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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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Atrial Longitudinal Strain Predicts New-Onset Atrial Fibrillation

A Systematic Review and Meta-Analysis

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in adults, with a prevalence of 2% to 4%.[1] AF is associated with a higher risk of cardiovascular events, including thromboembolism, stroke, left ventricular dysfunction, and heart failure (HF), with huge consequences on quality of life and public health. Identifying individuals at risk of developing AF could facilitate targeting preventive interventions and screening for early AF detection. Left atrial longitudinal strain (LAS) could provide additional information on atrial structure and function among traditional echocardiographic indexes. LAS is assessed by speckle-tracking analysis of the left atrial (LA) wall during the cardiac cycle. The atrial function studied by LAS consists of 3 phases: the reservoir (LASr), the conduit (LAScd) and the contraction (LASct) phase. During the last few years, some studies investigated the relationship of LAS with the risk of new-onset atrial fibrillation (NOAF). We performed a systematic review and meta-analysis to define the potential role and the clinical application of this functional parameter to predict NOAF.

The systematic review protocol and the statistical analysis methodology have been registered and reported in OSF.[2] Two expert cardiologists (B.D., A.C.) independently and systematically searched Medline, Cochrane Library, and Biomed Central for trials evaluating LAS derived from echocardiography and the occurrence of NOAF. The research was carried out in June 2022. The terms searched were: (atrial strain) AND (predict) AND (atrial fibrillation). This was supplemented by searching the reference lists of key reviews and all potentially relevant studies.

The database search yielded 761 records. After careful analysis 12 studies were finally selected for quantitative analysis (Figure 1A). Nine studies reported the univariate HR for the single-change unit of LASr, and 11 reported the adjusted HR from a multivariate model. All of the studies used a 2-chamber view approach (4-chamber and 2-chamber projections) for computing LAS. We focused our analysis on LASr.

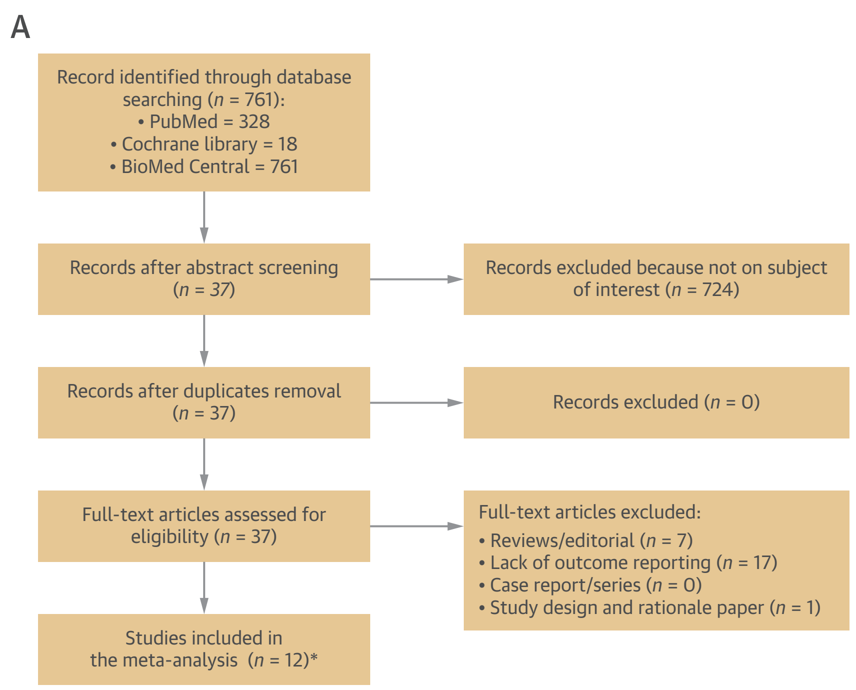
Overall, 2,039 patients were included in the primary analysis, showing a pooled HR with inverse variance mixed effect model for NOAF of 0.89 (95% CI: 0.88-1.31) for a single-change unit in LAS, with no significant heterogeneity ($I^2 = 13.4\%$; $P = 0.32$).

These results were also confirmed with sensitivity analysis using the leave-one-out approach. We performed a secondary analysis on 12 studies and 5,074 patients reporting adjusted HRs for LASr. All of the multivariable models included at least age as a covariate. The pooled HR was 0.96 (95% CI: 0.95-0.97) This analysis showed only minimal heterogeneity ($I^2 = 26.4\%$; $P = 0.185$). Visual assessment of the funnel plots did not suggest significant publication bias, as also supported by the results of Egger's test.

AF is part of the natural course of many cardiac diseases, and it has been reported that 20% to 30% of patients with HF have AF. The coexistence of AF and HF can be explained by sharing common risk factors (eg, older age, hypertension, diabetes, and obesity), comorbidities (eg, pulmonary and renal diseases), and common pathophysiologic mechanisms.

In HF, increased cardiac filling pressures and increased wall stress, autonomic and neuroendocrine dysfunction may lead to LA structural and functional remodeling with atrial fibrosis and electric instability, predisposing to the development of AF.[3] LA strain is a sensitive measure for detecting subclinical atrial impairment, and its use has grown exponentially in recent years. A recent meta-analysis of 40 studies and 2,542 patients showed an average reference value for LASr of 39% (95% CI: 39%-41%).[4]

FIGURE 1 **Outline of the Search Strategy and Pooled Analysis**

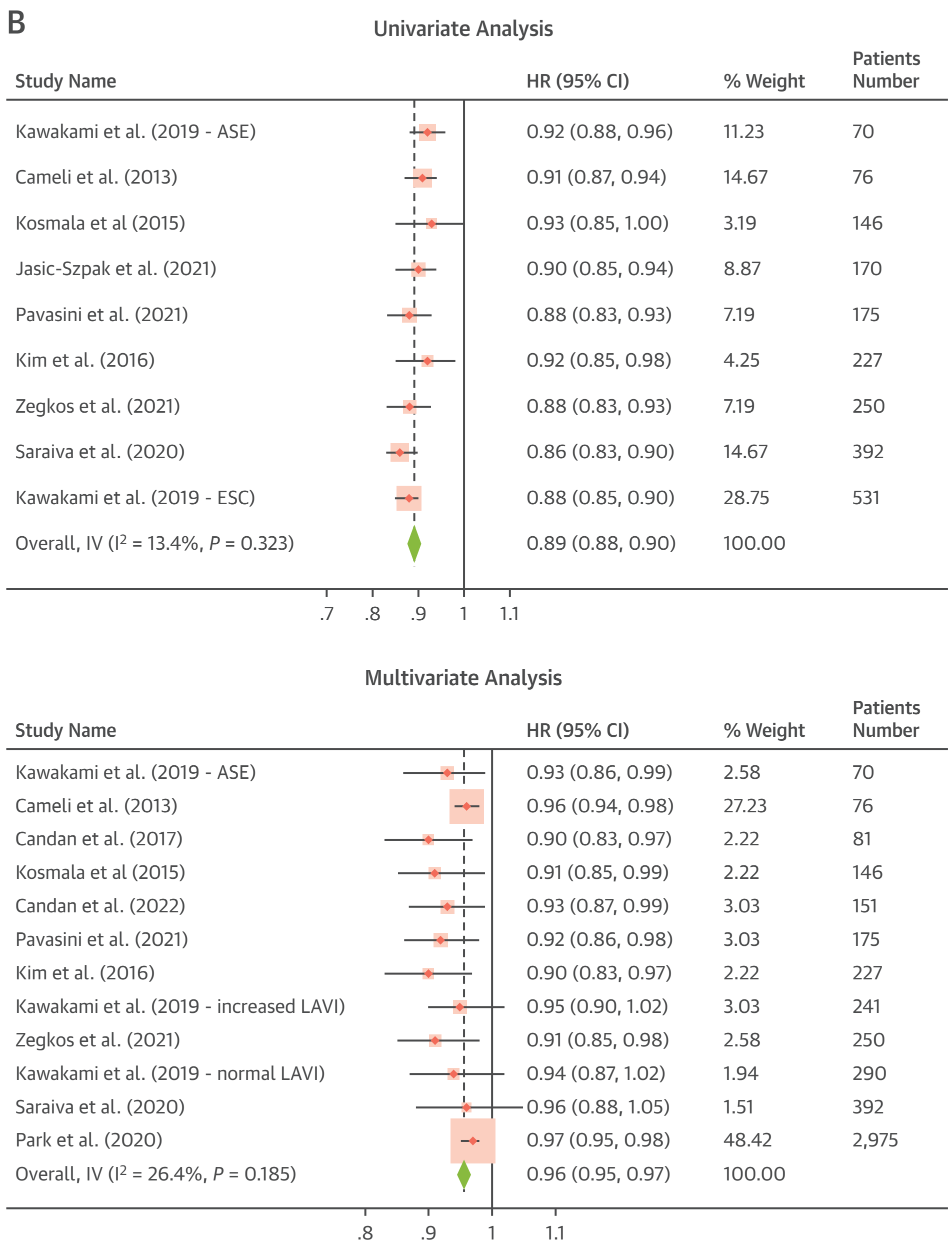


(A) Results of the search strategy according to the PRISMA flowchart and the references for the studies included in the quantitative analysis. **(B)** Univariate and multivariate pooled analyses using the inverse variance mixed effects model. Results from the multivariate analysis of the study by Kawakami et al[9] are presented in 2 groups (normal LAVI, enlarged LAVI), as in the original paper. *Park JJ, Park J-H, Hwang I-C, et al. Left atrial strain as a predictor of new-onset atrial fibrillation in patients with heart failure. *J Am Coll Cardiol Img.* 2020;13(10):2071-2081. Pavasini R, Fabbri G, Fiorio A, et al. Peak atrial longitudinal strain is predictive of atrial fibrillation in patients with chronic obstructive pulmonary disease and coronary artery disease. *Echocardiography.* 2021;38(6):909-915. Kawakami H, Ramkumar S, Pathan F, et al. Use of echocardiography to stratify the risk of atrial fibrillation: comparison of left atrial and ventricular strain. *Eur Heart J Cardiovasc Imaging.* 2020;21(4):399-407. Zegkos T, Ntelios D, Parcharidou D, et al. The predictive value of left ventricular and left atrial mechanics for atrial fibrillation and heart failure in hypertrophic cardiomyopathy: a prospective cohort study. *Int J Cardiovasc Imaging.* 2021;37(9):2679-2690. Kim D, Shim CY, Cho IJ, et al. Incremental value of left atrial global longitudinal strain for prediction of post stroke atrial fibrillation in patients with acute ischemic stroke. *J Cardiovasc Ultrasound*. 2016;24(1):20-27. Jasic-Szpak E, Marwick TH, Donal E, et al. Prediction of AF in heart failure with preserved ejection fraction: incremental value of left atrial strain. *J Am Coll Cardiol Img.* 2021;14(1):131-144. Candan O, Gecmen C, Kalayci A, et al. Left atrial electromechanical conduction time predicts atrial fibrillation in patients with mitral stenosis: a 5-year follow-up speckle-tracking echocardiography study. *Int J Cardiovasc Imaging.* 2017;33(10):1491-1501. Candan O, Cecmen C, Kahyaoğlu M, et al. Clinical utility of left atrial asynchrony and mechanical function in patients with hypertrophic cardiomyopathy. *Acta Cardiol Sin*. 2022;38(2):141-150. Cameli M, Lisi M, Reccia R, et al. Pre-operative left atrial strain predicts post-operative atrial fibrillation in patients undergoing aortic valve replacement for aortic stenosis. *Int J Cardiovasc Imaging.* 2014;30(2):279-286. Saraiva RM, Pacheco NP, Pereira TOJS, et al. Left atrial structure and function predictors of new-onset atrial fibrillation in patients with Chagas disease. *J Am Soc Echocardiogr.* 2020;33(11):1363-1374.e1. Kosmala W, Saito M, Kaye G, et al. Incremental value of left atrial structural and functional characteristics for prediction of atrial fibrillation in patients receiving cardiac pacing. *Circ Cardiovasc Imaging.* 2015;8(4):e002942. Kawakami H, Ramkumar S, Nolan M, et al. Left atrial mechanical dispersion assessed by strain echocardiography as an independent predictor of new-onset atrial fibrillation: a case-control study. *J Am Soc Echocardiogr.* 2019;32(10):1268-1276.e3. ASE = American Society of Echocardiography; ESC = European Society of Cardiology; IV = inverse variance; LAVI = left atrial volume index.

Continued on the next page

Left atrial longitudinal strain should be calculated as the longitudinal strain obtained from a non-foreshortened apical 4-chamber view. Recent guidelines suggest that biplane LA longitudinal strain (considering measurements obtained from both 4- and 2-chamber apical views) is an available option for measuring LAS.[5] Two methods are allowed to identify the reference frame of 0 strain, using: 1) the QRS complex to identify end-diastole; or 2) the P-wave to identify the initial atrial contraction. In both cases, it is recommended to use an electrocardiographic marker as a rough estimate and adjust the reference

FIGURE 1 Continued



frame according to the mitral inflow pattern (especially if the atrial contraction is chosen). In the present analysis, we gathered data from different studies in which LAS was always calculated by both 4- and 2-chamber apical views.

Preliminary findings from Russel et al[6] showed that LASr has higher accuracy in predicting the recurrence of AF after catheter ablation, especially in populations with normal left atrial volume index. In the same setting, similar findings were reported by Nielsen et al[7] showing an increased risk of AF recurrence (odds ratio: 1.03; 95% CI: 1.01-1.05) for each 1% decrease in LASr). Our pooled HR demonstrated similar prognostic importance also in patients without previous history of AF. We also observed that LASr consistently predicted NOAF in several patient groups: patients with HFrEF, HFpEF, Chagas disease, ischemic stroke, patients undergoing valvular replacement, and patients with COPD. Furthermore, it is noteworthy that multivariate analysis from most of the selected trials showed the independent prognostic value of LASr to predict NOAF and its addictive value over traditional echocardiographic parameters such as LA volume measurement. The decision to focus only on LASr was based on the lack of data for LASct and LAScd. Data on these parameters were available in only 3 trials.

This analysis has some limitations. Only studies that provided a Cox regression analysis with effect sizes related to a 1% increase in LASr were included. This provided a more reliable quantitative analysis but may have excluded further evidence on this subject, for example, in the setting of myocardial infarction (eg, the study by Kim et al[8] showed that LASr yields incremental prognostic utility vs LA geometry to improve NOAF detection after myocardial infarction). Furthermore, the pooled analysis of multivariable HR for LASr should be considered only "exploratory" because the adjustment set of covariates was slightly different in many studies. In contrast, age, an important modifier of LASr, was consistently included in every model, and this should be considered a point of strength.

This study showed strong evidence that LASr is a solid tool for predicting NOAF. Because of its informative role, analysis of atrial function should be part of the routine echocardiographic examination of all patients at high risk of AF.

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Measurement Accuracy of Right Ventricular Parameters Using 3D Echocardiography

Study-Level Meta-Analysis

The assessment of right ventricular (RV) morphology and function has gained increasing popularity because it provides incremental value over left chamber mechanical and functional parameters. Because the right ventricle has a complex shape, cardiac magnetic resonance (CMR) is the gold standard for the evaluation of RV volumes and right ventricular ejection fraction (RVEF), whereas 3-dimensional echocardiography (3DE) has also become an established method to quantify RV volumes and RVEF and has been independently associated with outcomes.[1] Meta-analyses regarding RV volumes and ejection fraction between CMR and 3DE were conducted at least 5 to 10 years ago.[2,3] In the last decade, echocardiographic equipment and RV quantification software incorporating artificial intelligence technology have advanced rapidly. We conducted a meta-analysis for measurement accuracy of contemporary 3DE-derived RV parameters compared with CMR.

A search was conducted in PubMed, Scopus, and Embase using the key words "three-dimensional echocardiography," "cardiac magnetic resonance,"