Coronary artery bypass grafting (CABG) alone in moderate ischemic mitral regurgitation: is CABG really enough?

Francesco Nappi[1], Cristiano Spadaccio[2,3]

[1]Cardiac Surgery Centre Cardiologique du Nord de Saint-Denis, Paris, France; [2]Department of Cardiothoracic Surgery, Golden Jubilee National Hospital, Glasgow, UK; [3]University of Glasgow Institute of Cardiovascular and Medical Sciences, Glasgow, UK

Correspondence to: Francesco Nappi, MD. Cardiac Surgery Centre Cardiologique du Nord de Saint-Denis, 36 Rue des Moulins Gémeaux, 93200 Saint-Denis, France. Email: francesconappi2@gmail.com.

Submitted Aug 05, 2016. Accepted for publication Aug 09, 2016.
doi: 10.21037/atm.2016.08.47
View this article at: http://dx.doi.org/10.21037/atm.2016.08.47

The randomized study described by Michler and co-authors recently appeared in *NEJM* reports the results of the 2-year outcomes of surgical treatment of moderate ischemic mitral regurgitation (IMR) (1). This paper nourishes and expands the discussion about functional or "secondary" mitral regurgitation occurring as a consequence of an active reversible ischemia or a complete infarction and reopens the debate arisen in the previous study of the Cardiothoracic Surgical Trials Network (CTSN) about the optimal treatment of IMR. Advances in the management of cardiovascular risk factors and acute coronary syndromes permit to effectively identify around 1.6 to 2.8 million patients in the United States suffering by functional IMR after a heart attack; about 10% of these patients suffer from an IMR of moderate entity. Despite the increase in the immediate survival, the lack of an optimized surgical treatment is responsible for a high rate of IMR recurrence (2) after surgery, transforming this pathological phenomenon into a chronic disease, with enormous societal implications.

The findings described by Michler *et al*. showed no difference among a combined approach including restrictive annuloplasty and coronary artery bypass grafting (CABG) *vs*. CABG alone in terms of left ventricular remodeling. These results reinforce the concept that IMR is sustained by reversible ischemia rather than by nonviable scar formation. Myocardial revascularization is therefore thought to play a significant contribution in left ventricular function as measured by means of the left ventricular end-systolic volume index (LVESVI), left ventricular ejection fraction, and global and regional wall motion. In surviving patients authors report no significant between-groups difference in LVESVI, at 2 years (41.2±20.0 mL in the CABG-alone group *vs*. 43.2±20.6 mL in the combined undersizing annuloplasty and CABP group, respectively). The rank-based assessment of the primary outcome of LVESVI including death at 2 years revealed a z score, 0.38; P=0.71. The same result was evident in terms of left ventricular ejection fraction (46.1%±10.5% in the CABG-alone group *vs*. 45.6%±10.0% in the associated surgery procedure group). However, MR recurrence was 3 times higher in the CABG-alone group at 2 years and patients developing MR experienced a significant worsening LVESVI and reverse remodeling. This presumably affected the absolute values of rehospitalization rate for heart failure, although not significant difference among groups was found. Moreover, echocardiographic evaluation revealed that at 2 years the relative percent improvement in the global wall-motion index was higher in patients free from moderate or severe MR in respect to those experiencing MR recurrence (16.5%±20.1% *vs*. 7.4%±16.7%, P=0.008).

As far as postoperative moderate or severe mitral regurgitation is concerned, the CABG-alone group was burdened by a significantly higher rate of MR recurrence in respect to the combined-procedure group (32.3% *vs*. 11.2%, respectively P<0.001) with moderate insufficiency affecting 43% of the patients in the CABG-alone versus 24.8% in the combined procedure (P=0.004); similarly, the proportion of patients with severe mitral regurgitation or needing mitral-valve reoperation was 11.4% in the CABG-alone group and 3.5% in the combined-procedure group (P=0.02).

Therefore, despite no changes in mortality or major

cardiac events, the CABG-alone approach was not able to break the vicious circle spiralling towards adverse LV and combination annuloplasty did not achieve either a complete resolution of the MR. This reflects the need arisen in some recent reports to address also the subvalvular apparatus in the context of mitral repair surgery (3). The rationale of this more "holistic" approach to the mitral valve is the correction of the altered ventricular geometry and imbalance between closing and tethering forces on the valve, together with revascularization (4,5). Under this light, the following two fundamental questions require a reply: is complete revascularization the only tenet of treatment to prevent progression of LV remodeling and MR recurrence? Should we also consider the geometrical restoration of tethering forces in the pathophysiological cascade of IMR?

The primary advantage produced by a complete and successful myocardial revascularization regards the recovery of the viable myocardium with further improvement in global and regional wall motion and reverse left ventricular remodelling. This effect has been noted in the first year after surgery in both the severe and moderate MR trial in *NEJM* (6,7). The second substantial effect of improved coronary perfusion is the improvement of mitral valve function subsequent to the reduction in the ventricular size and to the increased "closing forces". In support of this idea, the highest incidence of IMR recurrence in the 2-year study of the CTSN on surgical treatment for severe MR occurred in patients within the valve repair group who did not receive myocardial revascularization. On a total 54% rate of MR recurrence, 24% did not receive CABG.

IMR is sustained by a complex pathophysiological process involving the papillary muscles in terms of both their anatomical configuration and their dynamic blood perfusion. Clinical evidence and instrumental observations using high resolution CT scan have clarified the relationship between coronary blood flow and papillary muscles with particular emphasis on their peculiar morphology (3,8). In our series primary ischemic lesion or dysfunction of PM related to wall dyssincrony or LV dilation produced leaflet prolapse in 86.4% of IMR patients. Antero-lateral PM (ALPM) was involved in 18.2% and postero-medial PM (PMPM) in 63.8% respectively. In 13.6% the PM dysfunction or prolapse was determined by the necrosis of a restricted area of the myocardium adjacent to the PM, which was responsible for its abnormal traction and of its dyssyncrony (9).

Coronary distribution and the variability of PM anatomical configuration are responsible for a wide range of PM typologies of injury. Indeed distribution of blood supply to PM is uneven explaining the rare involvement of the anterior PM, which is perfused by both the left anterior descending coronary artery and diagonal branch. Additionally, the superficial location of the anterior PM in respect to the annulus and the relatively low tension borne by the PM protect this muscle from rupture. Conversely, the blood support of the posterior PM is furnished only by distal branches of either the right coronary or the circumflex artery and is therefore more sensitive to ischemia (10) [91% of the cases in our series (9)]. Furthermore, being located deep in the left ventricle a higher shear force is normally applied to this muscle with consequent higher chances of rupture or partial rupture. The microcirculation of the muscle itself relies in both an independent blood supply, provided by a well-identified arterial trunk perforating the PM from base to apex (Kugel's artery), and a segmental distribution. However, the morphology of the PM, the presence of muscular bridging and the relative position of the PM in respect to the ventricle profoundly influence the efficiency of the circulation and might enhance ischemic phenomena related to poor regional perfusion (11,12). Indeed, in case of discrete and individualized PM, as in type IV–V, the relative importance of the truncal system increases significantly with the apex being more prone to dysfunction or even rupture because of the fragility of its terminal irroration and the degree of physical stress (10). Additionally, the morphological variants of the posterior PM, which is the more common site of ischemic injury, are more complex than the anterior PM, presenting more frequently with subdivision into several heads (11,12).

IMR is frequently caused by a variable and complex degree of PM dysfunction (3). Dyssincrony, elongation limited to a single head or a partial PM rupture represent some among the heterogeneous manifestations of PM injury. Sometimes, leaflet prolapse, normally present in more than 30% of IMR cases, is sustained by an incomplete detachment of a head due to a rupture of its main insertion in the ventricle, with the body remaining fixed to the myocardial wall just via muscular bridges ('incomplete' papillary muscle rupture) (9).

Some of these patho-physiological principles might explain the results of the CTSN studies which showed a not negligible incidence of IM recurrence at 2 years follow-up (1,2). When failing to restore the physiological balance of tethering forces within the ventricle, correction of the mitral annulus with restrictive undersizing annuloplasty would not suffice to prevent mitral valve failure. Therefore,

surgical decision-making could be improved by identifying all those factors adversely affecting the balance between tethering forces and closing forces. In this context, surgery of subvalvular mitral apparatus may be the key to solve this physiopathological issue.

The characteristics of leaflet tethering have been described in details by Agricola and colleagues (13). These authors firstly described two echocardiographic patterns in IMR due to restricted motion according to the tethering characteristics; the asymmetrical pattern with predominant posterior tethering of both leaflets and the symmetrical pattern with predominant apical tethering of both leaflets. Each papillary muscle provides chordae to both leaflets, thus a posterior displacement of only the posteromedial papillary muscle invariably exerts traction on both leaflets (14). During LV remodeling, the development of tethering vectors consequent to LV cavity enlargement in the posterior, apical, and lateral directions is responsible for the different characteristics of mitral leaflets tethering among the two echocardiographic patterns described (13). In the asymmetrical pattern, the posterior leaflet is simply drawn more posteriorly than apically and its displacement is parallel to the posterior wall. This posterior restriction prevents the posterior leaflet to achieve its normal, coaptation point, normally located more anteriorly. As a final result, the coaptation point moves posteriorly, creating the mentioned asymmetrical tethering shape. In the symmetrical group there is a further apical and mediolateral tethering in addition to the posterior component. Echocardiographic result of these forces is a more apical tenting, with the coaptation point being displaced more apically. In the symmetrical group, the regurgitant jet usually has a central origin and direction because the systolic motion of both leaflets is likewise affected. Conversely, in the asymmetrical group, it is the movement of the posterior leaflet to be predominantly compromised causing the jet to be more posteriorly oriented. In our study the patients developing recurrence of IMR presented both central and eccentric regurgitation jets (5). This variability led us to think that the pathogenic mechanism is much more complex and we have developed a mathematical model describing the biomechanics of the mitral valve apparatus in all its components with the final aim to elaborate a decisional algorithm to support the surgical choices in IMR treatment (15).

Acknowledgements

None.

Footnote

Provenance: This is a Guest Commentary commissioned by Section Editor Busheng Zhang, MD, PhD (Department of Cardiac Surgery, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Michler RE, Smith PK, Parides MK, *et al*. Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation. N Engl J Med 2016;374:1932-41.

References

1. Michler RE, Smith PK, Parides MK, et al. Two-Year Outcomes of Surgical Treatment of Moderate Ischemic Mitral Regurgitation. N Engl J Med 2016;374:1932-41.
2. Goldstein D, Moskowitz AJ, Gelijns AC, et al. Two-Year Outcomes of Surgical Treatment of Severe Ischemic Mitral Regurgitation. N Engl J Med 2016;374:344-53.
3. Kalra K, Wang Q, McIver BV, et al. Temporal changes in interpapillary muscle dynamics as an active indicator of mitral valve and left ventricular interaction in ischemic mitral regurgitation. J Am Coll Cardiol 2014;64:1867-79.
4. Padala M, Gyoneva LI, Thourani VH, et al. Impact of mitral valve geometry on hemodynamic efficacy of surgical repair in secondary mitral regurgitation. J Heart Valve Dis 2014;23:79-87.
5. Nappi F, Lusini M, Spadaccio C, et al. Papillary Muscle Approximation Versus Restrictive Annuloplasty Alone for Severe Ischemic Mitral Regurgitation. J Am Coll Cardiol 2016;67:2334-46.
6. Smith PK, Puskas JD, Ascheim DD, et al. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014;371:2178-88.
7. Acker MA, Parides MK, Perrault LP, et al. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. N Engl J Med 2014;370:23-32.
8. Sanz J, Weinsaft JW. Ischemic mitral regurgitation: is mitral valve physiology moving from global to local? J Am Coll Cardiol 2014;64:1880-2.
9. Nappi F, Nenna A, Spadaccio C, et al. Predictive factors of long-term results following valve repair in ischemic mitral valve prolapse. Int J Cardiol 2016;204:218-28.
10. Estes EH Jr, Dalton FM, Entman ML, et al. The anatomy and blood supply of the papillary muscles of the left

ventricle. Am Heart J 1966;71:356-62.
11. Ramsheyi SA, Pargaonkar S, Lassau JP, et al. Morphologic classification of the mitral papillary muscles. J Heart Valve Dis 1996;5:472-6.
12. Victor S, Nayak VM. Variations in the papillary muscles of the normal mitral valve and their surgical relevance. J Card Surg 1995;10:597-607.
13. Agricola E, Oppizzi M, Maisano F, et al. Echocardiographic classification of chronic ischemic mitral regurgitation caused by restricted motion according to tethering pattern. Eur J Echocardiogr 2004;5:326-34.
14. Godley RW, Wann LS, Rogers EW, et al. Incomplete mitral leaflet closure in patients with papillary muscle dysfunction. Circulation 1981;63:565-71.
15. Nappi F, Spadaccio C, Fraldi M. Complete mitral valve repair: the new direction of travel. Towards geometry-based biomechanical modeling. J Am Coll Cardiol 2016. [Epub ahead of print].

Cite this article as: Nappi F, Spadaccio C. Coronary artery bypass grafting (CABG) alone in moderate ischemic mitral regurgitation: is CABG really enough? Ann Transl Med 2016;4(20):413. doi: 10.21037/atm.2016.08.47

