and may increase in a subgroup of patients[24-27]. These discrepancies across studies may be related to the different inclusion criteria in terms of MR aetiology (functional or degenerative) and severity, and to the timing of the postoperative echocardiographic examination. It appears that appropriate patient selection is crucial. Ideally, we would be able to identify those patients in whom MR will not improve or will progress following isolated AVR. In such patients the potentially increased surgical risk of a double valve procedure would be justified. Some predictors of MR progression following isolated AVR have been identified: increased left atrial size, poor LV ejection fraction, atrial fibrillation and, perhaps most importantly, degenerative as opposed to functional MR[12,13,17,18].

Transcatheter heart valve therapy for combined AS and MR

Transcatheter valve therapies have emerged as feasible alternatives to conventional open-heart surgery in many patients with valvular disease. For AS, the PARTNER (Placement of AoRTic TraNscathetER Valves) trials have demonstrated that transcatheter aortic valve implantation (TAVI) can offer a mortality benefit over medical management and is non-inferior to high-risk surgical aortic valve replacement[28,29]. For MR, edge-to-edge mitral valve repair with the MitraClip device (Abbott Laboratories, Abbott Park, IL, USA) is a valid alternative for selected high-risk patients[30].

The reported prevalence of at least moderate MR in patients with severe AS undergoing TAVI ranges between 2% and 40%[28,31-36]. In this setting MR is usually left untreated. Early TAVI studies actually excluded patients with more than moderate MR, leading some to conclude that severe MR was actually a contraindication to TAVI. Nevertheless, "off-label" use in such patients demonstrates that, as with surgical AVR, MR severity may decrease, remain unchanged, or even increase following TAVI.

Few and contrasting results have been reported in the literature in terms of the prognostic significance and magnitude of MR changes following TAVI. A sub-analysis of the PARTNER trial[37] reported that preoperative moderate or severe MR (mostly moderate) was associated with increased two-year mortality after surgical AVR, but not after TAVI, suggesting that TAVI may be a reasonable option in selected high-risk patients with combined aortic and mitral valve disease. As with the PARTNER sub-analysis, D'Onofrio et al[38] found that moderate or severe MR did not appear to be a significant risk factor for in-hospital mortality after TAVI. In contrast, Toggweiler et al[39] found that moderate or severe MR in patients undergoing TAVI was associated with a higher early, but not late, mortality rate. The difference in terms of prognostic impact of moderate to severe MR after TAVI might be explained by the higher proportion of patients with preoperative severe MR in Toggweiler's analysis compared with the PARTNER sub-analysis and D'Onofrio's study.

Little information is available with regard to changes in MR after TAVR. Durst et al[40] reported improvement in mild to moderate MR after TAVR with the SAPIEN valve (Edwards Lifesciences, Irvine, CA, USA) in 12 of 35 patients (34%). The absence of mitral annular calcification was associated with improved MR. Tzikas et al[41] reported a reduction in moderate to severe MR after TAVR with the CoreValve prosthesis (Medtronic, Minneapolis, MN, USA), improving in six of ten patients (60%), remaining unchanged in three patients (30%), and worsening in one patient (10%). Toggweiler et al[39] reported that MR diminished post-procedurally in 61% of patients with moderate or severe preoperative MR. At one-year follow-up MR had improved in 55% of patients, remained unchanged in 16%, and worsened in 1%. Patients with high transaortic gradients, with functional (as opposed to degenerative) MR, without pulmonary hypertension, and without atrial fibrillation were more likely to have reductions in MR at one-year follow-up. Recently, Hekimian et al[42] showed that MR significantly decreased at seven days after TAVI and remained unchanged afterwards. MR decreases were more marked in patients with baseline LV dilatation and dysfunction, while they did not differ according to aortic mean gradient, MR aetiology, or anterior mitral leaflet-device overlap. Similar to the surgical series, the heterogeneity of preoperative MR mechanism and degree, as well as the absence of homogenous quantification, is one of the explanations for these varying results.

Unger et al[43] examined the available evidence in order to investigate the possible influence of the type of transcatheter heart valve (THV) implanted on post-procedural MR changes. Admittedly, this analysis was limited by the heterogeneity of case selection, definitions, and follow-up across the available studies[43]. However, they did find that the effects of TAVI on MR may differ according to the type of prosthesis. As compared to the CoreValve prosthesis, the Edwards SAPIEN prosthesis was more often associated with improved MR and less frequently with worsened MR[44]. They speculated that these findings might be a consequence of extension of the CoreValve device deeper into the left ventricular outflow tract, with impingement on the anterior mitral leaflet movement or altered mitral annulus geometry. In line with this hypothesis is the observation that deep positioning of the prosthesis may be associated with MR worsening[44]. A second line of reasoning is based on the fact that the incidence of left bundle branch block (LBBB) and high degree conduction disorders requiring a pacemaker insertion are relatively high with the CoreValve device[45,46]. It is recognised that atrioventricular conduction disorders, LBBB, and right ventricular pacing are known to increase the prevalence and the severity of MR[47,48].

Recently, an appealing approach to the management of AS and MR has been described whereby TAVI is followed by percutaneous mitral valve repair with the MitraClip device (Abbott Vascular, Santa Clara, CA, USA)[49-53]. In the great majority of cases these procedures have been staged. Importantly, the presence of an aortic THV seems not to impact upon the future technical feasibility of a MitraClip repair. In contrast to the increased risk associated with mitral surgery performed for MR following prior isolated aortic valve surgery, prior TAVI does not seem to increase the risk of a subsequent MitraClip procedure. A "TAVI first" staging strategy might allow for the possibility of a spontaneous reduction in MR after isolated treatment of AS, and the potential to avoid an unnecessary additional procedure on the mitral valve. It seems likely that future transcatheter mitral interventions might offer additional options.

Summary

Moderate or severe mitral regurgitation is common in patients with severe aortic stenosis. The combination may be a relative indication for double valve surgery, particularly when MR is severe, degenerative, associated with left atrial dilation, chronic atrial fibrillation, or mitral annular calcium. However, in patients for whom open surgery is not desirable, TAVI may provide a reasonable therapeutic strategy with an expectation in selected patients that MR may improve, be better tolerated, or be amenable to staged transcatheter mitral interventions.

Conflict of interest statement

J. G. Webb is consultant for Edwards Lifesciences. The other authors have no conflicts of interest to declare.

Online data supplement

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