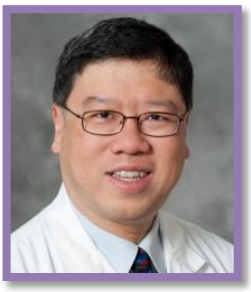
HEART FAILURE AND TRANSPLANTATION
Journal Watch
August
2015

Feras Khaliel, MD
King Faisal Specialist Hospital & Research Center
Riyadh, Saudi Arabia
f.khaliel@doctor.com



Andrew Kao, MD
St Luke's Mid America Heart Institute
Kansas City, Missouri, USA
akao@saint-lukes.org

Special Theme Issue:
ISCHEMIC MITRAL REGURGITATION

REVIEWS:

Functional ischemic mitral regurgitation (MR) occurs in up to 40% of patients after myocardial infarction. It is usually mild or moderate in severity but is associated with an increased incidence of heart failure and death. It is caused by left ventricular (LV) remodeling and dilatation after myocardial infarction, which tethers and pulls the mitral valve apart, resulting in MR. The mitral valve is normal in structure but is incompetent as a result of a dilated and dysfunctional left ventricle. The majority of patients have significant 3-vessel coronary artery disease and benefit from coronary artery bypass grafting (CABG). The long-term outcome with coronary artery revascularization alone remains poor, with a reported increased incidence of heart failure and death of up to 50%. (Aronson D, et al).

Chan KM, Punjabi PP, Flather M, Wage R, Symmonds K, Roussin I, Rahman-Haley S, Pennell DJ, Kilner PJ, Dreyfus GD, Pepper JR; RIME Investigators. "Coronary artery bypass surgery with or without mitral valve annuloplasty in moderate functional ischemic mitral regurgitation: final results of the Randomized Ischemic Mitral Evaluation (RIME) trial." ***Circulation*****. 2012 Nov 20;126(21):2502-10**

John Pepper and colleagues conducted a randomized, single blinded, multi-centered trial (RIME). They studied 73 patients with coronary artery disease (CAD), moderate ischemic MR, and LVEF>30%, dividing them equally into two groups. The first group underwent CABG, while the other group underwent combined MVR with CABG. One year after surgery, there was a greater improvement in the primary end point of peak oxygen consumption in the CABG plus MVR group compared with the CABG group (3.3 mL/kg/min versus 0.8 mL/kg/min; P= 0.001). There was also a greater improvement in the secondary end points in the CABG plus MVR group compared with the CABG group: left ventricular end-systolic volume index, MR volume, and plasma B-type natriuretic peptide reduction of 22.2 mL/m2 , 28.2 mL/beat, and 557.4 pg/mL, respectively versus 4.4 mL/m2 (P= 0.002), 9.2 mL/beat (P=0.001), and 394.7 pg/mL (P= 0.003), respectively. Operation duration, blood transfusion requirement, intubation duration, and hospital stay duration were greater in the CABG plus MVR group. Deaths at 30 days and 1 year were similar in both groups: 3% and 9%, respectively in the CABG plus MVR group, versus 3% (P= 1.00) and 5% (P= 0.66), respectively in the CABG group.

Smith PK, Puskas JD, Ascheim DD, Voisine P, Gelijns AC, Moskowitz AJ, Hung JW, Parides MK, Ailawadi G, Perrault LP, Acker MA, Argenziano M, Thourani V, Gammie JS, Miller MA, Pagé P, Overbey JR, Bagiella E, Dagenais F, Blackstone EH, Kron IL, Goldstein DJ, Rose EA, Moquete EG, Jeffries N, Gardner TJ, O'Gara PT,

Alexander JH, Michler RE; Cardiothoracic Surgical Trials Network Investigators. "Surgical treatment of moderate ischemic mitral regurgitation." *N Engl J Med*. 2014 Dec 4;371(23):2178-88.

Smith et al along with their colleagues from the Cardiothoracic Surgical Trials Network randomly assigned 301 patients with ischemic cardiomyopathy to CABG vs CABG plus mitral valve repair. Here they reported their 1 year outcomes with the main variable being examined being the left ventricular end systolic volume index (LVESVI). Both groups averaged 3 grafts, and both groups decreased their LVESVI by 9 ml/m^2 at 1 year. More patients in the CABG only group had moderate or severe MR at 1 year but the outcomes of cardiac/cerebrovascular events, death, readmissions, NYHA class (8-10% class 3-4) or quality of life (as measured by SF12, Minnesota Living With Heart Failure and EuroQol 5D) were similar between groups. Not surprisingly, the MVR group had longer bypass time, longer hospital stays and more neurologic events (9.6% vs 3.1%, p<0.03) compared to the CABG only group. Almost all patients were free of Canadian Cardiovascular Society Class 3-4 angina at follow-up. This study would suggest that the important treatment modality is revascularization, not mitral valve surgery. However, the follow-up in this study was short (1 year), and the long-term consequences of moderate to severe MR in the CABG only group may not yet have been apparent.

Maltais S, Schaff HV, Daly RC, Suri RM, Dearani JA, Sundt TM 3rd, Enriquez-Sarano M, Topilsky Y, Park SJ. "Mitral regurgitation surgery in patients with ischemic cardiomyopathy and ischemic mitral regurgitation: factors that influence survival." *J Thorac Cardiovasc Surg*. 2011 Nov;142(5):995-1001.

Maltais et al identified 431 patients (1993-2007) with ischemic cardiomyopathy (LVEF = 45%) and significant ischemic mitral regurgitation (> 2). Patients (44) with concomitant mitral stenosis were excluded from the analysis. A homogeneous group of 387 patients underwent combined coronary artery bypass grafting and mitral valve surgery: mitral valve repair in 302 (78%) and mitral valve replacement in 85 (22%). Uni- and multivariate analyses were performed on the entire cohort, and the predictors of mortality were identified in 2 distinct risk phases. Furthermore, the authors specifically examined the impact of mitral valve repair versus replacement by comparing 2 propensity matched subgroups. They reported the overall 1-, 5-, and 10-year survivals as 82.7%, 55.2%, and 24.3%, respectively, for the entire group. The risk factors for an increased mortality within the first year of surgery included previous coronary artery bypass grafting (hazard ratio = 3.39; P< 0.001), emergency/urgent status (hazard ratio = 2.08; P = 0.007), age (hazard ratio = 1.5; P = 0.03), and low left ventricular ejection fraction (hazard ratio = 1.31; P = 0.026). Thereafter, only age (hazard ratio =1.58; P< 0.001), diabetes (hazard ratio = 2.5; P = 0.001), and preoperative renal insufficiency (hazard ratio = 1.72; P = 0.025) were predictive. The status of mitral valve repair versus replacement did not influence survival, and this was confirmed by comparable survival in propensity-matched analyses.

Acker MA, Parides MK, Perrault LP, Moskowitz AJ, Gelijns AC, Voisine P, Smith PK, Hung JW, Blackstone EH, Puskas JD, Argenziano M, Gammie JS, Mack M, Ascheim DD, Bagiella E, Moquete EG, Ferguson TB, Horvath KA, Geller NL, Miller MA, Woo YJ, D'Alessandro DA, Ailawadi G, Dagenais F, Gardner TJ, O'Gara PT, Michler RE, Kron IL; CTSN. "Mitral-valve repair versus replacement for severe ischemic mitral regurgitation." *N Engl J Med*. 2014 Jan 2;370(1):23-32.

Acker et al. had a different hypothesis. They randomly assigned 251 patients with severe ischemic mitral regurgitation to undergo either mitral-valve repair or chordal-sparing replacement in order to evaluate the efficacy and safety of each approach. The primary end point was the left ventricular end-systolic volume index (LVESVI) at 12 months, as assessed with the use of a Wilcoxon rank-sum test in which deaths were categorized below the lowest LVESVI rank. At 12 months, the mean LVESVI among surviving patients was 54.6±25.0 ml per square meter of body-surface area in the repair group and 60.7±31.5 ml per square meter in the replacement group (mean change from baseline, −6.6 and −6.8 ml per square meter, respectively).

The rate of death was 14.3% in the repair group and 17.6% in the replacement group (hazard ratio with repair, 0.79; 95% confidence interval, 0.42 to 1.47; P = 0.45 by the log-rank test). There was no significant between-group difference in LVESVI after adjustment for death (z score, 1.33; P = 0.18). The rate of moderate or severe recurrence of mitral regurgitation at 12 months was higher in the repair group than in the replacement group (32.6% vs. 2.3%, P<0.001). There were no significant between-group differences in the rate of a composite of major adverse cardiac or cerebrovascular events, in functional status, or in quality of life at 12 months.

Gulack BC, Englum BR, Castleberry AW, Daneshmand MA, Smith PK, Perrault LP. "Repair or observe moderate ischemic mitral regurgitation during coronary artery bypass grafting? Prospective randomized multicenter data." *Ann Cardiothorac Surg*. 2015 May;4(3):266-72.

Gulack et al concluded recently this year: "Despite contradictory smaller studies, the largest studies regarding moderate mitral regurgitation demonstrate no survival benefit associated with CABG and concomitant MVR at one year." While it is likely that there is a subset of patients whose survival, functional status, or symptoms may improve with MVR; this subset of patients has yet to be definitively identified. Soon, the CTSN trial will report 2-year survival outcomes and thereby provide more evidence regarding the long-term impact of revascularization in IMR. Furthermore, this trial gathered specific data on neurologic function, functional status, cardiac wall motion, and detailed operative techniques. Planned subgroup analyses of the CTSN trial will be critical to our understanding of IMR and its treatment. In particular, the planned analysis of sub-segmental wall motion based on TEE and its impact on IMR will be paramount. In conclusion, the best clinical data available today supports isolated CABG as first line therapy in the short-term for moderate ischemic MR. Ongoing follow up and subgroup analyses of current data may identify groups of moderate IMR patients that would most benefit from concomitant MVR and CABG.

While the optimal approach to the treatment of significant ischemic mitral regurgitation remains to be defined, newer approaches are being studied. Scoville and Boyd just published a succinct review outlining the various approaches, including percutaneous edge-to-edge repair, minimally invasive mitral valve repair in combination with CABG, PCI or hybrid coronary revascularization. Stay tuned for more exciting developments in this important and controversial area of heart failure cardiology.

ARTICLES OF INTEREST:

1. Core Lab Analysis of Baseline Echocardiographic Studies in the STICH Trial and Recommendation for Use of Echocardiography in Future Clinical Trials. *J Am Soc Echocardiogr . 2012 March ; 25(3): 327–336. Doi:10.1016/j.echo.2011.12.002.*

2. Repair or replace for severe ischemic mitral regurgitation: prospective randomized multicenter data. *Ann Cardiothorac Surg* 2015;4(5):411-416.

3. Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation. *N Engl J Med. 2014 January 2; 370(1): 23–32*.

4. Optimal Surgical Management of Severe Ischemic Mitral Regurgitation: To Repair or to Replace? *J Thorac Cardiovasc Surg. 2012 June ; 143(6): 1396–1403. doi:10.1016/j.jtcvs.2011.05.030*

5. Smith PK, Puskas JD, Ascheim, DD et al for the Cardiothoracic Surgical Trials Network Investigators. Surgical Treatment of Moderate Ischemic Mitral Regurgitation. N Engl J Med 2014371:2178-2188

6. Scoville DH, Boyde JBH. A Novel Approach to Ischemic Mitral Regurgitation (IMR). Ann Cardiothorac Surg 2015;4:443-448

7. Is a good perioperative echocardiographic result predictive of durability in ischemic mitral valve repair? *J Thorac Cardiovasc Surg 2006;131:565-73*

8. A Novel Method of Percutaneous Mitral Valve Repair for Ischemic Mitral Regurgitation. *J Am Coll Cardiol Intv 2008;1:663–72*

9. Initial Results of Posterior Leaflet Extension for Severe Type IIIb Ischemic Mitral Regurgitation. *Circulation. 2009;119:2837-2843*

10. Mitral regurgitation surgery in patients with ischemic cardiomyopathy and ischemic mitral regurgitation: Factors that influence survival. *J Thorac Cardiovasc Surg 2011;142:995-1001*

11. Repair or observe moderate ischemic mitral regurgitation during coronary artery bypass grafting? Prospective randomized multicenter data. *Ann Cardiothorac Surg 2015;4(3):266-272*

12. Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation. Final Results of the Randomized Ischemic Mitral Evaluation (RIME) Trial. *Circulation. 2012;126:2502-2510.*

13. Management of severe ischemic cardiomyopathy: left ventricular assist device as destination therapy versus conventional bypass and mitral valve surgery. *J Thorac Cardiovasc Surg. 2014 Apr;147(4):1246-50*

14. Predicting recurrent mitral regurgitation after mitral valve repair for severe ischemic mitral regurgitation. *J Thorac Cardiovasc Surg. 2015 Mar;149(3):752-61.e1.*