



Management of Mild to Moderate Aortic Valve Disease undergoing Mitral Valve Surgery

Authors

Dr Sunil Dhar¹, Dr Amit Agarwal², Dr Mayank Yadav³, Dr Anubhav Gupta^{4*}

¹Senior Resident, Department: Department of CTVS, VMMC and Safdarjung Hospital

²Senior Resident, Department of CTVS, VMMC and Safdarjung Hospital

³Senior Resident, Department: Department of CTVS, VMMC and Safdarjung Hospital

⁴Professor & Head, Department: Department of CTVS, VMMC & Safdarjung Hospital

*Corresponding Author

Dr Anubhav Gupta

Professor & Head, Department: Department of CTVS, VMMC & Safdarjung Hospital, India

Introduction

The optimal management strategy of patients undergoing mitral valve intervention for rheumatic heart disease and having mild to moderate aortic valve disease is controversial. The decision making in this clinical setting is difficult as there are no guidelines on the management of combined valvular diseases. Mild aortic stenosis has a propensity of rapid progression however does it warrant a concomitant aortic valve replacement at the time of mitral valve intervention is not clear. In 2014 AHA guidelines recommended concomitant aortic valve replacement in patients with moderate aortic stenosis undergoing cardiac surgery for other indications including mitral valve surgery (*Level of Evidence: C*). These guidelines also recommended concomitant aortic valve replacement for moderate aortic regurgitation in patients undergoing surgery for ascending aorta, coronary artery bypass grafting (CABG), or mitral valve surgery (*Level of Evidence: C*).^[1]

Theoretically the type of mitral valve intervention also affects the above decision making. In patients undergoing balloon mitral valvotomy or mitral valve repair, which are likely to have future mitral valve procedure, can be dealt with a more conservative approach for the aortic valve disease than patients undergoing mitral valve replacement. With the above scenario in mind, we analysed the published literature on this subject using MEDLINE.

Hence, the aim of this study was to review all published literature on this clinical subset, allowing conclusions to be drawn regarding the progression of mild and moderate aortic valve disease and optimal surgical management.

Material & Methods

We conducted a MEDLINE and Google scholar database search for available literature on fate of aortic valve in patients undergoing Mitral Valve (MV) intervention and having mild to moderate aortic valve disease. In addition, the reference

sections of all relevant articles were searched to identify additional cases.

The collected data was evaluated in detail. nature of aortic valve disease, duration of follow-up, progression of aortic valve disease, need of redo surgery for aortic valve replacement and timing of aortic valve surgery was studied.

Results

There are 8 articles describing course of aortic valve disease progression in follow up period after mitral valve intervention. Total of 3047 patients included in all studies, 1514 patients (49.68 %) had mild to moderate aortic valve disease at time of mitral valve intervention.

Most of the authors had retrospective followed up of patients with mild to moderate aortic valve disease in which concomitant aortic valve replacement was not performed. However in two studies concomitant aortic valve replacement or repair was performed in one subset of patients. In all the studies mild and moderate aortic disease was clubbed together therefore conclusion regarding only mild or only moderate disease cannot be drawn. After pooled mean follow up of 15.19 years, only 136 patients (4.46 %) developed significant severe aortic valve disease. Summary of outcomes and results of all studies described in Table 1.

Discussion

Rheumatic heart valve disease is still the leading cause valvular heart disease in developing countries. In one-third of cases, there is simultaneous involvement of the mitral and aortic valve. Management of such patients is difficult because of large number of possible combination and lack of clear-cut guidelines. In patients with severe aortic valve disease, double valve replacement is the considerable option^[2]. However, in patients with mild to moderate aortic valve disease the decision making is challenging.

In order to decide the best approach, the clinician must review the course and rate progression of aortic valve disease. Unlike natural history of congenital or degenerative aortic stenosis, progression of aortic valve disease is poorly reported in literature. Rate of progression of mild aortic stenosis (AS) are neither uniform nor predictable.^[3] Decrease of aortic valve area ranging from 0.1 to 0.3 cm² or no progression of severity noted in various studies.^[4-11] Padial and colleagues in prospective observational study involving 127 patients, of which 67 patients had mild AR, 45 patients had moderate AR and 15 patients had severe AR, demonstrated that Aortic regurgitation (AR) is a progressive disease and the degree of regurgitation also increases in an important number of patients with initial Mild AR. the dilatation of left ventricle proportionately increases with the severity of AR at the time of presentation^[12]

Fate of AV disease after mitral valve intervention was studied by several authors.

Vautriand colleagues did a retrospective study in 131 patients undergoing mitral interventions, 59 patients (45%) of patients had mild to moderate aortic valve disease at time of intervention. Patient followed up for a mean follow-up of 13±7 years and observed aortic valve disease progressed in 96(73%) of patients but progressed to severe AVD in only 3 patients (2.29%). In the entire cohort only 6(5%) patients needed AVR out of which in 4 patients the primary indication of second surgery was dysfunction of prosthetic mitral valve. Most patients had mild disease, clinically 37 patients were in functional class III and 3 were in functional class IV. They concluded double valve replacement is not justifiable in patients having mild aortic valve disease at the time of mitral valve replacement, due to increased perioperative and long-term mortality and morbidity because there is minor progression of aortic valve disease during long term follow-up.^[13]

Author	Type of study	Country	Patients group	Outcome	No. of follow up years	Key Results	Comments
Mordehay Vaturi et. al. 1999,	Retrospective	Israel	131 Mitral intervention (101 MVR & 30 OMC) 59 AV disease, 7 AS, 58 AR 6 combined	96(73%) had AV disease 33 AS, 90 AR, 27 had combined disease Most patient had mild disease severe AS in 2 severe AR in 1	Average follow-up was 13±7 years	In 7 patients with AS 1 progressed from mild to moderate & 2 progressed from mod to severe -In 58 patients with AR 52 remained stable, 5 progressed from mild to moderate, 1 from mild to severe	Progression of AV disease over long period of follow-up seen in minor number.
Shiv Kumar Chaudhary et al 2001,	Retrospective	India	284 mitral valve procedure 18 mild AS 232 Mild AR 34 mixed lesions	Out of 284 patients 29 progressed to significant severity	Average follow-up was 10.8 years	In 232 patients with mild AR 11 progressed to significant AR 1 patient had severe AR & mod AS Out of 18 patients mild AS, 7 progressed to severe AS Patients with 34 mixed lesions 10 developed significant AV disease	Prophylactic AVR may not be recommended for mild aortic valve disease, if drawbacks of AVR are taken into consideration
Jong-Won Ha et.al. 2002,	Retrospective	Korea	275 patients with RHD underwent MV surgery -Group A 141 patient mild to mod AV disease, 104 mild AR, 37 mod AR , 5 mild AS, 2 mod AS -Group B 134 without coexisting AV disease	-22 patients in group A had progression of AV disease -6 patients in group B had progression of disease	Mean follow-up was 8.2 years for group A & 10.2 years for group B	9 progressed of AR, 8 from mild to mod AR, 1 from mod to severe AR -19 progressed of stenosis, 13 from none to mild, 3 from none to mod & 3 from mild to Mod disease - 3 progression of both stenosis & regurgitation	In patients with initial aortic valve lesions, progression of aortic valve disease is more frequent but progression to severity is uncommon
Narayan Namboodiri et.al. 2009,	Retrospective	India	200 patients isolated MV intervention -Group I 98, absent AV disease -Group II 102, isolated AV thickening in 16 patients, 69 patients had isolated AR with 18 trivial, 47 mild 4 had mod AR, 17 had combined disease, 16 mild AS & 1 mod AS	112 patients had AV di, 10 patients without AV disease at baseline had developed the condition -on completion of follow-up 38 patients had either mod or severe AV disease -No patients with Mod AS or AR at baseline progressed to severe AV disease	Mean follow-up period was 9.6 years	In patients with thickening only, none progressed beyond mild disease -among patients with trivial AR, 9 progressed to mild AR, 2 to mod AR, 5 developed mild AS & mild AR, 2 developed mild AS & mod AR -Among the 47 patients with mild AR, 25 remained mild, 8 developed mod AR, 3 developed mild AS & mild AR, 11 developed mild AS & mod AR - 4 patients with mod AR initially no progression in AR -Among 16 patient with mild AS, 6 progressed to mod AS & 2 progressed to severe AS	Patients with rheumatic MV disease showed only minor progression of AV disease and seldom requires AV surgery on the long term follow-up
Sanchez-Ledesma M et.al. 2008,	Prospective observational study	USA	676 PMV procedure performed -361 No AR -287 mild AR, 28 Mod AR	-No difference in overall survival rate and MVR rate -Rate of AVR was higher in mod AR group in comparison to mild AR group	Median follow-up of 4.11 years		Concomitant AR at the time of PMV does not influence procedural success and is not associated with inferior outcome. A minority of patients with MS and moderate AR who undergo PMV will require subsequent AVR on long-term follow-up

Bernal et al. 1998	Retrospective study	USA	<p>53 patients who underwent double or triple valve procedures (repair or replacement), predominantly having rheumatic mitral valve lesion associated with non-severe aortic valve disease. 25 patients had severe tricuspid valve disease.</p> <p>Patients with aortic valve disease, 66.1 % (n= 35) having pure aortic regurgitation , 18.9 % (n= 10) with mixed lesions and 15.1 % (n= 8) having pure aortic stenosis . 24 patients (45.3%) had mild aortic valve regurgitation (AR) and 21 patients (39.6%) with mod. AR.</p>	<p>All patients underwent aortic valve repair, out of 25 patients had severe Tricuspid valve lesions 24 were repaired and mitral valve repaired in 41 patients.</p> <p>49 surviving patients after 12 months of follow up, 10 patients found to have normal aortic valve, 30 patients (61.2%) found with mild residual lesions (25 with pure regurgitation, mixed in 4, 1 had stenosis). Moderate residual lesions in 9 patients (18.4 %).</p>	<p>Mean follow-up of 18.8 years (range 8 to 22.5 years)</p>	<p>Of the 49 surviving patients, 26 (53.1%) died during the late follow-up. The actuarial survival curve, including hospital mortality, was 35.4% +/- 8.7% at 22 years. For the subgroup of 28 patients who underwent mitral and aortic valve surgery, the actuarial survival curve at 22 years was 32.3% +/- 13%, whereas for the 25 patients who had triple-valve operation it was 37.0% +/- 10.1 Actuarial curves of survival free from structural deterioration of the repaired aortic valve at 22 years was 20.0% +/- 17.9% for patients with normal functioning valves, 33% +/- 11.4% for those with mild aortic lesions, and 22.2% +/- 13.9% for those with moderate residual lesions.</p>	<p>Long-term functional results of reparative procedures of non-severe aortic valve disease in patients with predominant rheumatic mitral valve disease have been inadequate at 22 years of follow-up. According to these data, conservative operations for rheumatic aortic valve disease do not seem appropriate.</p>
Hwang et al. 2014	Retrospective study	South Korea	<p>197 reported with Rheumatic mitral valve disease and mild aortic valve disease.</p> <p>Aortic valve untreated in 114 patients (no treatment group),</p> <p>Repaired in 40 patients (aortic valvuloplasty group AVP)</p> <p>Replaced in 43 patients (aortic valve replacement group AVR).</p>	<p>Echocardiographic data showed that more patients in the AVP and AVR groups had stenotic aortic valve pathology compared with the NT group.</p> <p>The aortic valve area and mean transvalvular pressure gradient in patients who had stenotic aortic valves were similar among the 3 groups</p> <p>The mitral valve was repaired in 37 patients.</p> <p>The AVP and NT groups underwent mitral valvuloplasty more frequently than the AVR group</p> <p>In 43 patients in the AVR group, bileaflet mechanical valves were used in 39 patients and bovine pericardial bioprostheses were inserted in 4 patients.</p>	<p>Mean follow up 9.5 years (1-20.16) years</p>	<p>In early period, there were no differences in operative mortality and postoperative complications among the 3 groups.</p> <p>In the NT group, significant AVD occurred in 8 patients. Progression-free survival in significant AVD at 5, 10, and 15 years was 98.7%, 91.3%, and 81.1%, respectively.</p> <p>In AVP group, Progression-free survival in significant AVD at 5, 10, and 15 years was 85.9%, 77.6%, and 69.8%, respectively.</p> <p>In AVR group, freedom from significant AVD at 5, 10, and 15 years was 90.4% 85.9% and 76.0%, respectively.</p>	<p>Mild aortic valve disease in patients undergoing rheumatic mitral valve surgery could be left untreated, because preventive aortic valve operation does not result in better clinical and echocardiographic outcomes.</p>
Do Jung Kim et al. 2018	Retrospective	Korea	<p>Total 1231 patients Mild AVD in 363 No AVD in 868 patients</p>	<p>Progressive AVD in 162 patients Significant AVD in 60 patients 37 patients needing AVR</p>	<p>20 years</p>	<p>Only 37 patients needed AVR primarily for mitral valve dysfunction requiring 2nd surgery with progressive aortic stenosis</p>	<p>Echocardiography at 5 year intervals after MVR for timing of AVR.</p>

Choudhary et al.^[14] followed 284 patients who underwent mitral valve intervention and had mild AV disease. Out of 232 patients who underwent mitral valve interventions and had initially mild AR only 6 (2.5%) progressed to moderate and 5 (2.1%) progressed to severe AR over an interval of 9 to 17 years (mean, 12.1±2.8 years). Those patients who had initial AS progressed more rapidly compared to those who had AR as initial

lesion. According to them, there is significant decrease in aortic valve area before gradient becomes detectable and this represents advance commissural fusion & valve deformity. This is in contrast to mild AR which can occur even with slight deformity of one or more leaflets. Other possible reason is that turbulence caused by stenotic valve may contribute to further leaflet damage and thus may lead to rapid progression of

the disease. They concluded that patients with mild aortic stenosis need close follow up still aortic valve replacement at time of initial mitral valve intervention not advisable.

In 2002, a retrospective case-control study by Ha et.al.^[15] including 275 patients having Rheumatic heart disease (RHD) who underwent mitral valve surgery (group A with 141 patients with mild to moderate aortic valve disease and group B with 134 without coexisting aortic valve disease). After a mean follow up of 8.2 years in group A and 10.2 years in group B, they observed aortic valve disease progression in 22 patients from group A and 6 patients from group B and only one patient progressed to severe lesion needed aortic valve replacement. In this study they suggested that there is no significant difference in either the survival rate or the event-free survival rate over the follow-up period between the two groups of mild aortic regurgitation and moderate aortic valve disease. Although the progression of aortic valve disease is more common in that group of patients who had initial lesions, progression to severe disease is uncommon. They suggested that mild and moderate aortic valve disease had slow rate of progression and prophylactic double valve replacement is not indicated.

In a similar retrospective study, Namboodiri et al.^[16] observed in 200 patients with isolated mitral valve intervention, of which 51 % of patients (n=102) had mild to moderate aortic valve disease while 98 patients(49%) had no AV disease. Patients were allocated to two groups, based on whether the AV disease was absent (group I, n=98) or present (group II, n=102) at baseline. The AV disease was categorized as thickening only (group IIA), isolated aortic regurgitation (AR) (group IIB), or combined aortic stenosis (AS) and AR (group IIC). No patient had isolated AS at baseline. 10 patients in group I developed new AV disease, which included AV thickening only (n=2), trivial-mild AR (n=7) and mild AS with trivial AR (n=1). Of 16 patients in group IIA, 11 developed isolated AR, and one patient progressed to have mild AS and AR. Among 69 patients in

group IIB, 22 (31.9%) developed AS, and all had either mild (n=8) or moderate (n=14) AR with mild AS. Group IIC included 17 patients with mild combined AV disease at baseline, except for moderate AS and moderate AR in one patient each. Among 16 patients with mild AS in group IIC, six progressed to moderate AS and two to severe AS. AR became moderate in 10 patients and severe in one patient. AV replacement was required in 2 patients who had mild disease at baseline and had progressed to severe AS. New combined AV disease with severe lesions was not observed in any patient.

After follow up period of 9.6 years, They observed minor progression of aortic valve disease in 50(25%) patients and only 2(1%) patients required aortic valve surgery during the entire follow up. They concluded that patients with no or mild AV disease at the time of MV intervention rarely develop severe AV disease, and seldom require AV surgery over the long-term follow up. The presence of mild AS at baseline is predictive in the minority of cases where AV disease will progress relatively more rapidly.

Hwang et al.2014,^[17] in a study of 197 patients with Rheumatic mitral valve disease and mild aortic valve disease, in which Aortic valve was left untreated in 114 patients (no treatment group), repaired in 40 patients (aortic valvuloplasty group AVP) and replaced in 43 patients (aortic valve replacement group AVR) and with a mean follow up of 9.5 years (1- 20.16 years) revealed that there were no differences in operative mortality and postoperative complications among the 3 groups in the early post-operative period. Only 8 patients among the non treated group developed significant AVD. In patients with significant AVD progression-free survival at 5, 10, and 15 years was 98.7%, 91.3%, and 81.1%, respectively. I Progression-free survival in in AVP group with significant AVD at 5, 10, and 15 years was 85.9%, 77.6%, and 69.8%, respectively. In AVR group, freedom from significant AVD at 5, 10, and 15 years was 90.4%, 85.9% and 76.0%, respectively. They concluded

that the preventive aortic valve operation does not result in better clinical and echocardiographic outcomes in patients with mild aortic valve disease in patients undergoing rheumatic mitral valve surgery if left untreated.

Do Jung Kim et al.^[18], reviewed 1231 patients operated over a period of 25 years who underwent mitral valve replacement. In 863 patients there was no AVD at the time of presentation and in 363 patients AVD was present. They noted no differences in postoperative complications or clinical outcomes were observed between groups. The 20-year overall survival was similar (without AVD 86.1% vs AVD 80.8%). Progressive AVD was observed in 162 patients, and significant AVD (grade >III) was observed in only 60 patients. Due to mitral valve (MV) dysfunction or severe aortic stenosis subsequent AVR was required in 37 patients. The 20-year freedom from significant AVD and subsequent AVR was significantly higher in the no AVD group than in the AVD group (96.5% vs 73.7%).

They concluded that progressive AVD did not significantly impact long-term survival during the follow-up period, those patients qualifying initially as mild AVD may eventually progress to significant AVD after the first 5 postoperative years. Therefore, aggressive echocardiography should be performed at 5-year lapse after mitral valve replacement to determine the appropriate timing of AVR.

Sanchez-Ledesma et al.^[19] in prospective observation study of 676 patients who underwent percutaneous mitral valve intervention, 315 patients (46.6%) had concomitant AR at the time of mitral valve intervention. The presence of concomitant AR did not influence the procedural success and is not associated with inferior outcome and only 2 patients with MS and moderate AR who undergo percutaneous mitral valve intervention required AVR on long term follow-up. The rate of aortic valve replacement was higher in patients with moderate AR than in patients with mild AR. Mean time to aortic valve replacement did not differ.

In a retrospective study by Bernal et al.^[20] in USA, 53 patients who underwent double or triple valve procedures (repair or replacement), predominantly having rheumatic mitral valve lesion associated with non-severe aortic valve disease. The actuarial survival curve, including hospital mortality, was 35.4% +/- 8.7% at 22 years. For the subgroup of 28 patients who underwent mitral and aortic valve surgery, the actuarial survival curve at 22 years was 32.3% +/- 13%, whereas for the 25 patients who had triple-valve operation it was 37.0% +/- 10.1. Actuarial curves of survival free from structural deterioration of the repaired aortic valve at 22 years was 20.0% +/- 17.9% for patients with normal functioning valves, 33% +/- 11.4% for those with mild aortic lesions, and 22.2% +/- 13.9% for those with moderate residual lesions. According to these data, conservative operations in forms of Aortic valve repair for rheumatic aortic valve disease do not seem appropriate.

Conclusion

In conclusion, the current review established the fact that concomitant AV disease progress slowly in case of RHD requiring mitral valve intervention and a small number of patients will require AVR in future. Double valve replacement is not advisable in this group of patients however those patients who have AS as the initial associated lesion will require stricter and more regular follow-up for early detection of progression of AV disease.

Study Limitations

The number of patients are relatively few(%) therefore the conclusions may be biased. Most studies mentioned above have clubbed mild to moderate AVD together and fine discretion between mild to moderate AVD in case of concomitant mitral valve disease needs to be investigated separately.

References

1. Nishimura,R.A.,Catherine,M.O.,Bonow,R.O.,Carabello,B.A.,Erwin,P.J.,Guyton,R.A. 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.*Circulation*,2014;129:2440-2492.
2. Mishra, P., Seth, H., Khandekar, J., Mohapatra, C., Ammannaya, G., Raut, C., et al. Double Valve Replacement (Mitral and Aortic) for Rheumatic Heart Disease: A 20-year experience with 300 patients.. *Journal of Cardio-Thoracic Medicine*, 2016; 4(3): 484-489. doi: 10.22038/jctm.2016.7427 .
3. Levinson GE, Alpert JS. Aortic stenosis. In: Alpert JS, Daten JE, Rahimtoola SH, eds. Valvular heart disease. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:207-8.
4. Wagner,S., Selzer, A. Pattern of progression of aortic stenosis: a longitudinal haemodynamic study. *Circulation*.1982;65:709-12.
5. Bogart, D.B., Murphy, B.L.,Wong BYS, Pugh DM, Dunn MI. Progression of aortic stenosis. *Chest*.1979; 76:391-6.
6. Faggiano P, Aurigemma GP, Rusconi C, Gaasch WH. Progression of valvular aortic stenosis in adults: literature review and clinical implications. *Am Heart J*. 1996;132:408-17.
7. Kennedy KD, Nishimura RA, Holmes DR, Bailey KR. Natural history of moderate aortic stenosis. *J Am CollCardiol*. 1991;17(2):313-9.
8. Cheitlin MD, Gertz EW, Brundage BH, Carlson CJ, Quash JA, Bode RS. Rate of progression of severity of valvular aortic stenosis in the adults. *Am Heart J*. 1979;98:689-700.
9. Otto CM, Burwash IG, Legget ME, Munt BI, Fujioka M, Healy NL, et al. Prospective study of asymptomatic valvular aortic stenosis. *Circulation* 1997;95:2262-70.
10. Lester SJ, Heilbron B, Gin K, Dodek A, Jue J. The natural history and rate of progression of aortic stenosis. *Chest*. 1998;113(4):1109-14.
11. Brener SJ, Duffy CI, Thomas JD, Stewart WJ. Progression of aortic stenosis in 394 patients: relation to changes in myocardial and mitral valve dysfunction. *J Am CollCardiol*. 1995;25(2):305-10.
12. Padiar LR, Oliver A, Vivaldi M, Sagie A, Freitas N, Weyman AE, et al. Doppler echocardiographic assessment of progression of aortic regurgitation. *Am J Cardiol* 1997;80:306-14.
13. Vaturi M, Porter A, Adler Y. The natural history of aortic valve disease after mitral valve surgery. *J Am CollCardiol*. 1999;33:2003-8.
14. Choudhary SK, Talwar S, Juneja R, Kumar AS. Fate of mild aortic valve disease after mitral valve intervention. *J Thorac Cardiovasc Surg*. 2001;122:583-6.
15. Ha JW, Choi SH, Chang BC, Nam CM, Jang Y, Chung N, et al. Is prophylactic aortic valve replacement indicated during mitral valve surgery for mild to moderate aortic valve disease. *Ann Thorac Surg*. 2002;74:1115-9.
16. Namboodiri N, Remash K, Tharakan JA, Shajeem O, Nair K, Titus T, et al. Natural history of aortic valve disease following intervention for rheumatic mitral valve disease. *J Heart Valve Dis*. 2009;18:61-7.
17. Hwang H.Y, Kim K.H, Ahn H, Attitude after a mild aortic valve lesion during rheumatic mitral valve surgery. *Journal of Cardiovascular Surgery*.2014;147(5):1540-46
18. Kim DJ, Joo H-C, Lee S-H, Chang B-C, Lee S. Natural history of mild aortic valve

disease untreated at the time of rheumatic mitral valve replacement. *Interact Cardio Vasc Thorac Surg* 2018;27:828–35.

19. Ledesma, M.S., Kim DJ, Joo H-C, Lee S-H, Chang B-C, Lee S. Natural history of mild aortic valve disease untreated at the time of rheumatic mitral valve replacement. *Interact Cardio Vasc Thorac Surg* 2018;27:828–35.
20. Bernal JM, Fernandez-Vals M, Rabasa JM, Gutierrez-Garcia F, Morales C, Revuelta JM. Repair of nonsevere rheumatic aortic valve disease during other valvular procedures: is it safe? *J Thorac Cardiovasc Surg.* 1998;115:1130-5.