



Percutaneous mitral valve repair: an evolving reality

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Secondary mitral regurgitation (MR), also known as functional MR, arises from changes in left ventricular geometry and function resulting in abnormal leaflet coaptation due to tethering of the mitral valve in patients with left ventricular dysfunction. Secondary MR is an independent risk factor for patients with heart failure (1,2). The 2017 AHA/ACC guidelines give a class IIb recommendation (level of evidence B) to isolated surgical mitral valve repair or replacement for patients with severe secondary MR who remain symptomatic (NYHA class III or IV) despite maximum tolerated guideline-directed medical therapy for heart failure (3). Meanwhile, the 2017 ESC/EACTS guidelines offer percutaneous repair as an alternative for these patients (class IIb recommendation; level of evidence C) (4). Percutaneous mitral valve repair with the use of MitraClip (Abbott Vascular, Santa Clara, CA, USA) has proven feasible, safe, and effective as an alternative for patients with severe symptomatic secondary MR and a high surgical risk in non-randomized studies (5). However, randomized data on hard clinical outcomes is lacking.

In this editorial, we refer to the randomized MITRA-FR trial published in the *New England Journal of Medicine* by Obadia *et al.* (6). MITRA-FR was a multicenter randomized clinical trial conducted in 37 centers in France. In this study, patients with severe secondary MR with a regurgitant volume of >30 mL per beat or an effective regurgitant orifice area (EROA) of >20 mm², a left ventricular ejection

fraction (LVEF) between 15% and 40%, and NYHA functional classes II–IV were randomized to percutaneous mitral valve repair with MitraClip plus medical therapy (152 patients) or medical therapy alone (152 patients). Patients were of advanced age (mean age 70.1±10.1 *vs.* 70.6±9.9 years) and mostly men (78.9% *vs.* 70.4%). Baseline characteristics were similar in both groups with the exception of prior myocardial infarction which was more common in the intervention group (49.3% *vs.* 34.2%). Mean EROA was 31±10 mm² (with 52% of patients having an EROA <30 mm²), LVEF was 33%±7%, and left ventricular end diastolic volume (LVEDV) was 135±35 mL/m². Device implantation was not attempted in eight patients and failed in six patients. Among the 138 patients who underwent successful device implantation, a single device was used in 63 patients (46%), two devices in 62 patients (45%), and three or more devices in 13 patients (9%). Periprocedural complications were seen in 21 patients (14.6%). Five patients (3.5%) had a vascular complication requiring transfusion or surgical intervention, 2 (1.4%) had cardiac embolism, and 2 (1.4%) had cardiac tamponade. The device was effective as 92% of patients experienced a reduction in MR to 2+ or lower and 76% had a reduction to 1+ or lower at the time of discharge. However, follow-up echocardiographic data was incompletely reported. The primary outcome of death or heart failure hospitalization at 12 months was met in 54.6% of patients in the intervention group and 51.3% of patients in the control group (OR

1.16; 95% CI, 0.73–1.84; P=0.53). Secondary outcomes including mortality, cardiovascular mortality, heart failure hospitalization, and major adverse cardiovascular events were similar in both groups. Per-protocol analysis results were consistent with the intention-to-treat analysis. The authors offered several possible explanations for the lack of clinical benefit which included the incomplete correction of secondary MR seen in some patients, the possibility that adverse clinical events were related to the underlying cardiomyopathy and that secondary MR was merely a marker of illness severity, and the prospect that the procedure may have been performed too late in the course of the progression of the disease.

Some limitations of the study are also worth noting. First, roughly 35% of patients in the intervention group may have had moderate MR at baseline and thus expected to derive less benefit from the intervention. Second, the elevated number of complications, device failure, and residual significant MR at 12 months may have dampened the potential benefit resulting from the intervention. Third, the trial appeared to have included a very high-risk population as evidenced by the high mortality seen at 12 months when compared to registry data. Fourth, incomplete follow-up data on echocardiographic parameters, functional status, and quality of life hindered further interpretation of these important parameters. Lastly, concerns remain regarding the possibility that the study was underpowered to detect smaller differences between the groups.

The COAPT trial by Stone *et al.* was published a month after the publication of the MITRA-FR trial in the *New England Journal of Medicine* (7). The COAPT trial demonstrated a significant improvement in all-cause mortality, cardiovascular mortality, heart failure hospitalization, NYHA functional class, 6-minute walk test, and quality of life in the intervention group at 24 months. In contrast to MITRA-FR, the COAPT trial was conducted in the United States and Canada, funded entirely by industry, and enrolled twice as much patients. Important differences in the studies include a higher EROA (41 ± 15 vs. 31 ± 10 mm²), lower baseline indexed LVEDV (101 ± 34 vs. 135 ± 35 mL/m²), lower procedural complications (8.5% vs. 14.6%), lower residual MR at discharge ($\leq 1+$ MR at discharge: 76% vs. 82%), and lower residual MR at 12-month follow-up ($\geq 3+$ MR 5% vs. 17%) in the COAPT trial (8).

The bottom line appears to be that patient selection is the key for optimal results following percutaneous mitral

valve repair with the use of MitraClip. Patients with more severe MR (as evidenced by higher EROA) and less dilated ventricles may benefit the most from the procedure. A third randomized clinical trial, the RESHAPE-HF2 trial, is currently underway and is expected to help continue to define the patients who will benefit the most from this intervention (9).

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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