

# Are adjunct subvalvular techniques more effective than isolated restrictive annuloplasty for treating ischemic mitral regurgitation?

Leonidas V. Athanasopoulos,<sup>1</sup> Marco Moscarelli,<sup>2</sup>  
Giuseppe Speziale,<sup>2</sup> Prakash P. Punjabi<sup>1</sup>  
and Thanos Athanasiou<sup>1</sup>

## Abstract

This review focused on whether subvalvular techniques are more effective than isolated restrictive annuloplasty in addressing ischemic mitral regurgitation (MR). Searching identified 445 papers and, following a selection process, we ended up with 10 articles. Two were propensity-matched studies, four retrospective and four prospective, non-randomized studies. The end points of interest were late recurrence of MR, other early echocardiographic outcomes of mitral function and early mortality. All studies focusing on echocardiographic measurements showed improved results in the groups where subvalvular repair techniques were used. In almost all studies, the recurrence of MR postoperatively was less when subvalvular techniques were used. No difference in early or in-hospital mortality was demonstrated in all four studies that included comparisons. We conclude that subvalvular techniques in combination with annuloplasty are safe and may better address ischemic MR than the use of annuloplasty ring alone.

## Keywords

mitral valve; ischemic mitral regurgitation; subvalvular; repair; papillary muscle

## Introduction

Ischemic MR is caused by global or localized left ventricular remodelling related to chronic coronary artery disease rather than pure valvular disease. Apart from decreased closing forces of the mitral valve due to ventricular systolic dysfunction and mitral annular dilatation, mitral valve tethering caused by left ventricular remodeling and subsequent papillary muscle displacement is the predominant cause of ischemic MR. Reduction annuloplasty by undersizing the mitral annulus 1–2 sizes has been the standard procedure for years. However, a recurrence of moderate-to-severe mitral regurgitation in 9–30% of patients within 6 months of repair has been noted,<sup>1,2</sup> which prompted the development of new techniques focusing on the subvalvular apparatus rather than the annulus and on how to improve on the predominant cause, the mitral valve tethering. We reviewed the literature to provide evidence on whether the use of adjunct subvalvular techniques are more effective than isolated restrictive annuloplasty.

## Methods

A literature review was performed from January 2000 to April 2016 with the use of PubMed database. The terms for search were: [ischemic mitral regurgitation] OR [approximation] OR [relocation] OR [chordal] AND [papillary muscle]. Studies identified in the references of these articles were also screened for suitability of inclusion. Figure 1 presents the flow chart of the selection process. Although this review focuses on comparisons of outcomes following annuloplasty vs. subvalvular techniques ± annuloplasty, we included studies with the absence of a control group when they

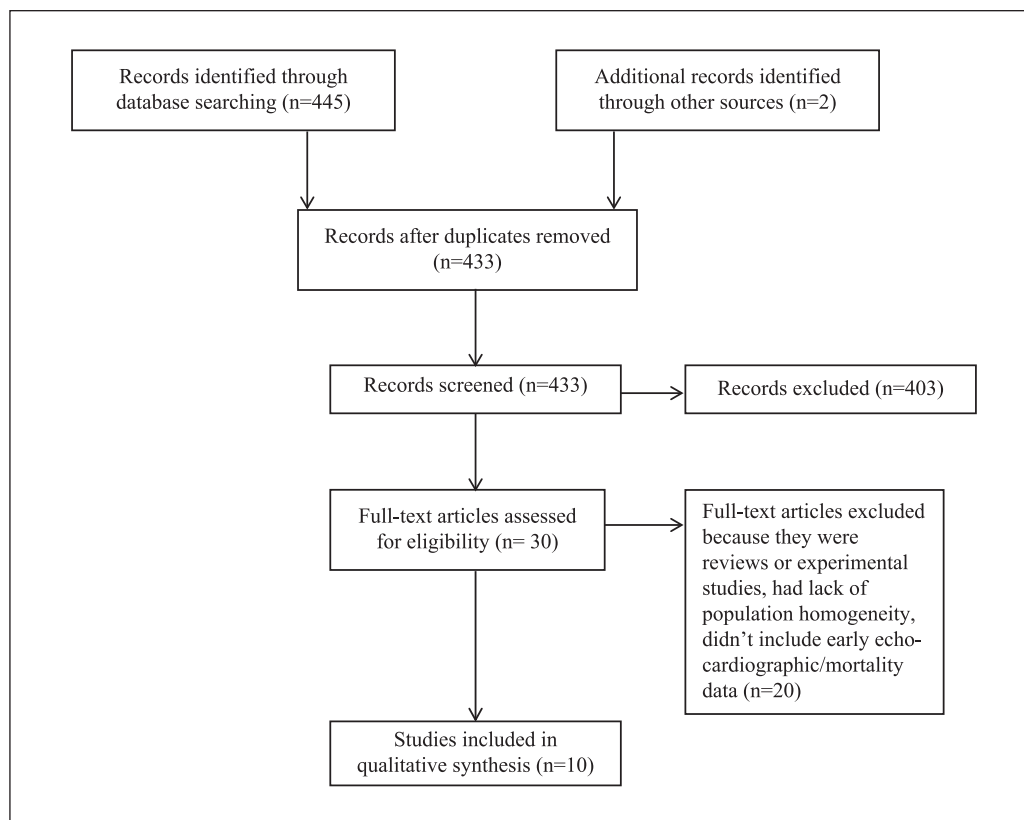
<sup>1</sup>Department of Cardiothoracic Surgery, Imperial College Healthcare NHS Trust, Hammersmith Hospital, London, UK

<sup>2</sup>Cardiac Surgery Department, Anthea Hospital, GVM Hospitals of Care and Research, Bari, Italy

### Corresponding author:

LV Athanasopoulos, 23 Ypsilantou Street, Kolonaki, Athens, 106 75, Greece.

Email: athanleon@hotmail.com



**Figure 1.** Flow chart depicting the selection of studies included in the review.

represented the only available literature evidence on the described technique.

## Results

Four hundred and forty-five articles were identified of which ten provided the best evidence, focusing mainly on the recurrence of mitral regurgitation (MR), early echocardiographic outcomes of mitral function and mortality. A summary of the findings is presented in Table 1. Almost all the studies concluded that a repair of the subvalvular apparatus in conjunction with an annuloplasty of the mitral valve had improved early echocardiographic outcomes and rates of MR recurrence. However, no difference in mortality was identified between patients who had a subvalvular repair or not.

Borger et al.<sup>3</sup> compared echocardiographic data in patients who had secondary chords cutting plus an annuloplasty and those undergoing an isolated conventional restrictive mitral annuloplasty. Measurements from intraoperative transesophageal echocardiogram demonstrated a more significant decrease in tenting area as well as increased reduction in the distance between the free edge of the anterior mitral valve leaflet and the posterior left ventricular wall in the chord-cutting group. No difference was noted in the postoperative

change of mitral annulus and tenting height as well as in the in-hospital mortality between the groups. However, patients in the chordal-cutting group had lower rates of recurrent MR.

Langer et al.<sup>4</sup> studied a matched group of 30 patients with severe leaflet tethering. Each group underwent a restrictive mitral annuloplasty plus an adjunctive papillary muscle repositioning with a transventricular suture (RING+STRING) or an isolated mitral annuloplasty (RING). Intraoperative echocardiogram demonstrated a decrease in tenting height and area. The distance between the posterior papillary muscle and the aorto-mitral continuity was also reduced. Recurrent MR>2+ was observed in six of the patients of the RING group and in only one in the RING+STRING group.

Hvass et al.<sup>5</sup> studied 37 patients who underwent an intraventricular peripapillary muscle sling completed by a mitral annuloplasty ring. The annuloplasty was normal or undersized. Early residual MR was none-to-trivial in 31 and mild in two of the patients. Ninety-five percent of the patients survived the postoperative period.

Fattouch et al.<sup>6</sup> matched two groups of 55 patients with severe MR with the use of propensity scoring analysis. One group had undergone papillary muscle relocation (PMR) in conjunction with normal-size mitral annuloplasty and

**Table 1.** Subvalvular Techniques.

Study	Patient group(s)	Outcomes	Key Results	Comments
Borger et al. (2007) J Thorac Cardiovasc Surg <sup>3</sup>	CC + RA = 43 RA = 49	Recurrent MR/ Early Mortality/Early Echocardiographic	Postop 4 patients had recurrent MR in the RA group and only 1 in the CC + RA group. No difference in in-hospital mortality (9% vs. 10%, p=0.9). Greater reduction in tenting area (53±3% vs 41±3%; p=0.01) and in the distance AMVL-posterior LV (24±3 vs. 11±4; p=0.01) in the CC + RA group.	Flexible, incomplete annuloplasty band/moderate undersizing used in both groups. Measurements taken at intraoperative transesophageal echocardiographic study. Limitations: Retrospective, non-randomized study, patients in the chordal-cutting group had a higher prevalence of recent MI
Langer et al. (2009) Circulation <sup>4</sup>	RING + STRING = 30 RING = 30	Recurrent MR/Early Echocardiographic	Recurrent MR>2+ was observed as early as 2 to 4 weeks after surgery in 6 patients of the RING group and only in 1 patient in the RING + STRING group. Ischemic MR improved in both groups. The tenting height (from 14±2 mm to 6±1 mm) and area (from 3.9±0.9 cm <sup>2</sup> to 1.0±0.2 cm <sup>2</sup> ) and the distance between the PPM and the aorto-mitral continuity reduced (from 44±4 mm to 37±3 mm) in the RING+STRING group.	Restrictive annuloplasty was performed in all patients. Measurements taken at intraoperative echocardiographic study. Limitations: Prospective, non-randomized study, use of semi-quantitative grading of MR severity
Hvass et al. (2010) J Thorac Cardiovasc Surg <sup>5</sup>	PMS + AR = 37	Residual MR/Early mortality	Early freedom from MR>1+; 94%. In-hospital mortality: 5%	The annuloplasty was normal or undersized. Limitations: small sample size, no control group
Fattouch et al. (2012) J Thorac Cardiovasc Surg <sup>6</sup>	PMR + AR = 55 RA = 55	Recurrent MR/ Early Mortality	Recurrent MR>2+ was observed in 3.7% of the PMR + AR group vs. 11.5% of the RA group; p=0.02. No difference in in-hospital mortality (3.6% vs. 5.4%; p=0.72)	In the PMR group, normal ring size was used. No early echocardiographic data reported. Limitations: small sample size
Manabe et al. (2012) Thorac Cardiovasc Surg <sup>7</sup>	PMA + RA = 14 RA = 13	Early Echocardiographic	No residual MR found in any of patients. In both groups, tethering angle of AMVL didn't change. Tethering angle of PMVL increased in both groups and the increase was lower in the PMA group.	Restrictive annuloplasty performed in all patients. Measurements taken 1 week postop. Limitations: small sample size, non-randomized study, selection bias might have affected results due to surgeon's preference, left ventriculoplasty was performed in 12 patients, possibly affecting results.
Cappabianca et al. (2013) Ann Thorac Surg <sup>8</sup>	CT + PPMR + AR = 49	Early mortality	In-hospital mortality: 2%, 6-week mortality: 2%	True-sized annuloplasty ring was used. Limitations: small sample size, retrospective study, no control group.
Wakasa et al. (2015) Ann Thorac Cardiovasc Surg <sup>9</sup>	RA = 30 PMA + AR = 26 PMA + AR + VP = 34	Recurrent of MR/ Early mortality	The hospital mortality rates did not significantly differ among the groups. Freedom from recurrence of MR didn't differ between the groups.	Restrictive annuloplasty performed in RA group and true-sized ring was used in the 2 other groups Limitations: Retrospective, non-randomized study, small sample size
Calaffiore et al. (2014) J Thorac Cardiovasc Surg <sup>10</sup>	CC + RA = 26 RA = 26	Residual MR/Early mortality	Residual MR was significantly lower in the CC + RA group than in the RA group (0.6±0.6 vs. 1.1±0.8, p=0.014) No early mortality occurred among the patients in the CC group.	A band was used in the CC group and a ring in the non-CC group. Limitations: small sample size, non-randomized study, a band was used in the CC group which provides suboptimal results compared to a ring.
Mandegar et al. (2011) Eur J Cardiothor-ac Surg <sup>11</sup>	PMA + AR + Dor = 15 AR + Dor = 15	Residual MR/Early Echocardiographic	MR decreased more in the PMA group (p=0.001). LVEF increased more in the PMA group (p=0.048). No difference in decrease in LVESV (p=0.12) and LVEDV (p=0.17) between the groups. More significant decrease in concavity area of the anterior leaflet in PMA group. Decrease in systolic and diastolic sphericity index was significant only in the PMA group.	Pericardial ring annuloplasty performed. Limitations: small sample size, no control group
Yamaguchi et al. (2013) Circ J <sup>12</sup>	RA = 14 RA + PMA + PMSU + SVR = 8	Recurrent MR/Early Mortality/ Early Echocardiographic	No 30-day in-hospital mortality. One month after surgery, residual moderate MR was not detected in either group. PMA group had lower LV volumes post-op. Posterior displacement of coaptation and coaptation depth decreased in both groups. In the PMA group, ALA and PLA were greater pre-op when compared to RA group, but decreased more to become less 1 year post-op.	Rigid ring annuloplasty used. Limitations: small sample size, non-randomized study

ALA: anterior mitral leaflet tethering angle; AMVL: anterior mitral valve leaflet; AR: annuloplasty ring; CC: chordal cutting; CT: cut and transfer; Dor: Dor procedure; LV: left ventricle; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricular ejection fraction; LVESV: left ventricular end-systolic volume; MR: mitral regurgitation; PMA: posterior mitral leaflet tethering angle; PMS: papillary muscle approximation; PMSU: papillary muscle sling; PMSU: papillary muscle suspension; PMVL: posterior mitral valve leaflet; PPMR: posterior papillary muscle; PPMR: posterior papillary muscle relocation; RA: restrictive annuloplasty; SVR: surgical ventricular restoration; VP: ventriculoplasty.

the other only a restrictive mitral annuloplasty (RA). No difference was identified in the in-hospital mortality between the groups. Two (3.6%) and three (5.4%) patients died in the PMR group and the isolated RA group, respectively. Recurrent MR rates were less in the PMR group.

Manabe et al.<sup>7</sup> compared patients who had papillary muscle approximation (PMA) and restrictive annuloplasty to those who had isolated annuloplasty. No residual MR was identified one week post-op for any of the patients. In both groups, the tethering angle of the anterior leaflet didn't change. The tethering angle of the posterior leaflet increased in both groups and the increase was lower in the PMA group. As the tethering angle is attenuated, but not completely eliminated, the authors conclude that PMA may not have a strong effect on mitral valve configuration.

Coppabianca et al.<sup>8</sup> investigated 49 patients who had coronary surgery plus mitral valve repair using the cut-and-transfer and posterior papillary muscle relocation techniques. All the patients received a true-size, semi-rigid, complete annuloplasty ring. The in-hospital mortality was 2% and all discharged patients were alive at six weeks.

Wakasa et al.<sup>9</sup> studied 90 patients who underwent a mitral valve repair. Thirty patients had a restrictive annuloplasty and 60 had a PMA along with a true-sized ring implanted. From these 60 patients, 34 also underwent a left ventriculoplasty. Thus, three different groups were created, as shown in Table 1. Hospital mortality rates did not significantly differ among the groups ( $p=0.9$ ). Freedom from recurrence of MR also didn't differ among them ( $p=0.58$ ).

Calafiore et al.<sup>10</sup> compared patients who underwent chordal cutting and a restrictive annuloplasty to those who had an isolated restrictive annuloplasty. A band was used in the former group and a ring in the latter one. The postoperative residual MR was significantly lower in the chordal-cutting group and no early mortality occurred in this group.

Mandegar et al.<sup>11</sup> studied 30 patients who underwent a true annuloplasty ring along with a Dor procedure to reconstruct the left ventricle. In half of these patients a PMA was also performed. The group who had a PMA showed greater decrease in MR and increase in left ventricular ejection fraction when compared to the other group. No difference was shown in the postoperative changes of left ventricular volumes between the groups. However, the concavity area of the anterior leaflet decreased more significantly in the PMA group and the systolic and diastolic sphericity index decreased significant only in this group.

Yamaguchi et al.<sup>12</sup> investigated 22 patients with severe ischemic MR who had a restrictive annuloplasty. In eight of them, a PMA, a papillary muscle suspension and a surgical ventricular restoration were also performed. In the whole series, there was no 30-day in-hospital mortality. Patients who had PMA had lower LV volumes

post-op. Posterior displacement of coaptation and coaptation depth decreased in both groups. It is important to note that, although the PMA group started with greater anterior and posterior mitral leaflet tethering angles, these decreased more in this group to become less one year post-op when compared to the other group.

## Discussion

Current guidelines support a mitral valve operation in patients with severe ischemic MR who undergo coronary artery bypass graft (CABG) surgery.<sup>13</sup> In a recent study comparing patients with moderate ischemic MR who either had a CABG alone or a combined CABG and a mitral valve repair, no difference was found in overall survival, hospital re-admissions or adverse events.<sup>14</sup> The two-year moderate or severe residual MR was higher in the CABG alone group. Furthermore, in the current literature, a controversy exists as to whether a mitral valve repair or a replacement is more beneficial. A few studies report no significant difference in postoperative survival between mitral valve repair and replacement,<sup>15-17</sup> but others have concluded that a mitral valve repair is preferable to replacement in terms of postoperative survival.<sup>18,19</sup> Acker et al.,<sup>20</sup> in the first prospective, randomized trial, again identified no difference in survival between patients undergoing a repair or replacement. However, a big difference was shown in 12-month residual MR (32.6% in the repair group vs. 2.3% in the replacement group). This observation can be explained by focusing on the subvalvular apparatus and, more specifically, on the effects of left ventricular dilatation, tethering of mitral leaflets and papillary muscle displacement toward the apex on overall valve competence.

There has been a previous meta-analysis<sup>21</sup> and a best evidence topic review<sup>22</sup> by Mihos et al. on the same topic and both have also demonstrated the supremacy of the subvalvular techniques in dealing with ischemic MR. We supplement our review by including additional papers and presenting the full gamut of available techniques for repair of the subvalvular apparatus. For homogeneity reasons, we have excluded studies which presented data from mixed populations.<sup>23,24</sup> As is evident from a review of the current literature, the subvalvular techniques deal with greater efficiency on this pathology than a simple annuloplasty.

The selection of the most suitable technique will be based on individual pathology characteristics. It is pivotal to have a detailed echocardiographic assessment preoperatively, which will aid in the selection process. A PMA or a RING + STRING technique will address an increased interpapillary muscle distance as well as an elevated tenting height whilst PMR will be helpful only on an elevated tenting area or coaptation depth based on the reported data.<sup>4,6</sup> Chordal cutting, on the other hand, will mobilize a restricted anterior leaflet and decrease the

tenting area and, finally, the cut-and-transfer technique will have an effect on decreasing the coaptation depth.<sup>3,8</sup>

## Conclusion

The various subvalvular techniques for addressing ischemic MR are safe as shown by the low mortality rates and the improved echocardiographic outcomes. Thus, it is important that they should be evaluated in larger studies to clarify their use in daily practice.

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