Editorial

Mitral valve repair for moderate ischemic mitral regurgitation

Daniel Hernandez-Vaquero, Rocío Díaz, Rubén Álvarez-Cabo, Carlota Vigil-Escalera, Jacobo Silva

Cardiac Surgery Department, Heart Area, Hospital Universitario Central de Asturias, Avenue Hospital Universitario Central de Asturias, Oviedo, Spain
Correspondence to: Daniel Hernandez-Vaquero, MD, PhD. Hospital Universitario Central de Asturias, Oviedo 33011, Spain. Email: dhvaquero@gmail.com.

Submitted Apr 29, 2016. Accepted for publication May 06, 2016.
doi: 10.21037/jtd.2016.05.41
View this article at: http://dx.doi.org/10.21037/jtd.2016.05.41

Any degree of ischemic mitral regurgitation (IMR) is present in 20% to 30% of patients after an acute myocardial infarction (AMI) and moderate severity IMR is developed in more than 10%. As the population ages and the survival rate following AMI increases, so will the number of people with IMR (1). IMR is associated with excess mortality regardless of management. So, patient survival has proven to be inversely correlated with the grade of MR. Even mild IMR post AMI dramatically increases cardiovascular mortality, with a 17% increase at 3.5 years compared to patients with similar degrees of ischemia but without MR (2).

After an AMI, left ventricular (LV) remodeling with LV dilatation and dysfunction lead to annular enlargement, reduction of the force available to close the leaflets, leaflet tethering and restriction of leaflet motion resulting in malcoaptation of absolutely normal leaflets and therefore IMR (3). Laplace's law (pressure is proportional to wall stress divided by radius of curvature) implies that once IMR is initiated, end-diastolic LV volume and wall stress increase in parallel with preload. The increase in wall stress leads to further LV remodeling, which culminates in a spiraling, self-perpetuating cycle of leaflet tethering (4). Pathophysiological causes of IMR and the way that coronary artery bypass grafting (CABG) or mitral valve repair (MVR) can break the vicious circle are summarized in *Figure 1*.

When the mitral regurgitation is severe, debate has focused on the choice between MVR or chordal-preserving mitral valve replacement as recently addressed by Goldstein D and colleagues (5) who randomized 251 patients with chronic IMR to undergo either mitral-valve repair or chordal sparing replacement with complete preservation of the subvalvular apparatus. At two years follow up, authors conclude that there were no difference with respect to LV reverse remodeling or survival but the rate of recurrence of moderate or severe mitral regurgitation was more than 15 times higher with mitral-valve repair (58.8% *vs.* 3.8%) resulting in more heart failure—related adverse events and cardiovascular admissions (5). A comprehensive and rigorous evaluation of this work has recently been published in this journal (6).

When the regurgitation is only moderate, debate has centered on the role of associated MVR versus isolated coronary artery by-pass grafting (CABG) (7).

European guidelines on valvular heart disease do not even address the surgical problem of moderate IMR and CABG saying only that "there is continuing debate regarding the management of moderate ischemic MR in patients undergoing CABG and, in such cases, valve repair is preferable" (8). Conversely, American guidelines consider surgical MVR at the time of CABG when the regurgitation is moderate as a class IIb recommendation (which indicates that the procedure may be considered with benefit ≥ risk but additional studies are needed) with a level of evidence C (expert opinion, no rigorous studies available) (9). With this level of uncertainty and patients on the operating table, a randomized clinical trial on this issue is a godsend for cardiac surgeons. Recently, Michler *et al.* (10) have published the 2-year outcomes of this clinical trial, which randomized 301 patients with moderate IMR and multivessel coronary artery disease to undergo either CABG alone or CABG and MVR. The primary end point was the degree of LV reverse remodeling, as measured by means of the LV end systolic volume index (LVESVI) on transthoracic echocardiography 1 year after randomization. All patients were followed for 2 years with end points measured at 6, 12, and 24 months. Secondary end points included findings on transthoracic echocardiography at other time points, rate of death, MACCE [defined as a composite of death, stroke, subsequent mitral-valve surgery, hospitalization for heart

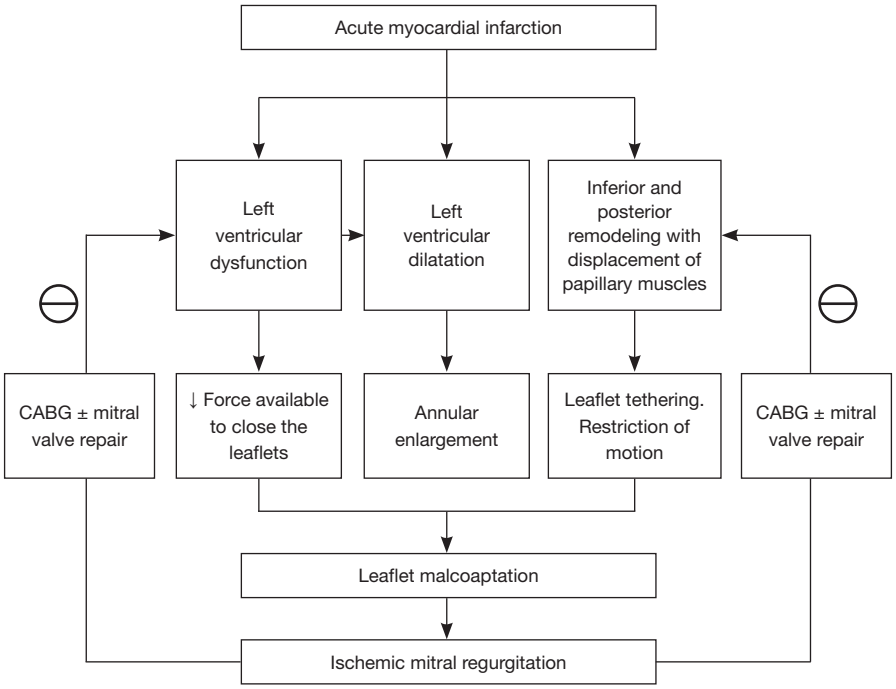

Figure 1 Pathophysiological mechanisms of ischemic mitral regurgitation and how CABG and MVR can break the vicious circle.

failure, or worsening New York Heart Association (NYHA) class], serious adverse events, degree of postoperative mitral regurgitation, quality of life, and rehospitalization. At 2 years follow up, authors concluded that the addition of mitral-valve repair to CABG had no incremental effect on reverse LV remodeling. However, patients who underwent CABG alone had 3 times higher prevalence of moderate or severe mitral regurgitation than those who underwent the combined procedure (32.3% *vs.* 11.2%, P<0.001). Conversely, this difference did not translate into higher rates of death, MACCE, serious adverse events (including heart failure), or readmission during these 2 years of follow-up. Moreover, patients who underwent CABG plus mitral-valve repair had higher self-reported exercise capacity. The addition of mitral-valve repair made the operation more difficult with longer cross-clamp or bypass times, which resulted in a longer postoperative length of stay during the index hospitalization, and significantly higher rates of serious neurologic events and supraventricular arrhythmias (10).

In summary, this trial conclude that patients who undergo CABG alone have less morbidity, same improvement on LV function and same rates of mortality (10.6% *vs.* 10%) and cardiovascular events than patients who undergo CABG plus MVR (10).

With these data, it would appear that the controversy is over and the problem is solved. However, not all that glitters is gold. What does IMR mean? In the current American guidelines functional or secondary mitral regurgitation occur not only due to completed infarction but also reversible ischemia. If mitral regurgitation was caused by reversible ischemia rather than by nonviable scar formation, successful myocardial revascularization can lead to reduced LV size, increased mitral-valve closing forces, improved papillary-muscle synchrony, and enhanced contractility of subjacent myocardium. All this would result in a global improvement of mitral valve function (*Figure 1*). So, if mitral regurgitation and ventricular dysfunction may be correctable by revascularization alone, the performance of MVR would only add operative risk without any benefit. In this trial (10), it is likely that many patients who were enrolled had mitral regurgitation caused by reversible ischemia rather than by nonviable scar formation, which resulted in an improvement of mitral valve function in two thirds of patients.

However, "IMR" has been defined as that "occurring more than 1 week after an AMI with (I) one or more LV segmental wall motion abnormalities; (II) significant coronary disease in the territory supplying the wall motion abnormality; and (III) structurally normal mitral valve

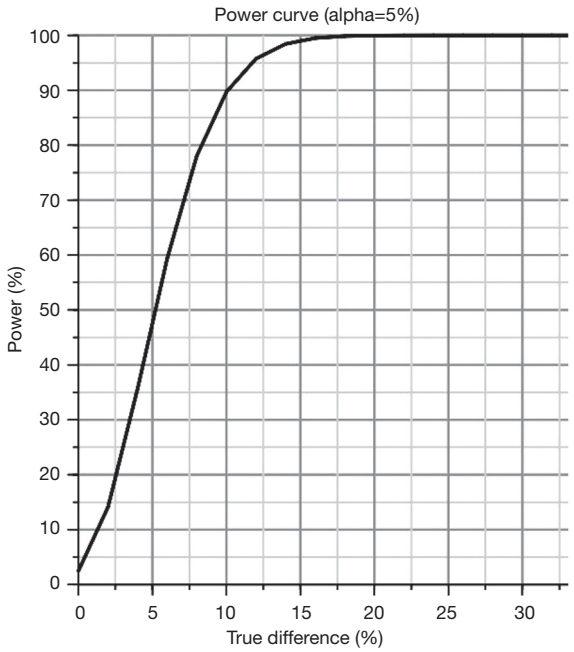

Figure 2 Statistical power to detect differences with 150 patients in each group and a mortality rate of 3% in one group.

leaflets and chordae tendineae." (7,11). In this situation, it is likely that there is not myocardial viability and therefore, MVR would be necessary. Unfortunately, many studies, like this trial (10), used the term more loosely, and these authors did not take into account this definition of IMR (7). However, this study teaches us that surgical decision making could be improved by conducting tests of myocardial viability identifying which patients are most likely to have an improvement in regional wall motion and global LV function after isolated CABG (10).

Other important limitation is that this study is unpowered to detect differences on clinical outcomes. Authors calculated that the enrollment of 300 patients would provide 90% power to detect a difference of 12 mL per square meter in the LVESVI between groups (12). This small number of patients is an advantage of analyzing continuous quantitative variables as some echocardiographic parameters. However, binomial clinical variables as mortality or cardiovascular events require a much higher number of patients. So, to achieve 90% power to detect differences in survival rates using log-rank test with an estimated HR of 1.2, the number of patients who need to be enrolled is more than 1,200. The power of this study with 301 patients would be 35%. This means that, although there were differences between treatments (HR =1.2), this study would detect them less than 50% of the times. With longer cross clamp and cardiopulmonary bypass times, the combined procedure is expected to have higher in-hospital mortality. However, this study does not provide this data. This is because it is simply not possible. To compare this important outcome with such number of patients using 90% power to detect differences, 3% of expected mortality rate in a group and a difference of ±2%, the number of patients needed would be around 4,000. With 150 patients per group, the difference between groups able to be detected is 10% (*Figure 2*). That means that, if the mortality of a group is 2%, the other one must have more than 12% in order to get a power of 90% [Calculations performed with STATA® IC 14.1 (StataCorp, College Station, TX, USA)].

In conclusion, two thirds of patients with moderate IMR and multivessel disease who undergo isolated CABG have mild or no IMR at 2 years follow up but probably this percentage varies depending on myocardial viability. Surgical decision making could be improved by conducting tests of myocardial viability on lateral, posterior and inferior territory identifying which patients are most likely to have an improvement in regional wall motion and therefore improve their mitral valve function after successful isolated myocardial revascularization. Patients with moderate IMR and multivessel disease who undergo either CABG alone or CABG plus MVR have similar LV function recovery at 2 years of follow up. Patients who undergo CABG and MVR have three times less significant IMR (32.3% *vs.* 11.2%) which leads to better self-reported exercise capacity at the expense of higher rates of neurological events, supraventricular arrhythmias and in-hospital morbidity. Nevertheless, since this study is not able to detect real differences on cardiovascular events or mortality, further research with greater number of patients and longer follow up is needed to know the relevance of adding MVR to CABG.

Acknowledgements

None.

Footnote

Provenance: This is an invited Editorial commissioned by the Section Editor Kai Zhu (Department of Cardiac Surgery, Zhongshan Hospital Fudan 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. Dayan V, Soca G, Cura L, et al. Similar survival after mitral valve replacement or repair for ischemic mitral regurgitation: a meta-analysis. Ann Thorac Surg 2014;97:758-65.
2. Perrault LP, Moskowitz AJ, Kron IL, et al. Optimal surgical management of severe ischemic mitral regurgitation: to repair or to replace? J Thorac Cardiovasc Surg 2012;143:1396-403.
3. Lee LS, Kwon MH, Cevasco M, et al. Postoperative recurrence of mitral regurgitation after annuloplasty for functional mitral regurgitation. Ann Thorac Surg 2012;94:1211-6; discussion 1216-7.
4. Roshanali F, Mandegar MH, Yousefnia MA, et al. A prospective study of predicting factors in ischemic mitral regurgitation recurrence after ring annuloplasty. Ann Thorac Surg 2007;84:745-9.
5. 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.
6. Hernandez-Vaquero D, Díaz R, Meana B, et al. Is chordal-preserving mitral valve replacement superior to valve repair in appropriately selected patients? J Thorac Dis 2016;8:6-9.
7. Sundt TM. Surgery for ischemic mitral regurgitation. N Engl J Med 2014;371:2228-9.
8. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur J Cardiothorac Surg 2012;42:S1-44.
9. Nishimura RA, Otto CM, Bonow RO, et al. 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 Practice Guidelines. J Thorac Cardiovasc Surg 2014;148:e1-e132.
10. 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.
11. Borger MA, Alam A, Murphy PM, et al. Chronic ischemic mitral regurgitation: repair, replace or rethink? Ann Thorac Surg 2006;81:1153-61.
12. Smith PK, Puskas JD, Ascheim DD, et al. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014;371:2178-88.

Cite this article as: Hernandez-Vaquero D, Díaz R, Álvarez-Cabo R, Vigil-Escalera C, Silva J. Mitral valve repair for moderate ischemic mitral regurgitation. J Thorac Dis 2016;8(7):1410-1413. doi: 10.21037/jtd.2016.05.41