Degenerative and functional mitral regurgitation (MR) constitute 2 separate disease entities. Although the pathophysiological problem is directly addressed by a successful intervention on the valve in the first case, the underlying ventricular disease persists in the latter.

Indications for surgery in MR are well defined for degenerative MR, in which relief of the valve lesion leads to relief of left ventricular volume overload. The timing of surgery is based on symptoms, left ventricular size and function, atrial fibrillation, and pulmonary hypertension. When following these criteria, surgery is associated with symptomatic improvement and a survival benefit. Nevertheless, up to 50% of patients, particularly the elderly and those who present with comorbidities or reduced ventricular function, are denied surgery despite having a clear indication for intervention.

Criteria for surgical intervention are less well defined in functional MR, in which the valve is structurally normal and regurgitation is caused by an imbalance between closing and tethering forces related to a ventricular pathology that is not entirely corrected by the relief of MR. From surgical experience, it is known that valve intervention leads to an initial reduction of MR, although the recurrence rate is high and a survival benefit has not been demonstrated so far. Furthermore, the surgical risk is frequently not negligible, and as a result, indications for surgery are not strong unless there is an indication for coronary artery bypass surgery. On a general basis, the first approach in these patients is the initiation of heart failure therapy, including cardiac resynchronization therapy when indicated, which has a proven survival benefit.

Nevertheless, a percutaneous approach to therapy for MR is an attractive concept for the management of inoperable and selected high-risk patients. The percutaneous MitraClip (Abbott Vascular, Abbott Park, IL) system has been adapted from the surgical edge-to-edge technique proposed by Alfieri et al. When introducing such a novel technique into clinical practice, several important questions need to be addressed regarding the safety of implantation, efficacy in reducing MR, the effect on symptomatic improvement, the effect on left ventricular remodeling, and last but not least, the effect on overall survival. Obviously, these questions need to be answered for both degenerative MR and functional MR.

The EVEREST I study (Endovascular Valve Edge-to-Edge Repair Study) was performed to demonstrate the feasibility, safety, and efficacy of the procedure. In a systematic review, it has been shown that the MitraClip can be implanted safely and effectively in high-risk surgical patients. Although in the EVEREST II trial (which randomized patients to MitraClip or surgical therapy), the majority of patients had degenerative MR, data from postapproval studies such as the ACCESS-EU trial (ACCESS-Europe: A Two-Phase Observational Study of the MitraClip System in Europe) and the TRAMI (Transcatheter Mitral Valve Interventions) registry indicate that the larger number of patients being treated in clinical practice have functional MR. These studies have confirmed an efficacious reduction in MR severity and symptomatic improvement for the majority of patients.

The present report by Grayburn et al demonstrates the effect of the reduction of MR on reverse left ventricular and left atrial remodeling after MitraClip implantation in 801 patients with severe MR derived from the EVEREST II study, the EVEREST II high-risk study, and the continued access EVEREST II (REALISM) study, as well as in 80 surgically treated patients. The study has the ability to separately assess the entities of degenerative and functional MR.

In patients with degenerative MR, a reduction of left ventricular end-diastolic volume from 140±40 to 120±35 mL was observed, whereas end-systolic volume remained rather stable at 53±21 and 50±20 mL at baseline and 12 months, respectively. These findings are explained by an effective reduction of volume overload.

In patients with functional MR, a reduction in left ventricular end-diastolic volume from 166±52 to 151±49 mL and of left ventricular end-systolic volume from 96±41 to 87±41 mL was observed. Furthermore, significant residual MR (3–4+) was associated with significantly less ventricular remodeling both in degenerative and in functional MR compared with lesser residual MR. Finally, reverse left atrial remodeling was also related to the magnitude of MR reduction observed with the intervention. Thus, the greater the reduction of MR, the more reverse remodeling can be expected.

The documented reverse remodeling in this large series is another important piece of information supporting the concept of percutaneous correction of MR. These data may also be seen in context with the findings of the MitraSwiss registry, which included 100 patients, in which the magnitude of residual MR after a MitraClip intervention was predictive of 1-year survival. The inclusion criteria for the EVEREST II trial required an ejection fraction >25% and a left ventricular end-systolic.
diameter <55 mm,\textsuperscript{13} and in the EVEREST II high-risk trial, patients with an ejection fraction <20% or left ventricular end-systolic diameter >60 mm\textsuperscript{14} were excluded. Indeed, the average ejection fraction at baseline in the present analysis was 44±11\% for patients with functional MR and 62±8\% for those with degenerative MR. The end-systolic diameters at baseline were 46±7 and 34±7 mm for patients with functional and degenerative MR, respectively. It is thus not proven that a similar extent of reverse remodeling can be expected in patients with very poor ventricular function and excessive left ventricular dilation. The potential futility of an intervention needs to be considered in such cases.

From the currently available data, it is justifiable to consider MitraClip implantation in inoperable or high-risk patients with degenerative MR when their valve anatomy is suitable.\textsuperscript{1} In secondary MR, the MitraClip procedure should be considered in inoperable or high-risk patients after optimization of medical therapy and after consideration of cardiac resynchronization therapy.\textsuperscript{3} Although there is increasing evidence that the procedure leads to reduction of MR, symptomatic improvement, and reverse ventricular remodeling in patients with functional MR, the important question regarding a potential survival benefit remains unanswered. A sufficiently powered randomized study comparing the survival of patients with functional MR receiving optimal medical therapy with survival of those undergoing MitraClip implantation is eagerly awaited. In the meantime, careful risk assessment and individualized decision making are required.\textsuperscript{15} The impact on reverse remodeling is one additional element to consider in the decision-making process.

Disclosures

Dr Rosenhek reports the receipt of lecture fees from Abbott and Edwards Lifesciences.

References


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