**Name of Journal:** *World Journal of Cardiology*

**Manuscript NO:** 40471

**Manuscript Type:** MINIREVIEWS

**Chronic ischemic mitral valve regurgitation, surgical perspectives**

Altarabsheh SE *et al*. Chronic ischemic mitral valve regurgitation

Salah Eldien Altarabsheh, Salil V Deo, Abeer Rababa’h, Yagthan M Obeidat, Osama Haddad

**Salah Eldien Altarabsheh,** Division of Cardiovascular Surgery, Queen Alia Heart Institute, Amman 11953, Jordan

**Salil V Deo,** Division of Cardiovascular Surgery, Harrington Heart and Vascular Institute, Case Western Reserve University, Cleveland, OH 44106, United States

**Abeer Rababa’h,** Department of Clinical Pharmacy, Jordan University of Science and Technology, Irbid 22110, Jordan

**Yagthan M Obeidat,** Department of Cardiac Surgery, AlMana General Hospital, AL Khobar 31952, Saudi Arabia

**Osama Haddad,** Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, OH 44195, United States

**ORCID number:** Salah Eldien Altarabsheh (0000-0002-1328-3340); Salil V Deo (0000-0002-4729-1461); Abeer Rababa’h (0000-0003-4619-2012); Yagthan M Obeidat (0000-0001-6551-9274); Osama Haddad (0000-0001-6308-6372).

**Author contributions:** Altarabsheh SE and Deo SV had almost equal contributions in writing the manuscript; Obeidat YM and Haddad O had equal contribution in editing the manuscript; Rababa’h A reviewed the manuscript.

**Conflict-of-interest statement:** We do not have any relevant disclosure pertaining to this study.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Correspondence to: Salah Eldien Altarabsheh, MD, Consultant Cardiac Surgeon,** Division of Cardiovascular Surgery, Queen Alia Heart Institute, Queen Rania St., Amman 11953, Jordan. salah936@yahoo.com

**Telephone:** +962-77-7181844

**Fax: +**962-2-7201075

**Received:** June 25, 2018

**Peer-review started:** June 26, 2018

**First decision:** July 9, 2018

**Revised:** August 4, 2018

**Accepted:** August 6, 2018

**Article in press:**

**Published online:**

**Abstract**

Chronic ischemic mitral valve regurgitation is a result of disturbed left ventricular geometry secondary to myocardial ischemia in the absence of intrinsic mitral valve pathology. It is a common complication after myocardial infarction, and patients who have ischemic mitral regurgitation (IMR) carries poorer prognosis compared to patients who have ischemic heart disease alone, and this is directly related to the severity of IMR. Medical therapy had limited efficacy, and surgical options including various repair techniques and valve replacement had been tried with variable success. Still there is intense debate among surgeons whether to interfere with moderate degree IMR at the time of coronary artery revascularization.

**Key words:** Mitral regurgitation; Myocardial infarction; Ring annuloplasty; Valve replacement

**© The Author(s) 2018.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Chronic ischemic mitral valve regurgitation is a valvular dysfunction secondary to myocardial infarction. Debates among surgeons surrounding the decision intervene and the type of intervention among surgeons in moderate degree of ischemic regurgitation. A comprehensive approach addressing the whole pathology of myocardial ischemia and ventricular dysfunction may be of value.

Altarabsheh SE, Deo SV, Rababa’h A, Obeidat YM, Haddad O. Chronic ischemic mitral valve regurgitation, surgical perspectives. *World J Cardiol* 2018; In press

**INTRODUCTION**

Chronic ischemic mitral regurgitation (IMR) is a complication that is determined by the extent and severity of myocardial infarction besides others, like ventricular dissynchrony and afterload[[1](#_ENREF_1)]. In contrast to primary mitral valve regurgitation caused by structural valve abnormality in which there is an increasing agreement among surgeons for therapeutic options, IMR management options are still a matter of debate among clinicians[[2](#_ENREF_2)].

An increasing consensus among authors indicates that a severe form of IMR should be corrected, however surgical intervention with moderate forms of IMR at the time of coronary revascularization is still a matter of debate[[3](#_ENREF_3)]. There had been evolution in surgical techniques of mitral valve repair over the years, however the continuous left ventricular remodeling process resulting in recurrence of the valve incompetence remained a major drawback of this approach[[4](#_ENREF_4)]. Mitral valve replacement preserving the subvalvular apparatus demonstrated a more durable valve competence and comparable left ventricular reverse remodeling and survival at 2 year follow up period in comparison with mitral valve repair[[5](#_ENREF_5)].

**DEFINITION AND BURDEN OF ISCHEMIC MITRAL VALVE REGURGITATION**

IMR is defined classically as mitral valve regurgitation due to a previous myocardial infarction[[1](#_ENREF_1)]. Based on this definition, left ventricular remodeling consequences following myocardial infarction are not considered which integral parts leading to the development of IMR. So IMR is a complication of myocardial infarction due to structural left ventricular dysfunction, in the presence of normal intrinsic mitral valve structure[[6](#_ENREF_6)]. This definition takes in consideration both the history of myocardial infarction as well as the resulting left ventricular abnormalities together. IMR is not a mitral valve disease per say, but a consequence of the disturbed closing and tethering forces related to the papillary muscles mechanics as a result of left ventricular remodeling following myocardial infarction[[6](#_ENREF_6)]. Secondary to some other mitral valve pathologies may coexist with a previous history of myocardial infarction like rheumatic or myxomatous mitral valve disease, however these don’t indicate an ischemic mitral valve disease, so the description of the mitral valve regurgitation depends on the mitral valve structure and the left ventricular structural dysfunction. Carpentier classification in 1983 characterized the pathophysiology of IMR to either 1. Mitral leaflet motion restriction in systole, type IIIb or 2. Isolated mitral annular dilatation, type Ia[[7](#_ENREF_7)].

IMR is a significant clinical problem that affects 1.6-2.8 million population in the united states and it may happens in 10%-20% of patients with ischemic heart disease[[5](#_ENREF_5),[8](#_ENREF_8)]. With the new technologies implemented in the current era of coronary artery interventions and the aging population one can expect that the incidence of IMR will increase, which had been demonstrated to have a significant negative impact on patient survival and the development of heart failure[[9](#_ENREF_9)].

Grigioni *et al*[[9](#_ENREF_9)] demonstrated in a propensity matched study including 173 surviving patients with Q wave after myocardial infarction that the prevalence of adverse events had been linked directly to the presence and degree of IMR. When patients are matched in their base line characteristics, those who have severe degree of IMR (ERO > 20 mm), are six time more liable to have heart failure compared to patients without IMR regardless of the symptomatology status (RR 6.4, 95%CI: 2.9 to 14.3; *P* < 0.0001). So detecting and quantifying IMR are highly crucial in planning treatment strategy following myocardial infarction.

**CHOICE OF SURGICAL INTERVENTION IN SEVERE IMR, REPAIR *VS* REPLACEMENT**

There is an agreement among clinicians that severe degree of IMR should be surgically approached, however moderate degree of IMR still a matter of debate[[10](#_ENREF_10)].The evolution of surgical approaches had many changes over the past years. Initially mitral valve replacement with excision of the mitral valve apparatus was the choice since it restores the competency of the valve, drawback of this approach is the impaired left ventricular function and geometry due to excision of the subvalvular apparatus[[8](#_ENREF_8)]. Mitral valve repair using ring annuloplasty was tempting solution since it preserves the subvalvular apparatus and theoretically preserves the mitral valve competency. Proponents of this therapeutic modality take in consideration the unique shape of the mitral annular configuration in determining the mitral competence by decreasing the leaflet stress during systole[[11](#_ENREF_11)]. This approach does work for type I IMR however it incompletely corrects type IIIb dysfunction, so the ideal solution is to adopt a comprehensive approach that will take all the aspects of the disease in consideration. Physiological changes are asymmetric in the left ventricle geometry as well as the annulus, so new advances had been designed even in the ring technology to reshape the annulus taking in consideration the saddle pattern of the mitral annular configuration[[12](#_ENREF_12)].

Till now decision making amongst surgeons had been a subject of intense debate whether to replace or repair severe chronic ischemic mitral valve regurgitation or just to replace it. The tradeoff considered always between the durability of mitral valve repair in correcting a regurgitant valve *vs* an adverse consequences of prosthetic valve insertion. Data from 251 patients who have severe ischemic mitral valve regurgitation enrolled in the cardiothoracic surgical trials network published in 2015[[5](#_ENREF_5)], demonstrated comparable degree of left ventricular reverse remodeling between mitral valve repair and replacement at one year follow up, However, the rates of recurrent mitral valve regurgitation amongst the survivors of the repair cohort was 32.6% at one year and 46% at 2-year follow up[[5](#_ENREF_5)]. Other forms of surgical options addressing the left ventricular geometrical changes had been tried with variable success rates. Fattouch *et al*[[13](#_ENREF_13)] reported a durable mitral valve repair with less than 3% recurrence rate of moderate mitral valve regurgitation by adopting papillary muscle relocation, non-restrictive mitral annuloplasty and myocardial revascularization in 115 patients with severe form of IMR.

Evidence from a propensity matched, retrospective study including 1006 patients with severe ischemic mitral valve regurgitation by Lorusso *et al*[[14](#_ENREF_14)] demonstrated that there was comparable incidence of untoward outcomes between the repair and replacement matched groups in the short and long term follow up periods. However, mitral valve repair remained the strongest predictor for the need for mitral valve re-operation[[14](#_ENREF_14)].

**MODERATE DEGREE OF IMR AT THE TIME OF CORONARY ARTERY BYPASS GRAFT**

There is general agreement among clinicians that significant IMR should be addressed at the time of coronary artery bypass graft  (CABG), however the drawback of this approach is that a combined procedure may increase the risk of surgery on a sick heart and doing coronary revascularization alone may improve ventricular status. Whether to interfere with moderate IMR at the time of CABG is a real debate over the past years in the world of cardiology and cardiac surgery, and this had led to the conduction of 4 randomized controlled trials which are the only ones published till now addressing this subject[[3](#_ENREF_3),[15-17](#_ENREF_15)].

Fattouch *et al*[[3](#_ENREF_3)] in their randomized trial in 2009 that included 102 patients concluded that a mitral valve intervention for significant functional mitral valve regurgitation at the time of CABG may improve the degree of functional mitral regurgitation, the New York Heart association functional class and left ventricular ejection fraction.

The randomized trial by Chan *et al*[[16](#_ENREF_16)] which included 70 patients in 2012, were also in agreement with Fattouch conclusions, and they demonstrated that there was an improvement in the degree of functional mitral regurgitation, reverse left ventricular remodeling and functional capacity when mitral valve repair was added to coronary artery revascularization in the presence of moderate degree of IMR.

A more recent conducted trial by Bouchard *et al*[[15](#_ENREF_15)] in 2014, demonstrated that there were no obvious clinical benefit of adding mitral valve intervention at the time of CABG after one year follow up, despite the tempting value early in the post-operative period, however the major drawback of this trial is that it included only 31 patients in both cohorts.

Smith *et al*[[17](#_ENREF_17)] again in 2014 published the largest trial which included 301 patients and demonstrated that there was some degree in the improvement of the mitral valve grade in association with mitral valve repair at the time of CABG, however the incidence of untoward events was increased.

Evidence from observational studies also had been a matter of argument since long time ago, Aklog *et al*[[18](#_ENREF_18)] demonstrated that there was clear superiority in performing mitral valve repair for moderate degree of IMR at the time of CABG compared to revascularization alone in correcting mitral valve incompetence in 136 patients.

Kang *et al*[[19](#_ENREF_19)] demonstrated in their study that included 107 patients that the addition of mitral valve intervention may increase operative mortality compared to patients who have CABG alone.

With these conflicting results in the randomized controlled trials addressing this issue, Altarabsheh *et al*[[20](#_ENREF_19)] published a systemic review and meta-analysis in 2017 that included the four randomized trials and seven relevant observational studies with a total of 1447 patients, and demonstrated clearly that the addition of mitral valve repair for moderate IMR at the time of CABG did not have survival or functional improvement at 5 year follow up period despite the fact that it may improve the degree of mitral valve competence.

**CONCLUSION**

IMR remains a real significant complication of myocardial infarction and continued to have therapeutic challenges. Complex mechanisms involving mitral annulus and subvalvular apparatus play a role, and ideal surgical repair should take the whole pathology in consideration. Future repair techniques which address disturbed left ventricular mechanics may be of value, and currently mitral valve replacement preserving the subvalvular apparatus is a valid surgical option. Moderate IMR could be addressed by coronary revascularization alone at the time of CABG.

**REFERENCES**

1 **Nappi F**, Spadaccio C, Chello M, Mihos CG. Papillary muscle approximation in mitral valve repair for secondary MR. *J Thorac Dis* 2017; **9**: S635-S639 [PMID: 28740718 DOI: 10.21037/jtd.2017.06.98]

2 **Tolis G Jr**, Sundt TM 3rd. Surgical Strategies for Management of Mitral Regurgitation: Recent Evidence from Randomized Controlled Trials. *Curr Atheroscler Rep* 2015; **17**: 67 [PMID: 26486511 DOI: 10.1007/s11883-015-0549-y]

3 **Fattouch K**, Guccione F, Sampognaro R, Panzarella G, Corrado E, Navarra E, Calvaruso D, Ruvolo G. POINT: Efficacy of adding mitral valve restrictive annuloplasty to coronary artery bypass grafting in patients with moderate ischemic mitral valve regurgitation: a randomized trial. *J Thorac Cardiovasc Surg* 2009; **138**: 278-285 [PMID: 19619766 DOI: 10.1016/j.jtcvs.2008.11.010]

4 **Hung J**, Papakostas L, Tahta SA, Hardy BG, Bollen BA, Duran CM, Levine RA. Mechanism of recurrent ischemic mitral regurgitation after annuloplasty: continued LV remodeling as a moving target. *Circulation* 2004; **110**: II85-II90 [PMID: 15364844 DOI: 10.1161/01.CIR.0000138192.65015.45]

5 **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; **370**: 23-32 [PMID: 24245543 DOI: 10.1056/NEJMoa1312808]

6 **Varma PK**, Krishna N, Jose RL, Madkaiker AN. Ischemic mitral regurgitation. *Ann Card Anaesth* 2017; **20**: 432-439 [PMID: 28994679 DOI: 10.4103/aca.ACA\_58\_17]

7 **Carpentier A**. Cardiac valve surgery--the "French correction". *J Thorac Cardiovasc Surg* 1983; **86**: 323-337 [PMID: 6887954]

8 **Boyd JH**. Ischemic mitral regurgitation. *Circ J* 2013; **77**: 1952-1956 [PMID: 23877709 DOI: 10.1253/circj.CJ-13-0743]

9 **Grigioni F**, Detaint D, Avierinos JF, Scott C, Tajik J, Enriquez-Sarano M. Contribution of ischemic mitral regurgitation to congestive heart failure after myocardial infarction. *J Am Coll Cardiol* 2005; **45**: 260-267 [PMID: 15653025 DOI: 10.1016/j.jacc.2004.10.030]

10 **Fattouch K**, Castrovinci S, Murana G, Moscarelli M, Speziale G. Surgical management of moderate ischemic mitral valve regurgitation: Where do we stand? *World J Cardiol* 2014; **6**: 1218-1222 [PMID: 25429333 DOI: 10.4330/wjc.v6.i11.1218]

11 **Grewal J**, Suri R, Mankad S, Tanaka A, Mahoney DW, Schaff HV, Miller FA, Enriquez-Sarano M. Mitral annular dynamics in myxomatous valve disease: new insights with real-time 3-dimensional echocardiography. *Circulation* 2010; **121**: 1423-1431 [PMID: 20231533 DOI: 10.1161/CIRCULATIONAHA.109.901181]

12 **Daimon M**, Fukuda S, Adams DH, McCarthy PM, Gillinov AM, Carpentier A, Filsoufi F, Abascal VM, Rigolin VH, Salzberg S, Huskin A, Langenfeld M, Shiota T. Mitral valve repair with Carpentier-McCarthy-Adams IMR ETlogix annuloplasty ring for ischemic mitral regurgitation: early echocardiographic results from a multi-center study. *Circulation* 2006; **114**: I588-I593 [PMID: 16820643 DOI: 10.1161/CIRCULATIONAHA.105.001347]

13 **Fattouch K**, Castrovinci S, Murana G, Dioguardi P, Guccione F, Nasso G, Speziale G. Papillary muscle relocation and mitral annuloplasty in ischemic mitral valve regurgitation: midterm results. *J Thorac Cardiovasc Surg* 2014; **148**: 1947-1950 [PMID: 24656671 DOI: 10.1016/j.jtcvs.2014.02.047]

14 **Lorusso R**, Gelsomino S, Vizzardi E, D'Aloia A, De Cicco G, Lucà F, Parise O, Gensini GF, Stefàno P, Livi U, Vendramin I, Pacini D, Di Bartolomeo R, Miceli A, Varone E, Glauber M, Parolari A, Giuseppe Arlati F, Alamanni F, Serraino F, Renzulli A, Messina A, Troise G, Mariscalco G, Cottini M, Beghi C, Nicolini F, Gherli T, Borghetti V, Pardini A, Caimmi PP, Micalizzi E, Fino C, Ferrazzi P, Di Mauro M, Calafiore AM; ISTIMIR Investigators. Mitral valve repair or replacement for ischemic mitral regurgitation? The Italian Study on the Treatment of Ischemic Mitral Regurgitation (ISTIMIR). *J Thorac Cardiovasc Surg* 2013; **145**: 128-139; discussion 137-138 [PMID: 23127376 DOI: 10.1016/j.jtcvs.2012.09.042]

15 **Bouchard D**, Jensen H, Carrier M, Demers P, Pellerin M, Perrault LP, Lambert J. Effect of systematic downsizing rigid ring annuloplasty in patients with moderate ischemic mitral regurgitation. *J Thorac Cardiovasc Surg* 2014; **147**: 1471-1477 [PMID: 23856201 DOI: 10.1016/j.jtcvs.2013.05.024]

16 **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; **126**: 2502-2510 [PMID: 23136163 DOI: 10.1161/CIRCULATIONAHA.112.143818]

17 **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; **371**: 2178-2188 [PMID: 25405390 DOI: 10.1056/NEJMoa1410490]

18 **Aklog L**, Filsoufi F, Flores KQ, Chen RH, Cohn LH, Nathan NS, Byrne JG, Adams DH. Does coronary artery bypass grafting alone correct moderate ischemic mitral regurgitation? *Circulation* 2001; **104**: I68-I75 [PMID: 11568033 DOI: 10.1161/hc37t1.094706]

19 **Kang DH**, Kim MJ, Kang SJ, Song JM, Song H, Hong MK, Choi KJ, Song JK, Lee JW. Mitral valve repair versus revascularization alone in the treatment of ischemic mitral regurgitation. *Circulation* 2006; **114**: I499-I503 [PMID: 16820626 DOI: 10.1161/CIRCULATIONAHA.105.000398]

20 **Altarabsheh SE**, Deo SV, Dunlay SM, Erwin PJ, Obeidat YM, Navale S, Markowitz AH, Park SJ. Meta-Analysis of Usefulness of Concomitant Mitral Valve Repair or Replacement for Moderate Ischemic Mitral Regurgitation With Coronary Artery Bypass Grafting. *Am J Cardiol* 2017; **119**: 734-741 [PMID: 28109559 DOI: 10.1016/j.amjcard.2016.11.024]

**P-Reviewer:** Li S, Ueda H, Said SAM **S-Editor:** Ji FF **L-Editor: E-Editor:**

**Specialty type:** Cardiac and cardiovascular systems

**Country of origin:** Jordan

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): 0

Grade D (Fair): D

Grade E (Poor): 0