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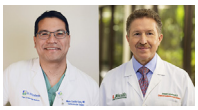

REPLY: IS PAPILLARY MUSCLE APPROXIMATION THE ANSWER TO ABSENT REVERSE REMODELING IN TRANSCATHETER EDGE-TO-EDGE REPAIR AND REDUCTIVE MITRAL ANNULOPLASTY?

Reply to the Editor:

The management of ischemic mitral regurgitation (MR) has been influenced by powerful datasets that can be summarized into 3 eras: the era of annular reduction[1,2]; the era of mitral replacement[3-5]; and the era of transcatheter edge-to-edge repair (TEER).[6] Throughout these periods, there have been positive animal and human studies supporting papillary muscle approximation (PMA) plus annuloplasty, including the only prospective randomized trial on the topic by Nappi and colleagues[7-9] Despite the beneficial effects on left ventricular (LV) remodeling and mitral valve geometry demonstrated with PMA, as well as its noninferiority to reductive annuloplasty (RA), this technique has not been widely adopted.

Nappi and Spadaccio,[10] in their letter to the editor on the recently published animal study by Xu and colleages,[7] summarize the strengths and weaknesses of RA and PMA techniques. PMA has been accompanied by an annuloplasty, more often a reductive one. They endorse the concept that RA perturbs ventricular geometry and torsion dynamics, inhibiting reverse remodeling that would otherwise result from correction of mitral regurgitation. Results from other studies suggest the absence of reverse remodeling is affected by more than RA's effect on ventricular geometry and torsion. The negative remodeling of ischemic ventricles inevitably leads to dilation and tethering of the mitral valve with leaflet tenting unless the process is attenuated or arrested. Reductive annuloplasty simply does not counteract this dilation process, as evidenced by Aker and colleagues.[4,11] COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) showed that TEER, while having no RA effects, improved mitral regurgitation but failed to arrest ventricular dilation and did not lead to reverse remodeling,[6,12] Furthermore, in studies of PMA plus restrictive annuloplasty by Nappi and colleagues[9] and Hvass and Joudinaud[8] reverse remodeling occurred and LV contractility improved suggesting PMA can inhibit LV dilation and allow reverse remodeling, that RA alone fails to achieve. The success of accepted therapies for ischemic MR have largely been based on their effect on diminishing leaflet tenting which impacts severity of MR more than left ventricular dysfunction, but this effect may be limited with isolated leaflet/annular interventions.[4,6,11,13]

Comparison of PMA outcomes with other therapies as evidenced by animal studies, retrospective and prospective randomized trials demonstrate an advantage of PMA in allowing reverse remodeling and improvement in left ventricular ejection fraction (LVEF),[7-9] but long-term survival is not different to that of RA and overall survival of all therapies remain suboptimal. Nappi and colleagues reported a significant decrease in major adverse cardiac and cerebrovascular events in the PMA group, demonstrating its long-term protective effect on the ventricle, but they found no significant difference in all-cause mortality at 5 years with 22.9% for the PMA group and 29.2% for the RA group.[9] The COAPT trial reported a 19% mortality at 1 year for TEER and 23% for medical management and a 2-year all-cause mortality risk of 29.1% in the TEER arm.[6] Importantly the preintervention severity of MR in the PMA trial was 4+ (severe), whereas 52.2% of patients in the COAPT trial had 3+ MR.[6,9] The Cardiothoracic Surgical Trials Network ischemic MR repair versus replacement trial showed a nonstatistically difference in 2-year mortality for repair versus replacement (19% vs 23.2% respectively).[11] Longer follow-up is needed to understand the benefit of PMA. One can then hypothesize that TEER allows early- and mid-term (up to 2 years) improvement of MR and survival because it improves the recurrent injury from MR, improves tenting height, maintaining a small posterior and anterior leaflet angle, and delaying LV dilation. RA fails during mid-term follow-up (up to 1 year) because it does not delay or prevent LV dilation. PMA has improved long-term LV remodeling (at 5 years) because it addresses both components of functional MR.[9]

Recurrence of moderate or worse mitral regurgitation in the PMA trial numerically favored PMA but was not statistically different between the PMA and RA arms until the fifth year, when a true difference occurred (27% vs 55.9%, respectively $P = .013$). The reoperation rate for the entire follow-up period was 6.2% for PMA versus

14.6% for the RA group but not statistically significant.[9] One can hypothesize that PMA fails to improve survival and quality-of-life metrics compared with RA alone because of the accompanying downsizing of the annulus. True sizing of the annulus has shown favorable short-term results.[8,14]

The degree of preoperative LV depression and LV dilation under which PMA is effective are not well delineated, but based on the PMA trial, a size of <60 mm LV end-diastolic diameter and LVEF >40%.[9] PMA combined with annuloplasty fails to yield a favorable result in those with mitral tethering other than the posteromedial papillary muscle restriction, profoundly depressed LVEF, and in those with overtly large ventricles. Should mitral valve replacement be the approach of choice in these nonresponders to PMA and TEER? Should mitral valve replacement be performed along with PMA? Will this ultimately lead to improved long-term results?

The aforementioned cited positive PMA results, absent intense medical optimization, and stringent patient selection present in a major transcatheter mitral repair trial, suggest there is a role for PMA in the management of ischemic MR and that it should be compared with the newly adopted percutaneous mitral therapies. As more data become available, better selection of patients would also lead to better longer-term outcomes for PMA. A necessary question is whether PMA should be accompanied by a RA or a true-sized annuloplasty. Additionally, would addressing the functional MR ventricle with PMA plus annuloplasty at earlier stages in the disease process improve survival and quality of life? It is time for prospective trials comparing transcatheter mitral therapies with surgery to include minimally invasive mitral surgery.

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