Indian Heart Journal xxx (xxxx) xxx

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

Prevalence of silent brain lesions in rheumatic mitral valve disease

Vatsal Singh [a], Lokesh Chaudhari [b], Darshan Krishnappa [b], Bhagya Narayan Pandit [c], Deepak Padmanabhan [d,*]

[a] Himalayan Institute of Medical Science, SRHU, Dehradun, India
[b] Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, India
[c] Dr Ram Manohar Lohia Hospital, ABVIMS, New Delhi, India
[d] Narayana Institute of Cardiac Sciences, Bengaluru, India

ARTICLE INFO

Keywords:
Rheumatic heart disease
Mitral valve disease
Stroke
Atrial fibrillation
Silent brain lesions

ABSTRACT

Background: Patients with rheumatic heart disease (RHD) are at high risk of stroke. Silent brain lesions (SBL) on brain MRI represent subclinical neurological injury, but their prevalence and predictors in RHD are not well defined.

Methods: We conducted a prospective, single-center study of consecutive adults with RHD and moderate-to-severe mitral valve disease. Patients with a history of stroke, hypertension, diabetes, smoking, or ventricular dysfunction were excluded. All participants underwent a standardized protocol including clinical assessment, electrocardiography, echocardiography, and 3T brain MRI.

Results: Among 79 patients (mean age 44.3 ± 11.4 years, 69.6% female), SBL were present in 14 (17.7%). Most patients (81%; $n = 64$) had atrial fibrillation (AF). The prevalence of SBL was similar between those with AF and those in sinus rhythm (17.2% vs. 20%). There were no significant differences in age, gender, valve lesion type (stenosis vs. regurgitation), left atrial size, or the presence of LAA thrombus between patients with and without SBL. The majority of SBL (85.7%) were located in cortical regions.

Conclusions: Silent brain lesions on MRI were detectable in 17.7% RHD patients with significant mitral valve disease, even in the absence of traditional stroke risk factors. We did not find any association between occurrence of these brain lesions and atrial fibrillation or left atrial enlargement. Alternative mechanisms like pro-thrombotic states or atrial cardiomyopathy may be responsible. These findings warrant further investigation into the clinical significance and management of subclinical brain injury in RHD.

1. Introduction

Rheumatic heart disease (RHD) is a significant cause of stroke in developing countries, where around 3 to 7.5% of all strokes are attributable to RHD.[1] The risk of clinical stroke in RHD is well-known but the burden of subclinical cerebrovascular injury remains poorly characterized, particularly in patients without AF.

Most of these patients are young and lack traditional risk factors. While stroke is often considered a sequela of left atrial (LA) enlargement and atrial fibrillation (AF),[2,3] other factors also contribute. These include altered hemodynamics with deranged cerebrospinal fluid drainage,[4] left atrial cardiomyopathy,[5] systemic inflammation,[6] auto-immunity[7] and increased thrombogenicity,[8] that predispose them to neurological insults. Furthermore, paroxysmal AF episode may remain undetected.

It is also important to note that the neurological insults from these factors do not always manifest as clinical stroke. Subclinical neurological injuries are identifiable on magnetic resonance imaging (MRI) as silent brain lesions (SBL).[9,10] This study aimed to determine the prevalence of SBL in RHD patients with significant mitral valve disease.

2. Methods

We conducted a single center prospective study among consecutively enrolled adult (>18 years) RHD patients with moderate to severe mitral stenosis or mitral regurgitation. The screening protocol included clinical examination, standard 12-lead electrocardiogram (ECG), and trans-thoracic echocardiography (TTE). AF was diagnosed based on ECG and

* Corresponding author. Narayana Institute of Cardiac Sciences, Bengaluru, India.
E-mail addresses: vatsalsingh27@gmail.com (V. Singh), drlokeshpc@gmail.com (L. Chaudhari), darshankrishnappa@gmail.com (D. Krishnappa), bnpandit1977@gmail.com (B.N. Pandit), deepak.padmanabhan@gmail.com (D. Padmanabhan).

https://doi.org/10.1016/j.ihj.2026.05.001
Received 3 March 2026; Received in revised form 5 May 2026; Accepted 16 May 2026
Available online 19 May 2026

medical records, and classified as paroxysmal (episodes lasting ≤7 days) or persistent (episodes lasting >7 days).[11] Echocardiographic evaluation and grading of valvular lesions followed World Heart Federation guidelines.[12] Left atrial (LA) size was measured in the parasternal long-axis view using M-mode. A transesophageal echocardiogram (TEE) was performed to assess for left atrial appendage (LAA) thrombus. Exclusion criteria were: severe non-mitral valvular disease, left or right ventricular dysfunction (left ventricular ejection fraction <50% or more than mild right ventricular dysfunction), prior history of stroke or transient ischemic attack, diabetes, hypertension, smoking, alcohol or intravenous drug use, and known neuropsychiatric illness.

Contrast-enhanced brain MRI was performed using a 3.0 T scanner with the following sequences: axial diffusion-weighted imaging (DWI), axial fluid-attenuated inversion recovery (FLAIR), axial T1-and T2-weighted imaging, and time-of-flight angiography. Brain lesions detected on MRI were categorized into white matter hyperintensities and cortical/subcortical lesions. White matter hyperintensities were defined as presence of hyperintense foci on FLAIR and T2-weighted imaging, located in periventricular or deep white matter. Cortical/subcortical lesions were defined as focal hyperintensities on T2/FLAIR with corresponding hypo-intensity on T1, ≥3 mm in size, in a vascular distribution. All the MRI scans were interpreted randomly by one of the two radiologists of the institution, blinded to the clinical data.

Statistical analysis was performed using *IBM SPSS software (version 21.0)*. Continuous variables are presented as mean ± standard deviation, and categorical variables as proportions and percentages. Groups with and without SBL were compared using the chi-square test for categorical variables and the *t*-test (parametric) or Mann–Whitney *U* test (non-parametric) for continuous variables.

3. Results

The study included 79 consecutive RHD patients with moderate-to-severe mitral valve disease, of whom 64(81%) had AF and 15(19%) were in sinus rhythm. Baseline characteristics are shown in Table 1. The mean age was 44.3 ± 11.4 years, and 55 (69.6%) were female. SBL were present in 14 patients (17.7%). Baseline clinical characteristics did not differ between patients with and without SBL.

Among the 64 patients with AF (mean age 46 ± 11.8 years), the prevalence of SBL was not significantly different from those in sinus rhythm (20% vs. 17.2%, respectively). LAA thrombus was detected in 7 (11.3%) patients with AF and 1(6.7%) patient in sinus rhythm ($p = 0.5$). All three patients with SBL in sinus rhythm had moderate-to-severe isolated mitral stenosis. The distribution of mitral valve lesions was: 41 (51.9%) with MS, 21 (26.6%) with MR, and 17 (21.5%) with mixed disease. The proportion of SBL in these groups was 19.5%, 19%, and 14.3%, respectively (Table 2). The number and distribution of SBL by rhythm is shown in Table 2 and Fig. 1. Since the number of events ($n = 14$) in comparison to the possible risk factors was very small, a regression analysis was not applicable.

Table 1
Baseline characteristics.

Parameters	SBL present ($n = 14$)	No SBL ($n = 65$)	P
Age (years)	48.6 ± 11.1	43.7 ± 11.6	0.154[a]
Gender (male)	6 (42.8%)	19(29.2%)	0.320[b]
Atrial Fibrillation	11(78.6%)	51(78.5%)	0.993[b]
Mitral valve area (cm^2)	1.3 ± 0.7	1.4 ± 0.7	0.392[c]
Moderate-severe mitral stenosis	8(57.1%)	33(50.7%)	0.826[b]
Moderate-severe mitral regurgitation	4(28.6%)	17(26.2%)	0.853[b]
Moderate-severe mixed mitral lesion	2(14.3%)	15(23.1%)	0.468[b]
Moderate-severe tricuspid regurgitation	7(50%)	22(33.8%)	0.255[b]
Left atrial appendage clot	2(14.3%)	6(9.2%)	0.570[b]
Left atrial size M-mode (cm)	5.1 ± 0.9	5.3 ± 1.1	0.140[c]

SBL-Silent brain lesions.
[a] *t*-test.
[b] chi-square test.
[c] Mann–Whitney test.

4. Discussion

Our study demonstrates that RHD patients without traditional stroke risk factors are predisposed to neurological injuries, detectable as SBL on MRI. SBL, including cortical lesions and white matter hyperintensities, represent neuronal demyelination or apoptosis, appearing as hyperintensities on T2-weighted or FLAIR sequences,[9,10] and are known to be associated with stroke and functional disability.[13,14]

The prevalence of SBL in our cohort was 17.7%. Patients with and without SBL did not differ in age, gender, or ECG and echocardiographic characteristics. A previous study of 53 mitral stenosis patients reported silent brain lesions in 24.5% of patients, with a higher incidence in those with AF and larger LA size.[15] In our study, the prevalence of SBL was similar in patients with sinus rhythm (20%) and AF (17.2%). The absence of association between SBL and AF should be interpreted in the context of a very small number of sinus rhythm patients ($n = 15$) and those with SBL in sinus rhythm ($n = 3$). AF may not be a prerequisite for SBL. According to previous reports, nearly 20% of systemic thromboembolisms occur without AF.[16]

The pathophysiology of SBL remains unclear. Certain non-AF related mechanisms may be predominant drivers of subclinical brain injury. Proposed mechanisms include left atrial cardiomyopathy, hypercoagulability, predisposition to LAA thrombus, hemodynamic changes, and systemic inflammation. Atrial cardiomyopathy has been linked to stroke, cognitive decline, and dementia.[17] Lee et al reported that mean right atrial pressure is independently associated with SBL volume in chronic valvular heart disease.[18] Our limited M-mode data of left atrium does not support this finding though. Interestingly, SBL are also documented in apparently healthy elderly subjects, with prevalence increasing with age and associated with dementia, gait abnormalities, and stroke risk [19–21].

The prevalence of SBL was similar across valve lesion types: 19.5% in MS, 19% in MR, and 14.3% in mixed disease. Notably, all patients in sinus rhythm with SBL had isolated MS. Most SBL were located in the cortical areas of the frontal and parietal lobes (85.7%). Basal ganglia lesions were present in 4 (28.5%) patients, and 1 (7.1%) had a cerebellar lesion. No distinct pattern was observed based on rhythm or valvular characteristics. Akdemir et al reported 47% cortical and 53% lacunar silent infarcts in RHD patients with mitral stenosis.[15] The variation in SBL type may be due to differences in regional blood supply.[9]

Although SBL are associated with adverse neurological outcomes, their long-term follow-up in RHD patients is unknown. The

Table 2
Prevalence of silent brain lesions in RHD patients, stratified by cardiac rhythm and type mitral valve pathology.

Patients	All	Sinus rhythm	Atrial Fibrillation	Types of SBL
Rheumatic mitral disease	$n = 79$ SBL = 14 (17.7%)	$n = 15$ SBL = 3 (20%)	$n = 64$ SBL = 11 (17.2%)	9 Cortical, 2 basal ganglia, 2 cortical + basal ganglia, 1 cortical + cerebellar
Isolated mitral stenosis	$n = 41$ SBL = 8 (19.5%)	$n = 13$ SBL = 3 (23.1%)	$n = 28$ SBL = 5 (17.9%)	6 cortical, 1 basal ganglia, 1 both
Isolated mitral regurgitation	$n = 21$ SBL = 4 (19%)	$n = 1$ SBL = 0 (0%)	$n = 20$ SBL = 4 (20%)	2 cortical, 1 basal ganglia, 1 both
Mixed mitral valve disease	$n = 17$ SBL = 2 (14.3%)	$n = 1$ SBL = 0 (0%)	$n = 16$ SBL = 2 (12.5%)	1 cortical, 1 cortical + cerebellar

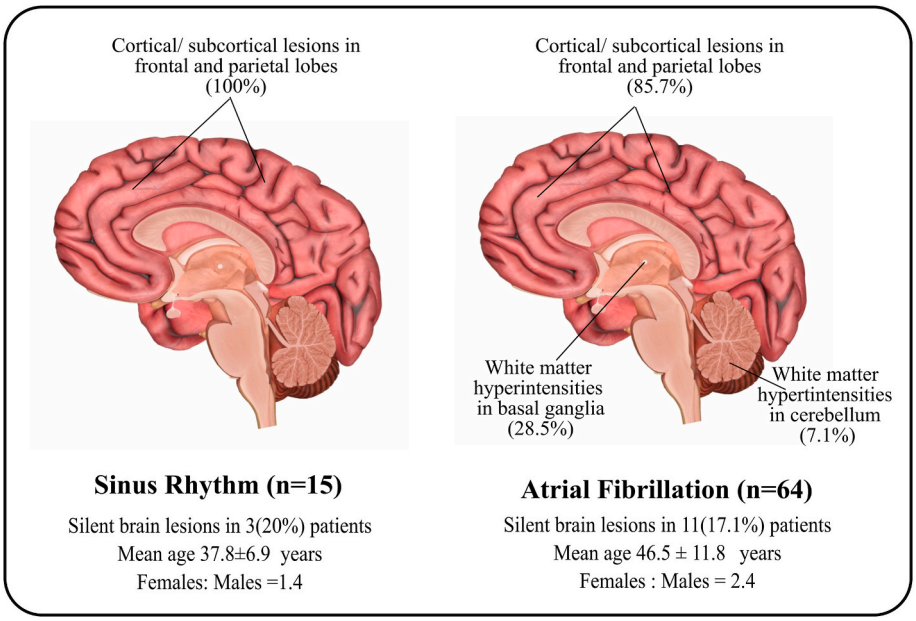

Fig. 1. Central illustration: distribution of silent brain lesions in rheumatic mitral valve disease patients.

neuropsychiatric consequences of SBL in this population remain largely unexplored, and there is no consensus on management, highlighting the limited pathophysiological understanding of these lesions.

4.1. Limitations

Our study has several limitations. The number of patients in sinus rhythm was low, particularly those with MR and mixed valve disease. We did not use the Fazeka's score to quantify SBL severity (that limits comparison of our findings to other studies) and lacked a control group to determine the incidental detection rate in a healthy, age- and sex-matched population. While SBL are typically reported in older populations (>60 years) and our cohort's mean age was 44.6 years, their presence in healthy young individuals cannot be ruled out. The echocardiographic assessment of left atrium was limited, including only M-mode data without volumetric analysis. Finally, we did not use long-term ECG monitoring to detect paroxysmal AF, so those patients could have been misclassified as having sinus rhythm.

5. Conclusion

Silent brain lesions were detected in 17.7% on brain MRI in RHD patients with significant mitral valve disease, absent a history of prior stroke or traditional risk factors. We did not detect any significant association of SBL with cardiac rhythm or left atrial characteristics. The paradigm for cerebral injury in RHD should be expanded beyond AF. Further prospective trials are needed to study clinical outcomes and management strategies in these patients.

Disclosures

None.

Presentation at a meeting

None.

Ethical statement

This study was performed with the approval of institutional ethical committee.

Source(s) of support

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *Lancet Infect Dis*. 2005;5(11):685–694.
2. Vasconcelos M, Vasconcelos L, Ribeiro V, et al. Incidence and predictors of stroke in patients with rheumatic heart disease. *Heart*. 2021;107(9):748–754.
3. Gupta A, Bhatia R, Sharma G, Prasad K, Singh MB, Vibha D. Predictors of ischemic stroke in rheumatic heart disease. *J Stroke Cerebrovasc Dis*. 2015;24(12):2810–2815.
4. Jefferson AL, Beiser AS, Himali JJ, et al. Low cardiac index is associated with incident dementia and Alzheimer disease: the framingham heart study. *Circulation*. 2015;131(15):1333–1339.
5. Chen LY, Ribeiro ALP, Platonov PG, et al. P wave parameters and indices: a critical appraisal of clinical utility, challenges, and future research. *Circ Arrhythm Electrophysiol*. 2022;15(4), e010435.
6. Franczyk B, Gluba-Brzózka A, Rysz-Górzyńska M, Rysz J. The role of inflammation and oxidative stress in rheumatic heart disease. *Int J Mol Sci*. 2022;23(24), 15812.
7. Carapetis JR, Beaton A, Cunningham MW, et al. Acute rheumatic fever and rheumatic heart disease. *Nat Rev Dis Primers*. 2016;2(1), 15084.
8. Toy JL, Lederer DA, Tulpule AT, Tandon AP, Taylor SH, McNicol GP. Coagulation studies in rheumatic heart disease. *Heart*. 1980;43(3):301–305.
9. Lin J, Wang D, Lan L, Fan Y. Multiple factors involved in the pathogenesis of white matter lesions. *BioMed Res Int*. 2017;2017:1–9.
10. Fazekas F, Enzinger C, Ropele S, Schmidt R. White matter changes. In: Wahlund LO, Erkinjuntti T, Gauthier S, eds. *Vascular Cognitive Impairment in Clinical Practice*. 1st ed. Cambridge University Press; 2009:131–138.
11. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J*. 2020. ehaa612.
12. Reményi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline. *Nat Rev Cardiol*. 2012;9(5):297–309.
13. Wong TY, Klein R, Sharrett AR, et al. Cerebral white matter lesions, retinopathy, and incident clinical stroke. *JAMA*. 2002;288(1):67–74.
14. Kuller LH, Longstreth WT, Arnold AM, et al. White matter hyperintensity on cranial magnetic resonance imaging: a predictor of stroke. *Stroke*. 2004;35(8):1821–1825.
15. Akdemir I, Dagdelen S, Yuce M, Davutoglu V. Silent brain infarction in patients with rheumatic mitral stenosis. *Jpn Heart J*. 2002;43:137–144.
16. Shenthar J. Management of atrial fibrillation in rheumatic heart disease. *Heart Rhythm O2*. 2022;3(6):752–759.

17. Kamel H, Okin PM, Longstreth WT, Elkind MS, Soliman EZ. Atrial cardiopathy: a broadened concept of left atrial thromboembolism beyond atrial fibrillation. *Future Cardiol*. 2015;11:323–331.
18. Lee WJ, Jung KH, Ryu YJ, et al. Association of cardiac hemodynamic factors with severity of white matter hyperintensities in chronic valvular heart disease. *JAMA Neurol*. 2018;75(1):80.
19. Ylikoski A, Erkinjuntti T, Raininko R, Sarna S, Sulkava R, Tilvis R. White matter hyperintensities on MRI in the neurologically non-diseased elderly: analysis of cohorts of consecutive subjects aged 55 to 85 years living at home. *Stroke*. 1995;26(7):1171–1177.
20. Debette S, Markus HS. The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: systematic review and meta-analysis. *BMJ*. 2010;341:c3666. c3666.
21. Garde E, Mortensen EL, Krabbe K, Rostrup E, Larsson HB. Relation between age-related decline in intelligence and cerebral white-matter hyperintensities in healthy octogenarians: a longitudinal study. *Lancet*. 2000;356(9230):628–634.