

Reply: Explaining differing outcomes from the COAPT and MITRA-FR trials using disproportionate and proportionate secondary mitral regurgitation



Marianna Adamo*, MD; Marco Metra, MD

Cardiothoracic Department, Civil Hospitals and University of Brescia, Brescia, Italy

We are thankful to Norris-Grey and colleagues for their comments¹ about our paper². There are a few considerations needed with respect to this letter.

First, our results should not be considered in contrast to Grayburn's hypothesis. There are two main explanations for the lack of differences in outcomes of patients with proportionate and disproportionate mitral regurgitation (MR). First, the sample size was relatively small and, using Grayburn's definition², the percentage of patients with proportionate MR was also low (22%). In addition, we had patients with "over-disproportionate" MR due to excessive effective regurgitant orifice areas (EROAs) less likely to be completely reduced. This latter aspect, as pointed out also by Norris-Grey et al, is the most relevant since MR >1+ at 30 days was the strongest predictor of poor outcome in our study². Indeed, the likelihood of having optimal procedural results should be considered as a major factor for the selection of MitraClip candidates⁴.

In addition to procedural results, Norris-Grey et al mention the possible impact of left atrial pressure (LAP) on MitraClip

outcomes⁵. They speculated that patients with normal LAP, having lower EROA, would have proportionate MR. However, no information about the relationship between MR severity and LV dimensions is reported in the study they cite. Moreover, chronic lung disease, but not LAP, was an independent predictor of outcome in that study⁵. Unfortunately, in our cohort LAP was available in less than 50% of patients; therefore, this parameter was excluded from the analysis. On the other hand, chronic lung disease was not associated with outcomes. However, in larger cohorts at longer follow-up, it was reported as a predictor of adverse events⁶. Intraprocedural monitoring of LAP is now recognised as paramount to guide the procedure and evaluate the MitraClip result. However, according to the above observations, a right heart catheterisation would also be helpful in the screening phase, especially in patients with a history of pulmonary disease, in order to identify those whose symptoms and/or pulmonary hypertension have a post-capillary component that may benefit from MR correction.

Finally, regarding the post-marketing surveillance results, we would like to clarify that the analysis included all the reports of

*Corresponding author: Cardiothoracic Department, Civil Hospitals and University of Brescia, Piazzale Spedali Civili 1, 25123 Brescia (BS), Italy. E-mail: mariannaadamo@hotmail.com

adverse events; therefore, the proportion of injuries, such as damage to the mitral valve apparatus (8%), was calculated on the total number of adverse events instead of the total number of patients treated⁷. Intraprocedural mortality and complications of the MitraClip procedure are very low and valve damage is extremely rare⁸. However, as stated by Norris-Grey et al, centre experience plays an important role⁹. In our study, two medium- and one high-volume centres were included; no differences were found in procedural complications or MR >1+ at 30 days among different centres (79% versus 67% versus 64%; p=0.312).

On the other hand, two-year mortality was quite high (39%) but perfectly in line with previous registries and trials^{10,11}. This is due to the high-risk profile of the patients treated, mostly affected by heart failure and other comorbidities. In this regard, further investigation for better selection of patients who may have a long-term benefit from this procedure is definitely needed.

Conflict of interest statement

M. Metra received consulting honoraria, for participation in steering committees or advisory boards or for speeches, from Abbott, Amgen, AstraZeneca, Bayer, Edwards, Fresenius, Novartis, and Servier. M. Adamo has no conflicts of interest to declare.

References

- Norris-Grey C, Ahmad M, Kirresh AZ. Letter: Explaining differing outcomes from the COAPT and MITRA-FR trials using disproportionate and proportionate secondary mitral regurgitation. *EuroIntervention*. 2020;16:e775-6.
- Adamo M, Cani DS, Gavazzoni M, Taramasso M, Lupi L, Fiorelli F, Giannini C, Branca L, Zuber M, Curello S, Petronio AS, Maisano F, Metra M. Impact of disproportionate secondary mitral regurgitation in patients undergoing edge-to-edge percutaneous mitral valve repair. *EuroIntervention*. 2020;16:413-20.
- 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.
- Adamo M, Metra M, Alfieri O. Percutaneous valve repair of functional mitral regurgitation: aiming at optimal and durable results. *Eur J Heart Fail*. 2020 May 27. [Epub ahead of print].
- Sims JR, Reeder GS, Guerrero M, Alkhouli M, Nkomo VT, Nishimura RA, Rihal CS, Eleid MF. Characteristics and outcomes of patients with normal left atrial pressure undergoing transcatheter mitral valve repair. *Heart*. 2020;106:898-903.
- Adamo M, Grasso C, Capodanno D, Rubbio AP, Scandura S, Giannini C, Fiorelli F, Fiorina C, Branca L, Brambilla N, Bedogni F, Petronio AS, Curello S, Tamburino C. Five-year clinical outcomes after percutaneous edge-to-edge mitral valve repair: Insights from the multicenter GRASP-IT registry. *Am Heart J*. 2019;217:32-41.
- Mahabir CA, DeFilippis EM, Aggarwal S, Bath A, Qamar A, Patel NK, Goldsweig AM, Vaduganathan M. The First 4 Years of Postmarketing Safety Surveillance Related to the MitraClip Device: A United States Food and Drug Administration MAUDE Experience. *J Invasive Cardiol*. 2020;32:E130-2.
- EGgebrecht H, Schelle S, Puls M, Plicht B, von Bardeleben RS, Butter C, May AE, Lubos E, Boekstegers P, Ouarrak T, Senges J, Schermund A. Risk and outcomes of complications during and after MitraClip implantation: Experience in 828 patients from the German TRANscatheter mitral valve interventions (TRAMI) registry. *Catheter Cardiovasc Interv*. 2015;86:728-35.
- Chhatriwalla AK, Vemulapalli S, Holmes DR Jr, Dai D, Li Z, Ailawadi G, Glower D, Kar S, Mack MJ, Rymer J, Kosinski AS, Sorajja P. Institutional Experience With Transcatheter Mitral Valve Repair and Clinical Outcomes: Insights From the TVT Registry. *JACC Cardiovasc Interv*. 2019;12:1342-52.
- Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ; COAPT Investigators. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. *N Engl J Med*. 2018;379:2307-18.
- Kalbacher D, Schäfer U, V Bardeleben RS, Eggebrecht H, Sievert H, Nickenig G, Butter C, May AE, Bekereldjian R, Ouarrak T, Kuck KH, Plicht B, Zahn R, Baldus S, Ince H, Schillinger W, Boekstegers P, Senges J, Lubos E. Long-term outcome, survival and predictors of mortality after MitraClip therapy: Results from the German Transcatheter Mitral Valve Interventions (TRAMI) registry. *Int J Cardiol*. 2019;277:35-41.