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Left Atrial Reservoir Strain in Mitral Valve Prolapse: A Systematic Review and Meta-Analysis of Clinical, Pathophysiological, and Prognostic Implications

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ADMINISTRATIVE INFORMATION**Support** - No funding.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY2026100106**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2026 and was last updated on 26 October 2026.**INTRODUCTION**

Review question / Objective To determine whether left atrial reservoir strain (LASr) is impaired in adults with mitral valve prolapse (MVP), and to assess its relationship with mitral regurgitation severity, atrial remodeling, MVP phenotype, and clinically relevant outcomes. The review also aims to quantify the difference in LASr between patients with MVP and control subjects and to explore the potential diagnostic and prognostic value of LASr across different clinical settings.

Rationale Left atrial reservoir strain (LASr) provides a sensitive measure of atrial mechanical function and may detect functional impairment before conventional markers such as left atrial enlargement or left ventricular systolic dysfunction become evident. In mitral valve prolapse (MVP), available studies have reported reduced LASr across heterogeneous clinical phenotypes, including patients with mild or absent mitral regurgitation as well as those with advanced

degenerative disease. However, the magnitude of LASr impairment, its relationship with MVP morphology and mitral regurgitation severity, and its potential prognostic value remain inconsistently defined across studies. A systematic synthesis is therefore needed to clarify the role of LASr in MVP, quantify differences versus control populations, and identify factors that may explain variability in reported findings.

Condition being studied Mitral valve prolapse (MVP), including its different morphological and clinical phenotypes, with particular attention to left atrial mechanical dysfunction assessed by left atrial reservoir strain (LASr). The review includes patients across the spectrum of mitral regurgitation severity, from absent or mild regurgitation to advanced degenerative disease requiring mitral valve intervention.

METHODS

Search strategy A systematic search will be conducted in PubMed/MEDLINE, Scopus, and

Embase from database inception to 2026. The strategy will combine terms related to left atrial deformation and function with terms identifying mitral valve prolapse and related phenotypes. Search concepts will include “left atrial strain,” “left atrial reservoir strain,” “atrial reservoir strain,” “left atrial longitudinal strain,” “left atrial deformation,” “PALS,” “LASr,” “LARS,” and “left atrial function,” combined with “mitral valve prolapse,” “MVP,” “Barlow disease,” “Barlow valve,” “bileaflet prolapse,” “mitral leaflet prolapse,” and “flail leaflet.” Controlled vocabulary, including MeSH and Emtree terms, will be used when available. Database-specific field tags and syntax will be applied for each platform. Reference lists of eligible articles will also be screened for potentially relevant studies.

Participant or population Adults with mitral valve prolapse (MVP), including Barlow disease, bileaflet or monoleaflet prolapse, and flail leaflet phenotypes. Patients will be eligible across the full spectrum of mitral regurgitation severity and clinical presentation, including asymptomatic individuals, patients with moderate-to-severe degenerative mitral regurgitation, and those undergoing mitral valve surgery. Studies including broader populations with primary mitral regurgitation will be considered only when data for patients with MVP can be separately identified.

Intervention Assessment of left atrial reservoir strain (LASr) using non-invasive cardiac imaging, primarily two-dimensional speckle-tracking echocardiography and, where available, cardiovascular magnetic resonance feature tracking. LASr will be considered as the index test/exposure of interest rather than a therapeutic intervention.

Comparator For the quantitative meta-analysis, the comparator will consist of control subjects without mitral valve prolapse and without relevant structural heart disease, whenever such a group is available. For prognostic and phenotype-based analyses, comparisons may also involve subgroups of patients with MVP defined by mitral regurgitation severity, valve morphology, mitral annular disjunction, or clinical outcome.

Study designs to be included Prospective and retrospective observational cohort studies, cross-sectional studies, case-control studies, and registry-based investigations reporting quantitative data on left atrial reservoir strain in adults with mitral valve prolapse. Both single-centre and multicentre studies will be eligible. Studies may address cross-sectional associations, disease

phenotyping, postoperative remodeling, or longitudinal clinical outcomes.

Eligibility criteria Studies will be eligible if they include adult patients with mitral valve prolapse and report extractable quantitative data on left atrial reservoir strain assessed by echocardiography or cardiovascular magnetic resonance. Studies involving Barlow disease, bileaflet or monoleaflet prolapse, and flail leaflet will be considered, irrespective of mitral regurgitation severity or clinical setting. Broader cohorts with primary mitral regurgitation will be included only when data for the MVP subgroup are separately available.

Eligible reports must provide original data from observational cohorts, cross-sectional studies, case-control studies, or registries. Studies will be excluded if they do not include MVP, do not report LASr or provide sufficient data for its extraction, assess only other atrial deformation indices, or lack adequate quantitative information for qualitative or quantitative synthesis. Reviews, meta-analyses, editorials, letters without original data, conference abstracts with insufficient information, case reports, and small descriptive case series will be excluded. For overlapping populations, the most informative report will be retained unless separate publications provide distinct non-duplicated outcomes.

Information sources Electronic searches will be performed in PubMed/MEDLINE, Scopus, and Embase from database inception through 2026. Reference lists of eligible full-text articles will also be examined to identify additional potentially relevant studies. Only published studies providing sufficient original quantitative data for the planned qualitative or quantitative synthesis will be considered.

Main outcome(s) The primary outcome will be left atrial reservoir strain (LASr) in patients with mitral valve prolapse, including its absolute values and its difference compared with control subjects when a suitable comparator group is available. For the quantitative synthesis, the principal effect measure will be the standardized mean difference in LASr between MVP and control groups.

Additional main outcomes will include the association of LASr with mitral regurgitation severity, left atrial remodeling, MVP phenotype, and clinically relevant events such as need for mitral valve surgery, postoperative atrial remodeling, cardiovascular events, and arrhythmic outcomes.

Additional outcome(s) Secondary outcomes will include relationships between LASr and conventional clinical or imaging markers of disease severity, including left atrial volume, pulmonary artery pressure, left ventricular systolic and deformation indices, mitral regurgitation severity, bileaflet involvement, Barlow phenotype, flail leaflet, and mitral annular disjunction. Where reported, associations with functional status, atrial fibrillation, ventricular arrhythmias, postoperative ventricular function, and residual left atrial enlargement will also be collected. Methodological differences in LASr assessment, including imaging modality, acquisition approach, and analysis software, will be explored as potential sources of between-study variability.

Data management Data from eligible studies will be independently extracted by two reviewers using a standardized electronic spreadsheet developed for this review. Extracted variables will include study characteristics, population features, clinical and echocardiographic data, mitral valve phenotype, mitral regurgitation severity, imaging modality and LASr methodology, as well as follow-up duration, clinical outcomes, and effect estimates when available. Each study will contribute one value per variable to the descriptive synthesis whenever possible. Missing data will not be imputed. Discrepancies between reviewers will be resolved through discussion and consensus. Extracted data will be checked for internal consistency before qualitative synthesis and meta-analysis.

Quality assessment / Risk of bias analysis

Methodological quality and risk of bias will be independently evaluated by two reviewers using the National Institutes of Health/National Heart, Lung, and Blood Institute (NIH/NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. The tool examines 14 methodological domains, including clarity of the research question, population selection, participation rate, eligibility criteria, sample-size justification, temporal relationship between exposure and outcome, validity and reliability of measurements, repeated exposure assessment, follow-up, assessor blinding, and control of potential confounding.

Each domain will be rated as Yes, No, Cannot Determine, Not Reported, or Not Applicable. An overall study-quality judgment of Good, Fair, or Poor will be assigned through qualitative appraisal of the applicable domains rather than by calculating a numerical score. Any disagreement between reviewers will be resolved by discussion

and consensus. Detailed guidance for domain interpretation will follow the NIH/NHLBI Study Quality Assessment Tools.

Strategy of data synthesis A qualitative synthesis will first describe the clinical, echocardiographic, and methodological characteristics of the included studies. Study-level continuous variables and proportions will be summarized using unweighted medians and minimum–maximum ranges when sufficiently reported.

For studies providing comparable LASr values in patients with MVP and control subjects, quantitative pooling will be performed using standardized mean differences (SMDs) with 95% confidence intervals. Both fixed-effect and random-effects models will be calculated, with the random-effects model considered primary because of anticipated clinical and methodological heterogeneity. Between-study heterogeneity will be assessed using Cochran's Q , I^2 , τ^2 , and τ .

Potential small-study effects will be explored by funnel-plot inspection and Egger's regression test when appropriate. Exploratory random-effects meta-regression will assess whether imaging modality and selected study-level clinical characteristics account for between-study variability. Robustness of the pooled estimate will be examined through leave-one-out sensitivity analysis. Statistical significance will be defined as a two-sided p value <0.05 .

Subgroup analysis Where sufficient data are available, subgroup analyses will explore differences in LASr according to clinically relevant MVP characteristics, including mitral regurgitation severity, bileaflet versus monoleaflet involvement, Barlow phenotype, presence of mitral annular disjunction, and surgical versus non-surgical clinical setting. Additional subgroup comparisons may consider imaging modality, particularly two-dimensional speckle-tracking echocardiography versus cardiovascular magnetic resonance feature tracking. Subgroup analyses will only be performed when the number of available studies and consistency of reporting allow meaningful quantitative comparison; otherwise, findings will be described narratively.

Sensitivity analysis The robustness of the quantitative findings will be assessed using a leave-one-out approach, sequentially excluding each study from the random-effects meta-analysis and recalculating the pooled standardized mean difference and 95% confidence interval. This analysis will be used to determine whether the

overall effect estimate is disproportionately influenced by any single study. Where appropriate, additional sensitivity analyses may be considered according to study quality or methodological differences, provided that the number of available studies is sufficient for meaningful comparison.

Language restriction Only studies published in English will be considered eligible for inclusion. No additional language restrictions will be applied.

Country(ies) involved Italy.

Other relevant information Any important deviation from the registered protocol occurring during completion of the review will be documented and justified in the final publication. As this study is based exclusively on previously published data, no individual patient-level information will be collected and no additional ethical approval is required.

Keywords Mitral valve prolapse; left atrial reservoir strain; left atrial strain; speckle-tracking echocardiography; mitral regurgitation; left atrial remodeling; risk stratification.

Dissemination plans The findings of this systematic review and meta-analysis will be submitted for publication in a peer-reviewed cardiovascular imaging or valvular heart disease journal. Results may also be presented at national or international scientific meetings. Any subsequent dissemination will report the methods and findings in accordance with PRISMA recommendations and will reference the INPLASY registration.

Contributions of each author

Author 1 - Andrea Sonaglioni - Drafted the manuscript.

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