Editorial

Transcatheter mitral valve repair in functional mitral regurgitation: who will benefit?

Aditya G. Parikh, Sean P. Pinney

Mount Sinai Medical Center, New York, NY, USA

Correspondence to: Sean P. Pinney, MD. Department of Advanced Heart Failure and Transplant Cardiology, One L. Gustave L Levy Place, Box 1030, New York, NY 10029, USA. Email: sean.pinney@mountsinai.org.

Submitted Mar 24, 2020. Accepted for publication Apr 14, 2020.
doi: 10.21037/acs-2020-mv-14
View this article at: http://dx.doi.org/10.21037/acs-2020-mv-14

Functional mitral regurgitation (MR) is a frequent finding in patients with ischemic or dilated cardiomyopathy and contributes to increased mortality (1). MR commonly develops in heart failure patients due to an imbalance between closing and tethering forces. The reduction in contractility associated with heart failure and a reduced ejection fraction, combined with leaflet tethering from papillary muscle displacement, produces MR of varying severity. The indications for intervention in degenerative (i.e., primary) MR are well defined, with surgical repair or replacement being the definitive therapies.

For patients with a prohibitive surgical risk, transcatheter interventions are becoming increasingly popular (2,3). In contrast, the management of functional (i.e., secondary) MR is more controversial. Functional MR is the result of myocardial disease and treatment is directed at the underlying cause, namely the treatment of cardiomyopathy. Thus, guideline-directed medical therapy (GDMT) and chronic resynchronization therapy (CRT) are the mainstays of treatment, with a focus on the reversal of adverse left ventricular (LV) remodeling. Surgical intervention for functional MR has yielded no difference in clinical outcomes, with high rates of recurrent MR (4). The development of a transcatheter edge-to-edge repair of the mitral valve (MV) using MitraClip (Abbott Laboratories, Menlo Park, California, USA) has created excitement for the treatment of secondary MR; however, two randomized controlled clinical trials, MITRA-FR and COAPT, showed contrasting results and focused attention on identifying a discrete population who can benefit from this technology (5,6).

Both COAPT and MITRA-FR randomized patients with LV dysfunction and symptomatic MR to MitraClip plus GDMT versus GDMT alone. COAPT showed that transcatheter MV repair resulted in lower rates of hospitalization for heart failure and all-cause mortality during twenty-four months of follow-up, compared to GDMT alone. In contrast, MITRA-FR showed no benefit of MitraClip over GDMT after twelve months. These contrasting outcomes may be due to underlying differences in baseline valvular and ventricular characteristics between the patient populations. The patients in COAPT had quantitatively more severe MR with larger effective regurgitant orifice area (EROA, 41±15 versus 31±10 mm^2) and smaller indexed left ventricular end diastolic volumes (LVEDV, 101±34 versus 135±35 mL/m^2) compared to patients in the MITRA-FR study. COAPT also excluded patients with a left ventricular end-systolic diameter (LVESD) >7 cm, a marker for advanced cardiomyopathy and remodeling.

One reason for the difference in MR severity between the two trials is the difference in the definition of MR severity. Enrollment in MITRA-FR was based on the 2012 ESC guidelines, which defined severe MR as having an EROA ≥0.2 cm^2. Meanwhile, COAPT used the 2006/2008 ACC/AHA guidelines, which defined MR as having an EROA ≥0.3 cm^2 (2,3). As such, the COAPT selection criteria produced a patient population with 'disproportionately' more severe MR with respect to the LV remodeling. In contrast, the MITRA-FR cohort had generally less severe MR in the context of more dilated and dysfunctional LV (7). Additionally, in COAPT, a review committee comprised of advanced heart failure specialists performed a careful assessment of the patients and oversaw advancement of

maximal tolerable doses of GDMT prior to randomization. Hence, these patients were medically optimized and only required few adjustments throughout the course of the trial. Although the results from the two trials appear contrasting, they provide complementary evidence; patients with heart failure and truly severe functional MR, without excessive LV dilation or remodeling, who remain symptomatic despite maximally tolerated GDMT, likely benefited from MitraClip intervention.

Notably, patients with stage D or end-stage heart failure were not included in the COAPT trial. Nevertheless, progression towards end-stage heart failure is inevitable in this population. Even in COAPT, nearly 8% of patients who received MitraClip required a left-ventricular assist device (LVAD) or heart transplant (HT) within three years. Whilst advanced therapies like LVAD and HT remain the therapies of choice for patients with end-stage heart failure, with two-year survival of approximately 85%, concomitant co-morbidities may delay treatment or make patients ineligible (8,9). Patients with pulmonary hypertension and elevated pulmonary vascular resistance are not eligible for HT due to elevated risk of right heart failure and death after transplantation. Additionally, in patients with concomitant biventricular dysfunction, isolated use of LVAD may not be a feasible alternative. Theoretically, percutaneous edge-to-edge repair could mitigate the degree of MR and in turn improve forward flow while reducing pulmonary pressures and right ventricular afterload. These changes in hemodynamics would favorably impact symptoms and functional capacity in patients awaiting transplantation.

Despite the theoretical appeal of MitraClip, real world outcomes caution against liberalization of such practice. In a meta-analysis performed by Belkin and colleagues, MitraClip implantation in advanced heart failure patients with left ventricular ejection fraction (LVEF) <35% and NYHA IV symptoms were associated with nearly 30% mortality within one year (10). Moreover, although creating a double-orifice MV with MitraClip placement has not been associated with significantly elevated trans-mitral gradients in patients with heart failure, the reduced area in combination with increased flow after LVAD placement might result in significantly elevated gradients, potentially limiting hemodynamic LVAD optimization.

In summary, functional MR is a frequent finding in patients with ischemic or dilated cardiomyopathy. GDMT and CRT promote reverse LV remodeling and should be the first-line treatment to ameliorate the severity of the functional MR. Unfortunately, despite their demonstrated efficacies, these therapies are significantly underutilized. Recent advances in transcatheter MV repair technologies have provided important groundwork that can help select heart failure patients with symptomatic functional MR despite GDMT. Identification of this subset of patients still needs further refining. In the meantime, a shared decision-making model with a multidisciplinary approach should be implemented to identify an individual's projected trajectory and candidacy for advanced therapies. While we await results of patient-level analysis of the MITRA-FR, COAPT and RESHAPE-HF2 studies, patient eligibility should be guided by, but not limited to, the exhaustive list of exclusion criteria outlined by the COAPT investigators, including maximizing GDMT prior to MitraClip intervention. This will appropriately restrict the population to which the MitraClip can or should be performed.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: SPP has received consulting fees from Abbott, CareDx, Medtronic, and Procyrion. AGP has no conflicts of interest to declare.

References

1. Nasser R, Van Assche L, Vorlat A, et al. Evolution of Functional Mitral Regurgitation and Prognosis in Medically Managed Heart Failure Patients With Reduced Ejection Fraction. JACC Heart Fail 2017;5:652-9.
2. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC); European Association for Cardio-Thoracic Surgery (EACTS), Vahanian A, et al. Guidelines on the management of valvular heart disease (version 2012). Eur

Heart J 2012;33:2451-96.
3. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;70:252-89.
4. Smith PK, Puskas JD, Ascheim DD, et al. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014;371:2178-88.
5. Obadia JF, Armoiry X, Iung B, et al. The MITRA-FR study: design and rationale of a randomised study of percutaneous mitral valve repair compared with optimal medical management alone for severe secondary mitral regurgitation. EuroIntervention 2015;10:1354-60.
6. Mack MJ, Abraham WT, Lindenfeld J, et al. Cardiovascular Outcomes Assessment of the MitraClip in Patients with Heart Failure and Secondary Mitral Regurgitation: Design and rationale of the COAPT trial. Am Heart J 2018;205:1-11.
7. Grayburn PA, Sannino A, Packer M. Proportionate and Disproportionate Functional Mitral Regurgitation: A New Conceptual Framework That Reconciles the Results of the MITRA-FR and COAPT Trials. JACC Cardiovasc Imaging 2019;12:353-62.
8. Mehra MR, Uriel N, Naka Y, et al. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. N Engl J Med 2019;380:1618-27.
9. Khush KK, Cherikh WS, Chambers DC, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-fifth Adult Heart Transplantation Report-2018; Focus Theme: Multiorgan Transplantation. J Heart Lung Transplant 2018;37:1155-68.
10. Belkin MN, Nnanabu J, Mehta PP, et al. Outcomes Following Mitraclip in Advanced Heart Failure Patients: A Meta-Analysis. J Heart Lung Transplant 2018;37:S201.

Cite this article as: Parikh AG, Pinney SP. Transcatheter mitral valve repair in functional mitral regurgitation: who will benefit? Ann Cardiothorac Surg 2021;10(1):161-163. doi: 10.21037/acs-2020-mv-14

