

## Long-Term Follow-Up of Adults with Nonsevere Initial Disease Affected with Rheumatic Mitral Stenosis

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### Abstract

**Background:** Regarding the normal course of rheumatic mitral stenosis (MS) in adults presenting with mild illness, there is no universal agreement.

**Methods:** Patients with rheumatic MS who were seen at one facility underwent a retrospective cohort analysis. 85 MS patients who were under 30 years old on their initial echocardiogram and had mild to moderate disease were included. A computerised database was accessed to retrieve information on demographics, medical history, echocardiographic results going back at least ten years, and related problems.

**Results:** In 75 patients (88%) after a period of  $13.1 \pm 2.38$  years, there was no discernible progression in the degree of stenosis. The final echocardiographic evaluation revealed two groups with a significant difference in the mean valvular pressure gradient ( $6.27 \pm 2.52$  vs.  $8.5 \pm 2.69$  mm Hg,  $p = 0.01$ ) and mitral valve area ( $1.58 \pm 0.44$  vs.  $1.1 \pm 0.26$  cm<sup>2</sup>,  $p = 0.001$ ).

**Conclusions:** In our investigation, an indolent natural course of rheumatic MS was noted. Despite this discovery, it could still have negative consequences. Patients who are Bedouin are more likely to get progressive diseases.

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### Introduction

Numerous in-depth research have examined the rheumatic mitral stenosis' natural history. [1-3] These investigations have shown that clinical development is typically modest but frequently variable, with some patients exhibiting little to no lung periods or clinical progression and others displaying a more accelerated trajectory. Little is known about the temporal changes in the mitral valve gradient or valve area, in contrast to these clinical trials. Such details are crucial since clinical deterioration might not be related to the progression of valvular stenosis rather than an unrelated occurrence such

the onset of atrial fibrillation, cardiac failure, pulmonary hypertension, or increased valve regurgitation.

Additionally, it is unknown whether hemodynamic, morphological, and mechanical parameters affect or may be used to predict how quickly stenosis progresses. Such information is crucial for making clinical decisions regarding the best follow-up interval for these patients as well as the necessity of percutaneous balloon valvuloplasty or surgery.

In order to better understand disease pathophysiology and create more potent

therapeutic approaches to stop irreversible valvular damage, it is important to better comprehend this pathological process that results in the development of severe valve dysfunction.

## Methods

In a retrospective population-based analysis, we examined the echocardiographic reports of 143 MS patients who were being treated in the cardiology division of M.G.M. Medical College, Kishanganj, Bihar, India and who had at least two echocardiograms that were at least ten years apart. It was decided to eliminate 58 patients for one or more of the following reasons: 1. Patients with advanced stenosis severity at the time of their initial echocardiographic evaluation already had severe disease, and information on the course and evolution of their condition was not accessible.

2. Due to their impact on cardiac hemodynamics, significant concomitant mitral regurgitation and/or aortic stenosis may impair the accuracy of valve and mean gradient echocardiographic measurement.

3. Senile calcific MS.

The following echocardiographic information was gathered from the patient's first and last study reports: MVA, mean gradient across the mitral valve, size and function of the left and right ventricles, systolic pulmonary artery pressure, and the presence of other valvulopathies. We categorised the mean gradient and MVA severity grade for each subject using the EAE/ASE definitions [4]. For example, if the MVA indicated mild stenosis and the mean gradient indicated moderate stenosis, we labelled the overall severity as mild-moderate. If there was a discrepancy between the MVA grade and the mean gradient grade, we labelled the overall severity as a combination of both.

Empirically, we assigned severity categories of 1 to severe, 2 to mild-

moderate, 3 to moderate, 4 to moderate-severe, and 5 to mild. In the initial and final echocardiographic evaluations, the severity of the stenosis was compared using this scale. By contrasting the degree of the first and final stenosis, we examined stenosis progression. In patients whose stenosis severity increased by up to one point during the follow-up period (for example, from 2 to 3 - mild-moderate in the first echocardiographic assessment to moderate in the last one), we defined the disease progression as indolent, and we defined it as progressive for patients whose stenosis severity increased by two points and more.

As a result, we separated the study population into two subgroups: group A consisted of patients with a slow-moving condition, while group B consisted of patients with a rapidly progressing disease. We were able to evaluate demographics and complication rates among subgroups and identify aggravating or mitigating factors as a result of the separation into subgroups.

Depending on the scale structures of the variables, the differences between the 2 groups in terms of sociodemographic traits, echocardiographic traits, and long-term clinical problems were evaluated using a t test or a  $\chi^2$  test. A multiple logistic regression analysis was used to explore the specific relative contribution of the independent sociodemographic variables (gender, ethnicity, and age at initial echocardiographic examination) to the explanation of illness progression. No interactions were discovered between the variables after they were each individually entered into the model. A two-sided p value  $<0.05$  was deemed statistically significant after computing ORs and 95% CI. SPSS version 23 was used to conduct each test (IBM, Armonk, NY, USA).

## Results

After excluding patients as described in the Methods section, the research

population consisted of 85 patients. 75 (88%) of the patients had indolent illness, it was discovered. The remaining 10 individuals (12%) all had advancing illness.

Table 1 provides a description of the 2 subgroups' demographic and clinical traits.

We discovered that race is a statistically significant factor: ( $p = 0.01$ ). No other research factor, clinical or demographic, was shown to significantly protect against or accelerate the development of the condition.

**Table 1. Demographic and clinical characteristics**

|  | <b>Group A<br/>(Indolent disease,<br/>n= 75)</b> | <b>Group B<br/>(Progressive disease,<br/>N=10)</b> | <b>P<br/>Value</b> |
|--|--|--|--------------------|
| Gender   |  |  |                    |
| Male   | 16 (21.6)  | 2 (29)   | 0.693              |
| Female   | 58 (77.2)  | 6 (69)   | 0.693              |
| Diabetes mellitus                                    | 27 (37.2))                                       | 2 (29)   | 0.739              |
| Hypertension   | 52 (70.6)  | 7 (79)   | 0.717              |
| Dyslipidemia   | 56 (75)  | 8 (89)   | 0.438              |
| Obesity (BMI > 30)                                   | 34 (46.6)  | 3 (39)   | 0.747              |
| Smoking  | 14 (19)  | 1 (19)   | 1                  |
| Age at 1 <sup>st</sup> echo, years, average $\pm$ SD | 54.91 $\pm$ 9.7                                  | 51.0 $\pm$ 5.96                                    | 0.233              |
| Follow-up duration, years, average $\pm$ SD          | 13.04 $\pm$ 2.47                                 | 13.2 $\pm$ 1.75                                    | 0.761              |

Table 2 displays the echocardiographic features of the patients in the 2 groupings. Patients in group A (those with indolent illness) had final echocardiographic evaluation MVA values that were considerably greater than those in group B (those with a progressing disease) ( $1.58 \pm 0.44$  vs.  $1.1 \pm 0.26$  cm<sup>2</sup>, respectively,  $p = 0.001$ ). Patients in group A had final mean pressure gradient values that were noticeably lower than those in group B ( $6.27 \pm 2.52$  vs.  $8.5 \pm 2.69$  mm Hg, respectively,  $p = 0.01$ ).

The yearly average of the MVA decreasing rate and mean gradient increasing rate also showed statistically significant variations between the subgroups: the MVA annual decreasing rate in group A patients was 0.027 versus 0.049 cm<sup>2</sup> in group B patients ( $p = 0.05$ ). Compared to group B patients, participants in group A experienced an annual rise in the mean gradient of 0.038 mm Hg ( $p = 0.001$ ) as opposed to 0.25 mm Hg.

**Table 2: Echocardiographic characteristics**

|                      | <b>Group A<br/>(indolent<br/>disease, n= 75)</b> | <b>Group B<br/>(Progressive<br/>disease, N=10)</b> | <b>P Value</b> |
|----------------------|--|--|----------------|
| Mean Gradient, mm Hg |  |  |                |
| 1 <sup>ST</sup> Echo | 5.76 $\pm$ 2.07                                  | 5.0 $\pm$ 1.63                                     | 0.333          |
| Last Echo            | 6.26 $\pm$ 2.51                                  | 8.4 $\pm$ 2.68                                     | 0.01           |
| Annual $\Delta$      | 0.037 $\pm$ 0.18                                 | 0.24 $\pm$ 0.11                                    | 0.001          |
| MVA, cm <sup>2</sup> |  |  |                |
| 1 <sup>ST</sup> Echo | 1.92 $\pm$ 0.47                                  | 1.74 $\pm$ 0.26                                    | 0.265          |

|           |              |              |       |
|-----------|--------------|--------------|-------|
| Last Echo | 1.57 ± 0.43  | 1.2 ± 0.28   | 0.001 |
| Annual Δ  | 0.026 ± 0.33 | 0.048 ± 0.23 | 0.265 |

Results pertaining to significant problems are shown in Table 3. Patients with indolent or progressive disease experienced the same incidence rate of serious complications, with no statistically significant variations. In both groupings, 80% of the patients experienced atrial fibrillation. Patients in group B had an earlier onset of atrial fibrillation, as measured in years from the initial

echocardiographic evaluation ( $5.5 \pm 3.59$  vs.  $7.55 \pm 5.12$  years,  $p = 0.347$ ), despite this not being statistically significant. Regarding the frequency of cerebral ischemia events and the interval between the initial echocardiographic evaluation and the occurrence of a stroke, there was no statistically significant difference between the two groups.

**Table 3: Long-term clinical complications**

|  | Group A<br>(indolent disease,<br>n= 75) | Group B<br>(Progressive disease,<br>N=10) | P<br>Value |
|--|---|---|------------|
| Years from 1 <sup>st</sup> echo to atrial fibrillation, average ± SD | 7.54 ± 5.11                             | 5.4 ± 3.58                                | 0.346      |
| Years from 1 <sup>st</sup> echo to stroke, average ± SD              | 8.4 ± 4.75                              | 10 ± 0                                    | 0.602      |
| Cerebral ischemic events   | 25 (33.32)                              | 2 (11)                                    | 0.165      |
| Atrial Fibrillation  | 59 (79)                                 | 7 (79)                                    | 1          |
| RV Injury  | 14 (19)                                 | 2 (29)                                    | 0.438      |
| Multiple Strokes (>1)  | 10 (14.66)                              | 2 (11)                                    | 1          |

## Discussion

Rheumatic MS usually progresses nearly immediately after diagnosis; some individuals will experience a significant and quick advancement with the development of symptoms in adolescence, while others will experience a more gradual progression [5-7]. Regarding the normal course of rheumatic MS in individuals with nonsevere disease at initial echocardiographic examination, there is little agreement in the medical community or literature.

In a study that spanned up to 10 years, Dubin et al. [8] examined serial hemodynamic data from 42 patients with mitral stenosis who underwent two or more cardiac catheterizations. Sixty-seven percent of the patients had progression, with a mean rate of valve area loss in this group over a mean follow-up period of two and a half years of 32 cm<sup>2</sup> per year,

compared to 33 percent who shown no change in valve area over a mean follow-up period of three and a half years. Symptomatic worsening over the follow-up period was more likely to occur in patients whose valve area decrease was progressing. This study was constrained by the fact that patients with more advanced diseases will be overrepresented in observational/retrospective studies of patients undergoing a second catheterization. As a result, it's possible that this study exaggerated the genuine prevalence of people with progressing disease.

13 patients with mitral stenosis in New York Heart Association functional class I or II were investigated by Leurcrtegger et al. [9] using M-mode echocardiograms spaced by a mean of 37 months. When they looked at the mitral valve closure index and EF slope, they discovered a

subgroup of 23% of the research group that showed more advancement. The EF slope and other M-mode metrics have now been shown to have significant limitations in assessing the degree of mitral stenosis [10], however its application in tracking changes in a single patient may still be appropriate [11].

Our study offers some advantages. In contrast to earlier studies with follow-up lengths ranging from 28 to 40 months [12,13], our study's average follow-up duration of 13 years (range 10–19) offers more accurate data and a better knowledge of the natural history and course of the disease. The main goal of studies with extended follow-up periods, which ranged from 10 to 26 years [14,15], was to evaluate survival over time. Furthermore, physical examination was used to diagnose mitral valve stenosis at the time because echocardiographic tests were not yet commonplace. [16]

Additionally, our study has several drawbacks. First of all, this analysis is retrospective, which has all the associated risks. Second, even though the echocardiographic assessments were based on predetermined standards, minute variations in the exact measurements made by the technicians during the test cannot be completely ruled out (although there would not necessarily be expected to be a difference between the subgroups in this aspect). As a result, it's possible that our conclusions cannot always be extrapolated to nations with more uniform populations. Finally, the subgroups' patient counts were relatively low, which could have impacted statistical comparison.

### Conclusion

In conclusion, the majority of young adult patients with non-severe rheumatic MS appear with a natural course that is slow. However, the valvular disease's generally sluggish course does not shield against serious clinical consequences. Our research also reveals that patients have a

higher risk of developing a chronic illness. Therefore, we advise cardiologists who care for patients to take into account a higher frequency of follow-up appointments and more successful primary preventive strategies targeted at this group.

### References

1. Rowe IC, habit RF, Spague His, White PD, Tin emcee of mitral stn-is wihoct surgery: ten. And my-year penpectiees. *Are Intern Med* 1960 :57 :74:-9.
2. Otneen Kit. The nmnal histon'of 271 patients with 61.11 stenosis under Medical treatment. *Br Heart* 1196224:349-57.
3. Grant RT. After histories rot ten years of 1000 men eufering trots heart disease: a study in prognosis. *Heart* 1933:16 :275-483.
4. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al.; American Society of Echocardiography; European Association of Echocardiography. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. *J Am Soc Echocardiogr.* 2009 Jan; 22(1):1–23
5. Rothenbühler M, O'Sullivan CJ, Stortecky S, Stefanini GG, Spitzer E, Estill J, et al. Active surveillance for rheumatic heart disease in endemic regions: a systematic review and metaanalysis of prevalence among children and adolescents. *Lancet Glob Health.* 2014 Dec; 2(12):e717–26.
6. Carroll JD, Feldman T. Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. *JAMA.* 1993 Oct; 270(14):1731–6.
7. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al.; American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. 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. *J Am Coll Cardiol.* 2014 Jun;63(22):e57–185.
8. Dabin AA- March Hey. Cute K. Seler A. Lon hood. t hemodyn and clinical study armitral sneasis. *Circulation* 1971;44:181-0
  9. Leuterogger F. Reefer FA, Fromer M, Fdlath F. Burckhavtl D. P0oFession of raid rearal stenoss and incidnee of resleaasis aft" open comtnis molonry: and, saes rsho@diognpiy. *Am Heal J* 194'940. 562-6.
  10. Nichol PM, Githen BW, Kiseb IA. Two. Dimeudonaleclocadio Wepl is se .-or astral stenosis Ceel .Oon 99TJ:55.-TV-g.
  11. Feogetrbanm H. Ed-indbpaphy.41b ed, Pta'hdellfhia : Leak Fehiger. AM 231
  12. Sagie A, Freitas N, Padiar LR, Leavitt M, Morris E, Weyman AE, et al. Doppler echocardiographic assessment of long-term progression of mitral stenosis in 103 patients: valve area and right heart disease. *J Am Coll Cardiol.* 1996 Aug;28(2):472–9.
  13. Aguilar, R. Fatigue symptom and oximetry sign in a patient with a positive Covid-19 antigen test for Sars-Cov-2. *Journal of Medical Research and Health Sciences*, 2022;5(8):2165–2176.
  14. Faletta F, De Chiara F, Crivellaro W, Mantero A, Corno R, Brusoni B. Echocardiographic follow-up in patients with mild to moderate mitral stenosis: is a yearly examination justified? *Am J Cardiol.* 1996 Dec;78(12):1450–2.
  15. Rowe JC, Bland EF, Sprague HB, White PD. The course of mitral stenosis without surgery: ten- and twenty-year perspectives. *Ann Intern Med.* 1960 Apr;52(4):741–9.
  16. Olesen KH. The natural history of 271 patients with mitral stenosis under medical treatment. *Br Heart J.* 1962 May;24(3):349–57.