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Long-term Outcomes of Mitral Valve Repair Versus Replacement for Degenerative Disease: A Systematic Review

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Abstract: The short-term advantage of mitral valve repair versus replacement for degenerative disease has been extensively documented. These advantages include lower operative mortality, improved survival, better preservation of left-ventricular function, shorter post-operative hospital stay, lower total costs, and fewer valve-related complications, including thromboembolism, anticoagulation-related bleeding events and late prosthetic dysfunction. More recent written data are available indicating the long-term advantage of repair versus replacement. While at some institutions, the repair rate for degenerative disease may exceed 90%, the national average in 2007 was only 69%. Making direct comparisons between mitral valve repair and replacement using the available studies does present some challenges however, as there are often differences in baseline characteristics between patient groups as well as other dissimilarities between studies. The purpose of this review is to systematically summarize the long-term survival and reoperation data of mitral valve repair versus replacement for degenerative disease. A PubMed search was done and resulted in 12 studies that met our study criteria for comparing mitral valve repair versus replacement for degenerative disease. A systematic review was then conducted abstracting survival and reoperation data.

Keywords: Degenerative mitral valve disease, long-term survival mitral valve repair, mitral valve replacement, myxomatous degeneration.

INTRODUCTION

Degenerative disease is the most common etiology of mitral regurgitation in Western countries, affecting around 2% of the population [1, 2]. Degenerative mitral valve disease is characterized by morphological changes in the connective tissue of the valve resulting in abnormal valve function. This disease spans a range of presentations from isolated prolapse of a single leaflet scallop –most often P2- to bileaflet prolapse with excessive leaflet tissue and annular dilation [3, 4]. These changes appear to be mediated through glycosylaminoglycan and other extracellular matrix alterations that, over time, result in a weaker connective tissue and subsequent valve dysfunction [5].

In recent years, mitral valve repair has become the procedure of choice for treating isolated mitral regurgitation and this trend continues to increase with time. While the repair rate for isolated mitral valve disease increased from 51% to 69% from 2000 to 2007, this rate is still much lower than the 90% or higher rate that some institutions achieve, with higher volume centers tending to achieve better repair rates [6-8]. Additionally, the repair rate has remained much lower among the elderly than their younger counterparts [9]. Mitral valve repair techniques are improving over time, leading to more durable and better functioning repairs [10-12]. The advantages of mitral valve repair include lower operative mortality, improved survival, better preservation of left-ventricular function, shorter post-operative hospital stay, lower total costs, and fewer valve-related complications, including thromboembolism, anticoagulation-related bleeding events and late prosthetic dysfunction. Earlier literature has established the superiority in short-term outcomes of mitral valve repair [13-17]. More recently, single institutional studies have focused on the long-term survival of mitral valve repair versus replacement. Compared to other etiologies of mitral regurgitation, degenerative disease is the most amenable to repair and has the best survival with post-operative longevity that is equal to the general population in appropriately referred patients. Accordingly, patients with degenerative disease stand the most to gain by receiving optimal surgical therapy [18]. The purpose of this review is to systemically summarize the survival and reoperation data available for repair versus replacement in degenerative mitral valve disease.

MATERIALS AND METHODS:

A systematic review of English articles on human trials from 1990 to March 2014 was done on PubMed using the search terms "mitral valve repair versus replacement." Additionally, relevant literature from the references section of the above studies was used. Studies that were included had to 1) have a direct comparison between mitral valve repair and replacement, 2) mitral regurgitation had to be stated as due to degenerative disease or be due to prolapse not caused by ischemic disease, rheumatic fever, or endocarditis and 3) include long-term (>1yr) survival outcomes. Using our search terms, a total of 190 articles were retrieved. 178 did not meet the inclusion criteria and were therefore excluded. 12 studies qualified for our study and were reviewed in de-

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tail. 9 of these studies compared primary mitral valve repair versus replacement and 3 were comparing re-repair versus replacement after a primary mitral valve repair. This review represents a contemporary analysis of the current long-term survival and reoperation data.

OUTCOMES

Key preoperative characteristics are listed in Table **1**. The most significant difference in baseline characteristics between the repair and replacement groups was their NYHA (New York Heart Association) classification. In 6 out of the 12 studies in our review, the MVP group had significantly better NYHA classification. In 3 of 12 studies, the MVP (mitral valve repair) group was also younger and had a higher percentage of male patients. Most of the baseline characteristics were better for the MVP group in Gillinov *et al*. 2008. Other differences in characteristics between the two groups, in general, did not reach statistical significance. The difference in baseline characteristics between repair and replacement groups is a challenging aspect of comparing outcomes between the two procedures. Better preoperative NYHA classification and ejection fraction have been shown to be very strong predictors of survival. In the majority of the studies, ejection fraction was not significantly different, however NYHA status was better in half of the studies in the MVP group [19-22]. Additionally, age and female gender have also been shown to be poor predictors of post-operative outcomes including survival [23-27]. All studies performed risk adjustment to account for these differences, with all but one using multivariable analysis.

Table 1. Preoperative patient characteristics.

Study	# subjects		Mean age		Male (%)		Diabetes (%)		Renal failure (%)		NYHA III/IV (%)		A fib (%)		Mean EF (%)		Conc. CABG (%)	
	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR
Daneshmand *et al*. 2009	705	284	60.9*	65.3	53.9	48.2	10.6	10.9	3.4	3.5	52.2	52.8	11.4*‡	7‡	50.8*	53.5	24.4	32
Gillinov *et al*. 2008	3051	235	57*	70	68*	51	1.5*	3.9	NA	NA	14*	29	16*	33	58*	56	NA	NA
Lee *et al*. 1997	167	22 SVP, 89 no SVP	66	63.4 SVP, 65.1 no SVP	68.3*	63.6 SVP, 52.8 no SVP	-	-	-	-	71.9	81.8 SVP, 60.2 no SVP	51.5	68.2 SVP, 60.2 no SVP	-	-	-	-
Mohty *et al*. 2001	679	238	64	66	69	65	5.3	6.7	-	-	44.5*	69.5	38.6*	51.8	62	62	27.4	26
Suri *et al*. 2006	1173	238		64	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Zhou *et al*. 2010	241	78	67.3	69.8	51	57.7	10.8	7.7	6.6	11.5	28.6*	47.4	24.9	23.1	-	-	13.7	19.2
Gillinov *et al*. 2003	447	223	67	67	75	69	10	14	2	3	35*	44	21	25	-	-	100	100
Chikwe *et al*. 2011	105	34	83	83	47	56	11	24	7*	24					58	55	36*	62
Gog-bashian *et al*. 2006 ∞	147/71	36/38	75/77	77/78	51/68	42/55	5/13	6/13	4/13	6/26	62/75	61/79	44/27	56/28	57/56*	58/51		
Zegdi *et al*. 2008 †	21	22	55	66	71	77	-	-	-	-	24	45	5	32	71	67	-	-
Dumont *et al*. 2007 †	68	120	57*	63	73*	57	-	-	-	-	12*	33	12*	31	53	50	-	-
Suri *et al*. 2006 †	64	81	64	67	77	65	-	-	-	-	44*	51	11	12	57	56	-	-

* $p < .05$ compared to MVR

∞ In sets with two numbers separated by a "/" first number is without performance of concomitant CABG, second is with CABG

† all data based on reoperation after primary mitral valve surgery

‡ any preoperative arrhythmia

SVP = subvalvular preservation

SHORT-TERM SURVIVAL AFTER PRIMARY MITRAL VALVE SURGERY

Operative mortality was used for short-term survival when available and 30-day mortality was used otherwise. In all of the eight studies that reported short-term data, survival was improved with MVP compared to MVR (mitral valve replacement); this difference reached statistical significance in four studies. These results are available in Table **2**. In Gogbashian *et al.,* there was a survival advantage in patients undergoing isolated mitral valve surgery, but this wasn't evident in patients receiving concomitant CABG [28]. Because the short-term survival advantage of repair has been evaluated in numerous studies and was not the major focus of our review, this data is included only for completeness.

LONG-TERM SURVIVAL AFTER PRIMARY MITRAL VALVE OPERATION

The most popular method for reporting long-term survival was in 5,10, and-15 year survival rates. These data were used when available. When these weren't available, the published survival rates at the given intervals were used. These rates are available in Table **2**. All studies showed improved long-term survival for MVP compared to MVR. After adjusting for baseline characteristics, which were in general worse for the MVR groups, the survival advantage was still statistically significant in all studies except in Gillinov *et al.*2008. In Gillinov 2008, they adjusted for baseline differences by creating 195 propensity-matched patients for repair from the 235 patients receiving replacements. Survival was similar (P=.8) between these two groups [29]. In Gogbashian *et al.,* mitral valve repair

Table 2. Survival and operative mortality data.

Study	Short-term Operative Mortality		1yr		5 yrs		6 yrs		7 yrs		10 yrs		12 yrs		15 yrs	
	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR	MVP	MVR
Daneshmand *et al*. 2009	2.3%	3.5%	-	-	-	-	-	-	-	-	-	-	-	-	Adjusted survival was 7.3% better*	
Gillinov *et al*. 2008	0.6%*	2.1%	-	-	95*	80	-	-	-	-	87*	64	-	-	68*	44
Lee *et al.* 1997	1.2%	0% SVP, 4.5% no SVP	-	-	-	-	67.8	63.3 no SVP, 80.8 SVP	-	-	-	-	-	-	-	-
Mohty *et al*. 2001	-	-	-	-	86*	71	-	-	-	-	68*	49	-	-	37*	29
Suri *et al*. 2006	0.7%*	5.6%	-	-	88.7*	74.6	-	-	-	-	70.6*	52.5	-	-	41.5*	29.3
Zhou *et al*. 2010	2.5%*	9%	94*	80.4	84.4*	64.6	-	-	-	-	-	-	-	-	-	-
Gillinov *et al*. 2003	4.0%	6.4%	92	88	79*	70	-	-	-	-	59*	37	-	-	-	-
Chikwe *et al*. 2011			71*	56												
Gogbashian *et al*. 2006 ∞	0.7*/1.4%	13.9/5.3%	95*/89	81/89	81*	63					48	50				
Zegdi *et al*. 2008 †	0%	5.0%	-	-	-	-	-	-	95*	69	-	-	-	-	-	-
Dumont *et al*. 2007 †	0%*	6.7%	-	-	-	-	-	-	-	-	-	-	81	45	-	-
Suri *et al*. 2006†	1.6%	4.9%	96	94	76 *	60	-	-	-	-	-	-	-	-	-	-

Numbers under "yrs" column indicate percent survival, unless otherwise stated

* P<0.05 compared to MVR

∞ In sets with two numbers separated by a "/" first number is without performance of concomitant CABG, second is with CABG. At 5 years, only data without CABG was available

† all data based on reoperation after primary mitral valve surgery

SVP = subvalvular preservation

Table 3. Reoperation data.

Study	MVP	MVR
Daneshmand *et al.* 2009	95.4% at 20 yrs	96.6% at 20 yrs
Gillinov *et al.* 2008	94% at 5,10 yrs	95%, 92% at 5,10 yrs
Lee *et al.* 1997	-	-
Mohty *et al*. 2001	93%, 89%, 84% at 5,10,15 yrs	93%, 85%, 77% at 5,10,15 yrs
Suri *et al.* 2006	No significant difference between MVP and MVR	
Zhou *et al*. 2010	98.7%, 97.6% at 1,5 yrs	95.5% at 1,5 yrs
Gillinov *et al*. 2003	-	-
Gogbashian *et al*. 2006 ∞	93.9%/98.2% at 10 years	100%/100% at 10 years
Zegdi *et al*. 2008 *	95% at 7 yrs	95% at 7 yrs
Dumont *et al.* 2007 *	93% at 10 yrs	87% at 10 yrs
Suri *et al.* 2006 *	No significant difference between MVP and MVR	

Percentages indicate freedom from reoperation

∞ In sets with two numbers separated by a "/" first number is without performance of concomitant CABG, second is with CABG

* all data based on reoperation after primary mitral valve surgery

was found to be an independent predictor of survival. However, when patients were divided if concomitant CABG was preformed, the survival benefit disappeared and was only seen in patients with isolated valve surgery. Concomitant CABG was a predictor of late mortality in this study, a finding that has been known for decades. In these patients it is plausible to think that due to their reduced long-term survival, the benefit of repair is less able to be realized [28].

Of particular importance to the long-term survival focus of this study, two of the publications found the survival advantage of repair to increase over the course of follow-up. In Daneshmand, they preformed an area under the curve analysis, after multivariable risk adjustment, to compare the survival of repair to replacement. In this analysis, replacement patients achieved 92.7% of repair survival during 15 years; 99.3% for years 0 to 5, 95.1% for years 5 to 10, and 78.7% for years 10 to 15 [30]. In Gillinov 2003, the survival advantage of repair only became apparent after two years post operation. Both of these results help to validate the long-term survival advantage and durability of repairing the valve, rather than the difference coming from a reduction in short-term mortality [31].

It has been previously shown that the elderly are less likely to receive mitral valve repair compared to a series of all-comers [9]. Perhaps part of the reason factoring into this discrepancy is that, due to age and increased comorbidities, a perceived reduction in the benefit of repair will be achieved and also a hesitancy to have to return to the OR for an unsuccessful repair. Two of the studies in this review, Chikwe *et al.*2011 and Gogbashian *et al.* 2006, looked at patients over 80 and 70 years old respectively. Both of them found repair to still remain an independent predictor of survival, despite the inherent reduced longevity compared to younger counterparts [9, 28, 32].

Complex pathology is often the reason surgeons defer to replacing the valve. This was evident in two of the studies of this review that stratified by leaflet prolapse. In these publications, anterior and bileaflet prolapse were predictive of valve replacement [11, 12]. This is unfortunate, as an independent survival advantage was shown for repair of both anterior and posterior leaflet prolapse in Mohty *et al*. In Suri *et al*. the survival advantage of repair was still significant when looking at bileaflet prolapse as well. While there was also an improved survival with anterior leaflet repair, it was not significant (P=.26) [11]. Furthermore, it is unlikely that the inability to repair a valve is predictive of reduced survival. Lee *et al.* looked at the survival of replacement patients during the initial study phase, most of whom would have had repairs given modern techniques, with more recent replacement patients where the valves were largely irreparable and found no survival difference [30].

Presumably anterior and bileaflet prolapse are replaced more often because of surgeon's hesitation about the success and durability of repair in this setting and the possible need for bail-out replacement. Longer bypass times and higher rates of failure in complex pathology also may contribute to this decision. Zhou *et al.* and Lee *et al.* looked specifically at conversion to mitral valve replacement after a failed repair within the same operation. Both of them found no difference in long-term survival between this replacement group after failed repair and primary replacement without attempting repair, despite longer bypass times. These results should favor a policy of always attempting to repair a valve initially for degenerative disease [22, 30]. Nevertheless, patients with more complex pathology may benefit from referral to high volume mitral valve centers [7].

DURABILITY OF MITRAL VALVE REPAIR VERSUS REPLACEMENT

In the publications in this review, mitral valve repair was found to have long-term durability equaling that of replacement, and in some contexts, better. Reoperation data was recorded as freedom from reoperation during the stated time intervals in Table **3**. When reoperation statistics were reported as reoperation rate, we used "1- reoperation rate" to determine the freedom from reoperation for the stated time interval. When analyzed over the course of the study, no publication found a difference in the likelihood of reoperation between the MVP and MVR groups, either after primary mitral valve surgery or after reoperation of a failed repair. These findings should counteract the notion still held by many that mitral repair may commit the patient to a second intervention while mitral replacement is viewed as a definitive fix.

Furthermore, the use of a bioprosthesis was found to be associated with higher reoperation rates, increasing sharply around 10 years [11, 12]. Common risk factors for reoperation amongst those who received a primary repair were greater than mild residual regurgitation at discharge, lack of annuloplasty ring, which is uncommon in current surgical practice, use of chordal shortening, which has also largely given way to chordal replacement, and anterior leaflet repair [11, 12, 22]. While anterior leaflet repair is often technically more difficult than posterior repair leading to the higher published rates of reoperation, these differences were largely seen in the first half of the studies that examined this topic, presumably due to recent advancement in surgical techniques. In the 1990's, compared with the 80's, the risk found with repair of an anterior leaflet was greatly diminished. When it was analyzed, reoperation for repairs of all subtypes of leaflet prolapse were reduced in the second halves of studies; In Mohty *et al*., it was reduced to the point that repair in the 90's was independently associated with freedom from reoperation compared with valve replacement [11, 12]. Although no study focused on reoperation rates from just 2000 on, we would expect this trend of improved durability of mitral valve repair to continue due to further improvement in surgical techniques.

SURVIVAL AFTER REOPERATION

Three studies in our review looked at long-term survival for reoperation after a failed mitral valve repair [33-35]. These studies all excluded patients who had a replacement after a failed repair within the same operation. All studies found improved long-term survival for re-repair compared to replacement. In general however, the baseline characteristics were worse for the patients undergoing replacement after a failed repair compared to re-repair. Two studies accounted for this by multivariate analysis. In Suri *et al*. re-repair was still found to be an independent predictor of survival after adjusting for baseline characteristics, whereas in Dumont *et al*. the advantage lost its significance P=.13 [33, 34].

The mechanisms behind the improved survival advantage comparing primary mitral valve repair to replacement should theoretically be maintained for reoperation, the main ones being reduced operative mortality, better preservation of left-ventricular function, and reduced valve-related complications [13-16]. All publications reported reduced operative mortality for re-repair compared to replacement. Additionally, one publication included follow-up echocardiographic data and reported that patients with a re-repair had better follow-up left ventricular dimensions and function compared to replacement; there were no differences between the groups in this regard preoperatively.

The rates of re-repair in these studies ranged from 36-49%. Previous studies on reoperation for degenerative disease have reported re-repair rates as low as 10% [36]. The causes behind reoperation are either procedure-related or valve-related. The primary examples of procedure-related failure are incomplete primary repair, suture dehiscence, systolic anterior motion of the anterior leaflet of the mitral valve causing left ventricular outflow obstruction and residual mitral regurgitation, or hemolysis. Progression of degenerative disease and endocarditis are the main examples seen for valve-related related failure. Procedure-related failure should be able to be corrected by re-repair. The rates of this type of failure ranged from 42%-56%. Additionally, as progression of degenerative disease should also be able to be re-repaired in most cases, the rates of re-repair should ideally be higher than what we observed through this review. Presumably, these rates are lower than what is possible due to the surgeon's reluctance to confront the perceived idea of another failure and the inherent difficulty of complex repairs. Again, these may be patients who would benefit from referral to specialized mitral valve surgeons.

LIMITATIONS

The results of this review are all based on nonrandomized, retrospective studies which carry their own inherent biases. We are unable to account for the intraoperative factors that account for the performance of repair or replacement. In general patients who receive mitral valve replacement have a worse preoperative profile. All studies however, performed risk adjustment to account for differences in baseline characteristics. A key limitation was the lack of echocardiographic data in these reviewed publications, especially in follow-up. Preoperative ejection fraction is the strongest predictor of survival after mitral valve surgery [20]. Additionally, mitral valve repair has been previously shown to be a predictor of better post-operative left ventricular function which is itself predictive of survival [14]. This follow-up echocardiographic data would allow for a more definitive assessment of the functional outcomes of mitral valve repair versus replacement.

CONCLUSIONS

There is an abundance of literature supporting the short-term survival benefits of mitral valve repair versus replacement. More recent literature has been published regarding the long-term benefits of repair. This paper aimed to review and summarize these publications. Mitral valve repair was shown to be largely independently associated with superior long-term survival with similar rates of reoperation. Additionally, the longer patients were followed, the more mitral valve repair gained a survival advantage over replacement.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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ABBREVIATIONS

NYHA = New York Heart Association

MVP = Mitral valve repair

MVR = Mitral valve replacement

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