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# Left Atrial Longitudinal Strain as a Tool for Detecting Left Atrial Appendage Spontaneous Echo Contrast in Atrial Fibrillation

**Ibrahim Mohieddin Mohammed, Maha Hamed Elsebaei, Ahmed Shafea Ammar, Mohammed Ali Elsayed Ibrahim, Alaa Elsayed salama**

*Cardiology Department, Faculty of Medicine, Zagazig University, Egypt*

***Corresponding author:** Mohammed Ali Elsayed Ibrahim

**Email:** mohammedzankal80@gmail.com,

**Abstract**

Atrial fibrillation (AF) is the most prevalent sustained cardiac arrhythmia, affecting approximately 2% of the population with substantial thromboembolic risk. The left atrial appendage (LAA) serves as the primary site of thrombus formation in non-valvular AF, accounting for up to 90% of cardiac emboli. Spontaneous echo contrast (SEC), detected by transesophageal echocardiography (TEE), represents blood stasis and serves as a validated marker of thrombogenic risk. However, TEE's semi-invasive nature limits its routine use. Left atrial longitudinal strain (LALS), measured non-invasively via speckle-tracking echocardiography, quantifies atrial myocardial deformation and reflects mechanical function. Recent evidence demonstrates strong inverse correlations between reduced LALS and LAASEC severity. Studies show that LALS cut-off values of 8-12% predict dense SEC with sensitivities and specificities exceeding 80-85%, providing incremental value beyond $CHA_2DS_2$-VASc scores and conventional echocardiographic parameters. This review synthesizes current evidence examining the relationship between LALS parameters and LAASEC in AF patients, explores underlying pathophysiological mechanisms, and discusses clinical applications for non-invasive thromboembolic risk stratification.

**Keywords:** Atrial fibrillation, left atrial strain, speckle-tracking echocardiography, spontaneous echo contrast, left atrial appendage, thromboembolic risk, stroke prevention, reservoir strain, $CHA_2DS_2$-VASc score

## Introduction

Atrial fibrillation (AF) represents the most common sustained cardiac arrhythmia encountered in clinical practice, affecting approximately 2% of the general population with prevalence rates demonstrating a marked upward trajectory in recent decades. This arrhythmia is characterized by disorganized atrial electrical activity and loss of coordinated atrial mechanical contraction, resulting in significant hemodynamic consequences and substantially increased risk of adverse cardiovascular outcomes. Among the most serious complications associated with AF are thromboembolic events, particularly ischemic stroke, which occur at rates five times higher in AF patients compared to individuals in sinus rhythm. (1)

The pathophysiological basis for this elevated thrombotic risk lies primarily in blood stasis within the left atrial appendage (LAA), a trabeculated pouch-like structure that serves as the anatomical site of thrombus formation in up to 90% of non-valvular AF cases. The mechanisms underlying LAA thrombogenesis are multifactorial, encompassing Virchow's triad of blood stasis, endothelial dysfunction, and hypercoagulability, all of which are amplified in the setting of atrial fibrillation. (2)

Traditional clinical risk stratification tools, most notably the $CHA_2DS_2$-VASc score, have been widely adopted to guide anticoagulation decisions in AF management. However, these scoring systems rely exclusively on clinical

variables and do not incorporate direct assessment of atrial structural or functional abnormalities, potentially limiting their discriminatory capacity in certain patient subgroups. (3)

Transesophageal echocardiography (TEE) remains the gold standard imaging modality for direct visualization of the LAA and detection of thrombus or spontaneous echo contrast (SEC), a dynamic smoke-like echocardiographic appearance reflecting erythrocyte aggregation under conditions of low shear stress. Despite its diagnostic superiority, TEE is semi-invasive, requires conscious sedation or general anesthesia, carries procedural risks, and is not suitable for routine screening or serial monitoring. (4)

Consequently, there exists substantial clinical interest in identifying non-invasive imaging markers that can enhance thromboembolic risk stratification and guide clinical decision-making regarding anticoagulation intensity, pre-procedural screening, and timing of rhythm control interventions. Left atrial longitudinal strain (LALS), assessed through speckle-tracking echocardiography (STE), has emerged as a promising functional biomarker that quantifies atrial myocardial deformation throughout the cardiac cycle and provides comprehensive evaluation of atrial mechanics. (5)

This review synthesizes current evidence examining the relationship between LALS parameters and left atrial appendage spontaneous echo contrast in patients with atrial fibrillation, explores the underlying pathophysiological mechanisms, evaluates diagnostic and prognostic implications, and discusses potential integration into contemporary AF management paradigms. (6)

**Epidemiology and Clinical Burden of Atrial Fibrillation**

The global burden of atrial fibrillation has increased substantially over recent decades, with current estimates suggesting that over 33 million individuals worldwide are affected by this arrhythmia. The prevalence of AF demonstrates strong age-dependency, rising from less than 0.5% in individuals younger than 50 years to approximately 10-15% in those aged 80 years and older. Multiple large-scale epidemiological studies have documented that AF prevalence is higher in men than women across all age groups, though women tend to develop AF at older ages and experience more severe symptoms and higher stroke rates. (7)

The lifetime risk of developing AF is approximately 1 in 3 for individuals aged 55 years and older in developed countries. Beyond its high prevalence, AF confers substantial morbidity and mortality, with affected individuals experiencing a five-fold increase in stroke risk, three-fold increase in heart failure incidence, two-fold increase in dementia risk, and approximately 1.5 to 2-fold increase in all-cause mortality compared to age-matched controls in sinus rhythm. (8)

Ischemic stroke represents the most devastating complication of AF, occurring at an annual rate of approximately 5% in untreated patients, with approximately one in five of all strokes attributable to atrial fibrillation. AF-related strokes tend to be more severe, associated with larger infarct volumes, higher disability rates, and increased mortality compared to strokes from other etiologies. The recognition that most AF-related thrombi originate from the left atrial appendage has prompted development of both pharmacological (anticoagulation) and mechanical (LAA occlusion devices) strategies for stroke prevention, yet accurate identification of individual patient risk remains challenging and represents an area of active investigation. (10)

**Pathophysiology of Thrombogenesis in Atrial Fibrillation**

The pathophysiological mechanisms underlying thrombus formation in atrial fibrillation are complex and multifactorial, reflecting interactions between hemodynamic alterations, structural remodeling, and prothrombotic blood constituents. At the hemodynamic level, loss of coordinated atrial contraction during AF results in dramatically reduced blood flow velocities within the left atrium and particularly within the left atrial appendage, where the complex trabeculated anatomy and narrow orifice predispose to stagnation. (11)

Studies using intracardiac echocardiography and Doppler techniques have demonstrated that LAA emptying velocities decrease from normal values of 60-80 cm/s during sinus rhythm to less than 20-25 cm/s in AF, with values below 20 cm/s strongly associated with presence of spontaneous echo contrast and thrombus formation. This marked reduction in flow velocity creates regions of blood stasis where normal washout mechanisms are

compromised, allowing time-dependent processes of erythrocyte aggregation and fibrin network formation to proceed. (12)

At the cellular and molecular level, AF is associated with a systemic hypercoagulable state characterized by platelet activation, endothelial dysfunction, and alterations in coagulation cascade proteins. Biomarker studies have documented elevated levels of von Willebrand factor, soluble P-selectin, thrombin-antithrombin complexes, prothrombin fragments, and D-dimer in AF patients compared to controls, reflecting ongoing thrombotic and fibrinolytic activity even in the absence of visible thrombus. (13)

Endothelial dysfunction, manifested by reduced nitric oxide bioavailability and increased expression of procoagulant molecules such as tissue factor and thrombomodulin, contributes to local prothrombotic conditions within the atrial endocardium. Structural remodeling of the atrial myocardium represents another critical component of the thrombogenic substrate in AF. (14)

The process of atrial remodeling encompasses electrical, contractile, and structural changes that occur in response to sustained atrial arrhythmia and hemodynamic stress. Electrical remodeling involves shortening of atrial action potential duration and effective refractory period, contributing to maintenance and perpetuation of the arrhythmia itself. Contractile remodeling manifests as impaired atrial systolic function even after restoration of sinus rhythm, a phenomenon termed "atrial stunning" that may persist for days to weeks following cardioversion. (15)

Structural remodeling is characterized by progressive atrial enlargement, myocyte hypertrophy, interstitial fibrosis with excessive collagen deposition, fatty infiltration, and inflammatory cell infiltration, all of which contribute to mechanical dysfunction and reduced atrial compliance. The left atrial appendage undergoes particularly pronounced remodeling in AF, with studies demonstrating increased fibrosis, endocardial denudation, and extracellular matrix reorganization that further compromise contractile function and promote thrombogenesis. (16)

The concept of "atrial cardiomyopathy" has emerged to describe this substrate of structural and functional atrial abnormalities that exist independent of the rhythm status and contribute to both arrhythmia perpetuation and thromboembolic risk. Recognition that atrial cardiomyopathy may develop prior to clinical AF onset and persist after rhythm restoration has important implications for risk stratification and suggests that assessment of atrial function, rather than rhythm status alone, may provide superior prognostic information. (17)

**Table (1). Initial Evaluation of Atrial Fibrillation (14).**

| *Test* | *Purpose* |
|---|---|
| Chest radiography | Identify possible pulmonary disease (e.g., pneumonia, vascular congestion, chronic obstructive pulmonary disease) |
| Complete blood count | Identify comorbid conditions (e.g., anemia, infection) |
| Complete metabolic profile | Identify electrolyte abnormalities that may cause or exacerbate atrial fibrillation |
| | Assess kidney and liver function and blood glucose level |
| Echocardiography | Assess heart size and shape; chamber sizes and pressures; valve structure and function; presence of pericardial effusion; wall motion abnormalities; systolic and diastolic function |
| Electrocardiography | Diagnose atrial fibrillation and identify other arrhythmia (e.g., atrial flutter, atrial tachycardia) |
| | Identify other cardiac conditions (e.g., left ventricular hypertrophy, ischemia, strain, injury) |
| Thyroid-stimulating hormone measurement | Identify hyperthyroidism |

**Left Atrial Appendage Anatomy and Spontaneous Echo Contrast**

The left atrial appendage is a tubular, hooked structure that extends from the anterolateral wall of the left atrium, positioned between the left upper pulmonary vein and the left ventricle. Embryologically, the LAA represents a remnant of the primordial left atrium and possesses distinct structural and functional characteristics that differentiate it from the main left atrial body. (18)

The LAA exhibits significant anatomical variability in morphology, with classification systems describing four primary shapes: chicken wing (48%), cactus (30%), windsock (19%), and cauliflower (3%). Studies have demonstrated that certain LAA morphologies, particularly the chicken wing configuration, are associated with lower stroke risk, possibly due to more favorable flow dynamics and reduced propensity for stasis. (19)

The internal architecture of the LAA is characterized by extensive trabeculation with numerous pectinate muscles that create a complex network of recesses and crevices where blood flow may be particularly sluggish. The LAA orifice, which connects to the main left atrial chamber, demonstrates considerable size variability ranging from 10 to 40 mm in diameter, with larger orifices generally associated with higher flow velocities and lower thrombogenic risk. (20)

From a functional perspective, the LAA contributes to left atrial compliance and serves as a reservoir during ventricular systole, potentially modulating left atrial pressure and preventing excessive pressure elevation during volume loading. The LAA also possesses endocrine function, with LAA myocytes producing and secreting atrial natriuretic peptide in response to atrial stretch, thereby participating in volume and blood pressure regulation. (21)

In the setting of atrial fibrillation, LAA contractile function becomes severely impaired or absent, transforming this structure from an active participant in atrial mechanics to a passive, stagnant pouch predisposed to thrombus formation. Spontaneous echo contrast, also termed "smoke" or "sludge," represents a dynamic echocardiographic phenomenon characterized by slowly swirling, cloud-like echoes distinct from random background noise. (22)

The physical basis of SEC reflects erythrocyte aggregation into rouleaux formations under conditions of low shear stress, with the aggregates being sufficiently large to generate detectable ultrasound backscatter. Histopathological studies have demonstrated that regions exhibiting SEC contain increased fibrinogen concentrations and activated platelets, representing an intermediate stage along the continuum from normal blood to organized thrombus. (23)

The severity of SEC can be graded using a standardized classification system ranging from grade 0 (absent) to grade 4+ (severe), with higher grades characterized by increasingly dense, slowly swirling echoes that persist throughout the cardiac cycle. Dense SEC (grades 3-4) has been consistently associated with elevated thromboembolic risk comparable to that of visible thrombus, with several studies documenting stroke rates of 12-15% per year in patients with severe SEC compared to 3-5% in those without this finding. (24)

The presence and severity of SEC correlate strongly with LAA emptying velocity, with SEC typically appearing when velocities fall below 25-30 cm/s and becoming progressively denser as velocities decline further. Additional clinical and echocardiographic factors associated with SEC include persistent or permanent AF (compared to paroxysmal), larger left atrial size, lower left ventricular ejection fraction, mitral stenosis or regurgitation, recent heart failure exacerbation, and higher $CHA_2DS_2$-VASc scores. (25)

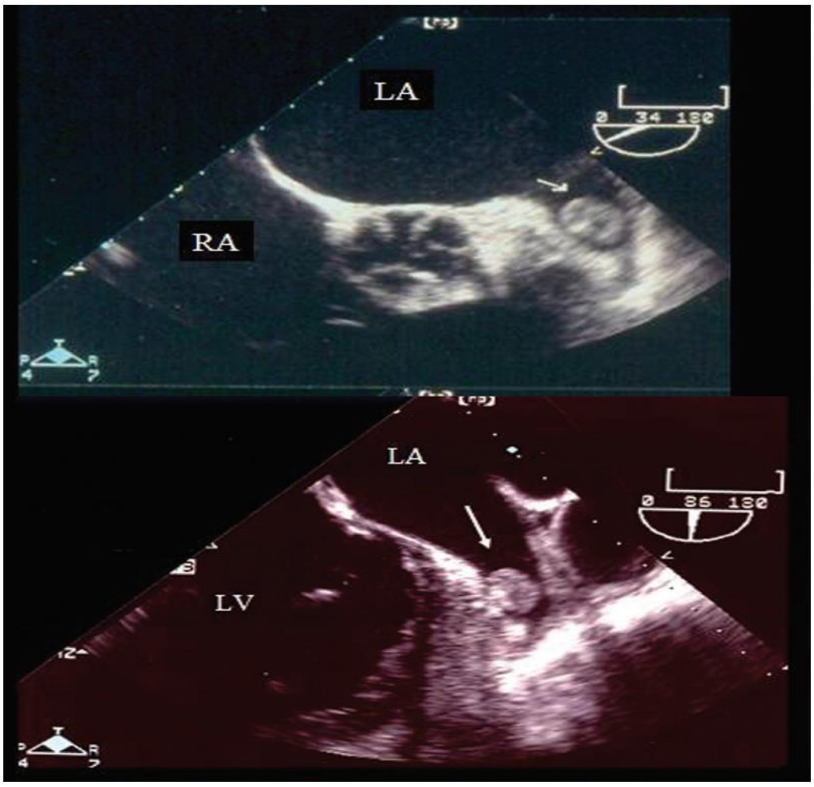


**Fig. (1). Transesophageal echocardiographic image of thrombi (arrows) in the left atrial appendage. (LA = left atrium; LV = left ventricle; RA = right atrium.) (23).**

**Current Risk Stratification Approaches in Atrial Fibrillation**

Clinical risk stratification represents a cornerstone of contemporary AF management, guiding decisions regarding anticoagulation therapy, rhythm versus rate control strategies, and procedural interventions. The $CHADS_2$ score, introduced in 2001, represented the first widely adopted clinical prediction rule for stroke risk in AF, incorporating five variables: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack (the latter weighted with 2 points). (26)

While the $CHADS_2$ score demonstrated reasonable predictive performance and ease of clinical application, subsequent analyses revealed that a substantial proportion of patients classified as low or intermediate risk (scores 0-1) still experienced thromboembolic events, suggesting inadequate sensitivity for identifying all at-risk individuals. The $CHA_2DS_2$-VASc score was developed to address these limitations by expanding the risk factor set to include vascular disease, age 65-74 years (in addition to age ≥75), and female sex, thereby providing more granular risk stratification particularly in the lower risk categories. (27)

Multiple validation studies across diverse populations have confirmed that the $CHA_2DS_2$-VASc score demonstrates superior predictive performance compared to $CHADS_2$, particularly in identifying truly low-risk patients (score 0 in men, 1 in women) who may safely forego anticoagulation. Current international guidelines from the European Society of Cardiology, American College of Cardiology/American Heart Association, and other major societies recommend using the $CHA_2DS_2$-VASc score as the primary risk stratification tool, with oral anticoagulation recommended for men with scores ≥1 and women with scores ≥2. (28)

Despite the widespread adoption and validation of the $CHA_2DS_2$-VASc score, several important limitations persist. First, the score demonstrates only modest discriminatory capacity with C-statistics typically ranging from 0.60 to 0.68, indicating that substantial overlap exists in event rates across score categories. Second, the score does not account for individual variations in atrial structure, function, or remodeling severity, despite recognition that these factors fundamentally influence thrombogenic substrate. (29)

Third, the binary classification of risk factors (present/absent) does not capture disease severity or control status—for example, well-controlled versus poorly controlled hypertension or diabetes. Fourth, the score shows limited ability to predict stroke risk in specific subgroups such as young patients with lone AF or those with significant atrial cardiomyopathy despite low clinical risk scores. (30)

Recognition of these limitations has stimulated research into biomarker-based and imaging-based approaches to enhance risk stratification. Circulating biomarkers including troponin, natriuretic peptides, growth differentiation factor-15, and markers of renal function have shown independent associations with stroke risk and may provide additive prognostic information when combined with clinical scores. Similarly, echocardiographic parameters such as left atrial volume index, left atrial ejection fraction, presence of left atrial fibrosis on cardiac magnetic resonance imaging, and LAA morphology and function have all demonstrated associations with thromboembolic events. (31)

**Principles of Speckle-Tracking Echocardiography and Strain Imaging**

Speckle-tracking echocardiography represents a major advancement in quantitative cardiac imaging, enabling objective assessment of myocardial deformation independent of angle dependency and tissue Doppler limitations. The fundamental principle underlying STE involves tracking the motion of natural acoustic markers, termed "speckles," which are created by constructive and destructive interference of ultrasound waves reflected from myocardial structures smaller than the ultrasound wavelength. (32)

These speckle patterns are relatively stable and unique within a given myocardial segment, allowing frame-by-frame tracking throughout the cardiac cycle using sophisticated pattern-matching algorithms. Unlike tissue Doppler imaging, which measures velocities along the ultrasound beam direction and is therefore highly angle-dependent, speckle-tracking can assess motion in any direction within the imaging plane, providing true two-dimensional strain measurements. (33)

The technical process of strain analysis begins with acquisition of standard two-dimensional grayscale echocardiographic images at frame rates of 60-80 frames per second, which represents an optimal balance between temporal resolution and tracking accuracy. Higher frame rates improve temporal resolution but may degrade speckle pattern consistency, while lower frame rates may miss rapid deformational events. (34)

Following image acquisition, the endocardial border is manually traced at a reference time point (typically end-systole for ventricular strain, end-diastole for atrial strain), and the software automatically generates an epicardial contour to define a region of interest encompassing the myocardial wall. This region is then divided into segments (typically 6 segments per standard view), and the tracking algorithm follows the speckle patterns within each segment throughout the cardiac cycle. (35)

The software quantifies the distance between acoustic markers within each segment and calculates strain as the percentage change in length relative to the original dimension. Strain values are expressed as percentages, with negative values indicating shortening, positive values indicating lengthening, and zero indicating no deformation. For left atrial strain analysis specifically, positive strain values during ventricular systole reflect atrial reservoir function as the atrium fills and stretches. (36)

Left atrial strain assessment provides three distinct functional components corresponding to the three phases of atrial function. Reservoir strain (LARs or peak atrial longitudinal strain, PALS) represents the peak positive strain value achieved during ventricular systole and reflects the atrium's capacity to store pulmonary venous return while the mitral valve is closed. Conduit strain represents passive atrial emptying during early diastole when the mitral valve opens and blood flows into the ventricle driven by the atrioventricular pressure gradient. (37)

In patients with atrial fibrillation, the absence of atrial mechanical systole eliminates the contractile component, but reservoir and conduit functions can still be assessed, with reservoir strain (PALS) being the most reproducible and clinically relevant parameter. Multiple studies have established that left atrial reservoir strain provides superior prognostic information compared to volumetric measurements such as left atrial volume index, likely because strain directly quantifies myocardial function rather than simply reflecting chamber size. (38)

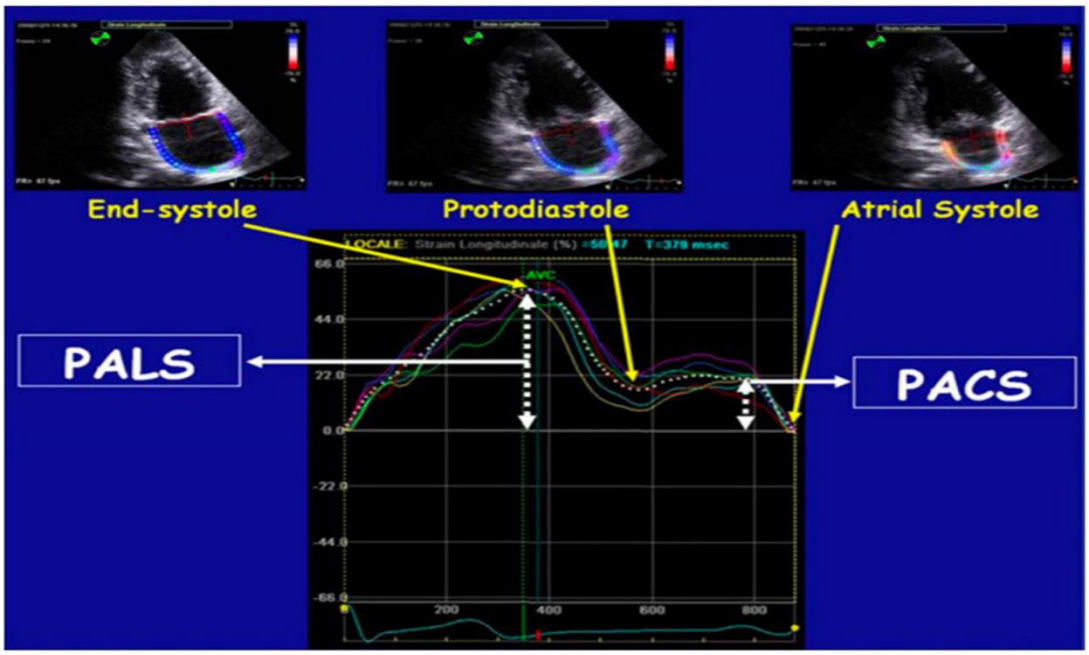


**Fig. (2). Left atrial strain. Measurement of peak atrial longitudinal strain (PALS) at the end of reservoir phase. The dashed curve represents the average atrial longitudinal strain during the cardiac cycle (35).**

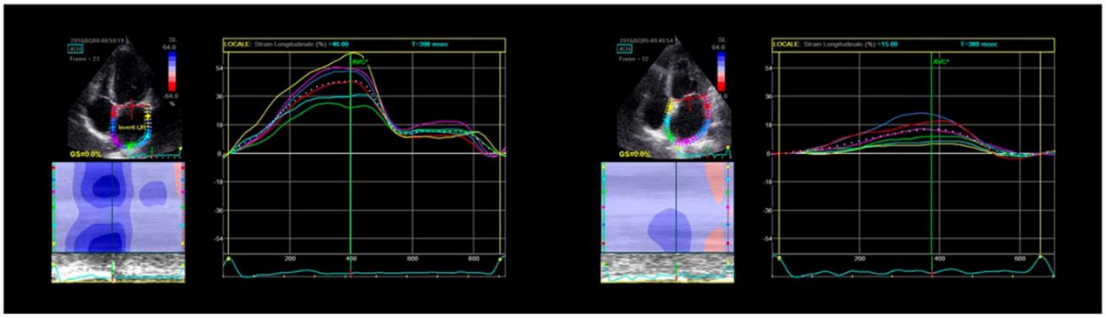

**Fig. (3). Atrial strain in atrial fibrillation. Comparison between atrial strain in a healthy subject (left) and a patient with atrial fibrillation (right). Note in the latter subject, besides a reduced PALS, the disappearance of PACS, the second deflection of the curve, relative to the atrial systole (35).**

**Left Atrial Strain and Atrial Remodeling in Atrial Fibrillation**

The progressive nature of atrial fibrillation has been well described, with the condition tending to advance from paroxysmal to persistent and eventually permanent forms in many patients. This progression reflects ongoing atrial remodeling processes that create an increasingly favorable substrate for arrhythmia maintenance. Left atrial strain parameters have demonstrated exceptional sensitivity for detecting early stages of atrial remodeling, often identifying functional impairment before significant structural changes become apparent on conventional imaging. (39)

Studies comparing patients with paroxysmal versus persistent AF have consistently shown that those with persistent forms exhibit significantly lower reservoir strain values, reflecting more advanced atrial dysfunction. Furthermore, in patients with paroxysmal AF, reduced baseline strain values predict progression to persistent forms, suggesting that strain assessment may identify individuals at risk for arrhythmia advancement who might benefit from early aggressive rhythm control strategies. (40)

The relationship between left atrial strain and atrial fibrosis has been investigated using cardiac magnetic resonance imaging with late gadolinium enhancement, which can directly visualize fibrotic tissue within the atrial wall. These studies have demonstrated strong inverse correlations between the extent of atrial fibrosis and

reservoir strain values, with more extensive fibrosis associated with progressively lower strain measurements. This relationship likely reflects the fact that fibrotic tissue is mechanically inert and cannot contribute to active myocardial deformation. (41)

Left atrial stiffness, another important parameter of atrial mechanical function, can be estimated non-invasively by calculating the ratio of E/e' (a marker of left ventricular filling pressure) to left atrial reservoir strain. Patients with AF demonstrate significantly elevated LA stiffness compared to controls, and higher stiffness values correlate with increased risk of AF recurrence after catheter ablation and cardioversion. The ability to quantify atrial stiffness using readily available echocardiographic parameters represents an important advance in functional assessment. (42)

In the context of rhythm control strategies, left atrial strain has shown value in predicting outcomes following both electrical cardioversion and catheter ablation. Patients with preserved pre-procedural strain values demonstrate higher rates of successful cardioversion and sustained sinus rhythm maintenance, while those with severely depressed strain are more likely to experience early AF recurrence. These findings suggest that strain assessment could help identify optimal candidates for rhythm control interventions versus those in whom a rate control strategy might be more appropriate. (43)

Following successful cardioversion or ablation, serial strain measurements have documented gradual improvement in atrial mechanical function over subsequent weeks to months, a process termed "reverse remodeling." The degree of strain improvement correlates with long-term maintenance of sinus rhythm, with patients demonstrating significant functional recovery being less likely to experience AF recurrence. Conversely, failure to show strain improvement despite apparent rhythm control may indicate persistent atrial substrate abnormalities and predict arrhythmia relapse. (44)

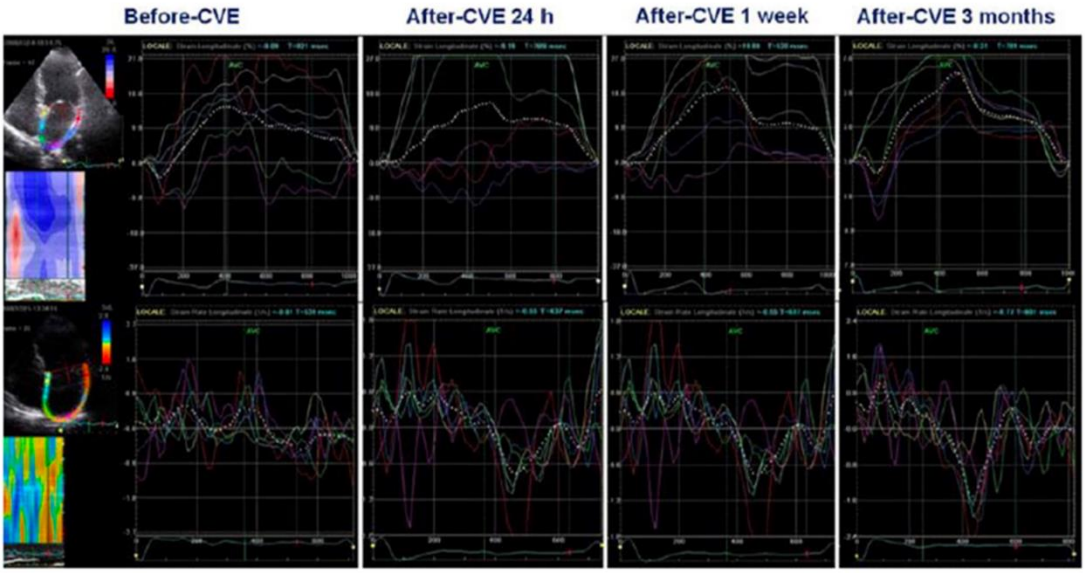


**Fig. (4). Atrial strain and electrical cardioversion. Evaluation of left atrial strain (above) and strain rate (below) in a patient before and after electrical cardioversion (CVE): it is important to highlight the reappearance of the second deflection of the atrial strain curve and the progressive improvement of PALS (44).**

**Relationship Between Left Atrial Strain and LAA Function**

The functional relationship between the main left atrial body and the left atrial appendage has important implications for understanding thrombogenic risk in atrial fibrillation. While these structures are anatomically continuous, they may exhibit somewhat independent mechanical behavior, particularly in the setting of atrial arrhythmias. However, accumulating evidence suggests that global left atrial strain parameters correlate well with LAA-specific functional indices, supporting the concept of a unified atrial mechanical substrate. (45)

Multiple studies have demonstrated significant positive correlations between left atrial reservoir strain and LAA emptying velocity, one of the most established markers of LAA function. Patients with reduced global LA strain values consistently exhibit lower LAA emptying velocities, suggesting that impaired atrial mechanical function affects both the main chamber and the appendage. This relationship persists across different AF subtypes and remains significant after adjustment for clinical variables and conventional echocardiographic parameters. (46)

The correlation between LA strain and LAA ejection fraction, calculated as the percentage change in LAA area between systole and diastole, has also been investigated. Studies have found moderate to strong correlations between reduced reservoir strain and impaired LAA ejection fraction, with both parameters reflecting underlying atrial contractile dysfunction. The concordance between these measurements suggests that assessment of global LA strain may provide indirect information about LAA mechanical function without requiring TEE. (47)

From a pathophysiological perspective, the relationship between LA strain and LAA function likely reflects shared mechanisms of atrial remodeling affecting both structures. The electrical, structural, and contractile changes that impair main LA function similarly affect the appendage, resulting in parallel deterioration of mechanical performance. Additionally, reduced LA compliance and elevated filling pressures, which contribute to decreased strain values, also adversely impact LAA flow dynamics and emptying. (48)

Several investigations have specifically examined whether LA strain can predict LAA thrombus presence. These studies have generally found that patients with LAA thrombus demonstrate significantly lower reservoir strain values compared to those without thrombus, and in multivariate analyses, strain often emerges as an independent predictor of thrombus presence alongside traditional risk factors. The diagnostic performance of strain for thrombus detection typically yields areas under the curve of 0.75-0.85, indicating good discriminatory ability. (49)

**Left Atrial Strain and Spontaneous Echo Contrast**

The association between reduced left atrial strain and presence of spontaneous echo contrast represents one of the most clinically relevant applications of strain imaging in atrial fibrillation. Multiple studies across diverse patient populations have consistently demonstrated that patients with SEC, particularly dense SEC (grades 3-4), exhibit significantly lower LA strain values compared to those without this finding. These associations remain robust after adjustment for age, sex, AF type, $CHA_2DS_2$-VASc score, and conventional echocardiographic parameters. (50)

A landmark study by Ma and colleagues examined 338 patients with non-valvular AF who underwent both transthoracic echocardiography with strain analysis and TEE for SEC assessment. This investigation found that patients with high-grade SEC (grades 3-4) had markedly reduced reservoir strain (15.01±8.93% vs 21.78±10.25%, $p<0.001$) and contractile strain (10.20±5.11% vs 14.89±6.28%, $p<0.001$) compared to those with low-grade or absent SEC. ROC curve analysis identified a reservoir strain cut-off of <8.85% as predictive of grade 3 SEC with sensitivity of 86.7% and specificity of 84.3%. (51)

Similar findings have been reported in other cohorts, with consistent observations that strain parameters progressively decline as SEC severity increases. Patients with grade 0 SEC typically demonstrate near-normal or mildly reduced strain, those with grades 1-2 show moderate impairment, and those with grades 3-4 exhibit severely depressed values often below 10-12%. This dose-response relationship strengthens the biological plausibility of the association and suggests that strain may serve as a continuous marker of thrombogenic risk. (52)

When comparing the predictive performance of different strain parameters, reservoir strain (PALS or LARs) generally demonstrates the strongest associations with SEC, likely because this parameter reflects overall atrial compliance and storage function, which are fundamental determinants of blood flow dynamics. Contractile strain, while also significantly associated with SEC in patients with paroxysmal AF or intermittent sinus rhythm, provides less information in those with permanent AF due to absence of coordinated atrial contraction. (53)

Multivariate regression analyses have consistently identified LA strain as an independent predictor of high-grade SEC even after adjustment for multiple confounding variables. In the Ma et al. study, reservoir strain remained

significantly associated with dense SEC (OR 0.52, 95% CI 0.33-0.83, p=0.006) after controlling for age, sex, AF type, $CHA_2DS_2$-VASc score, LA diameter, LA volume index, and LAA emptying velocity. These findings suggest that strain provides unique information about atrial mechanical function not captured by conventional parameters. (54)

The incremental value of adding strain assessment to clinical risk scores has been formally evaluated in several studies. When combined with $CHA_2DS_2$-VASc score, LA strain significantly improved the discriminatory capacity for predicting dense SEC or thrombus, with the combined model achieving C-statistics of 0.85-0.90 compared to 0.65-0.70 for $CHA_2DS_2$-VASc alone. This substantial improvement in predictive performance suggests potential clinical utility for strain-enhanced risk stratification. (55)

Studies have also examined whether strain can identify high-risk patients within specific $CHA_2DS_2$-VASc score categories. Among patients with low-to-moderate clinical risk scores (0-2), those with reduced strain values demonstrated significantly higher prevalence of SEC compared to those with preserved strain, suggesting that functional imaging may help refine risk assessment in individuals otherwise classified as lower risk. Conversely, some high $CHA_2DS_2$-VASc score patients with preserved strain showed lower SEC rates than expected, potentially identifying a subset who might tolerate less aggressive anticoagulation, though this remains speculative and requires prospective validation. (56)

**Diagnostic Performance and Optimal Cut-off Values**

Establishing optimal cut-off values for left atrial strain in predicting LAASEC represents an important step toward clinical implementation. However, reported threshold values have varied somewhat across studies, reflecting differences in patient populations, imaging equipment, analysis software, and statistical approaches. Nevertheless, certain patterns have emerged that may guide clinical interpretation. (57)

For reservoir strain (PALS), reported optimal cut-offs for predicting high-grade SEC or thrombus have ranged from approximately 8% to 15%, with most studies identifying values in the 10-13% range. A study by Puwanant and colleagues found that PALS <17.9% predicted LAA thrombus with 87% sensitivity and 88% specificity, while another investigation identified <12% as the optimal threshold for dense SEC. The variability in these values likely reflects different prevalence rates of SEC/thrombus in study populations and different definitions of the outcome of interest. (58, 59)

The diagnostic accuracy of LA strain for detecting high-grade SEC or thrombus, as assessed by ROC curve analysis, has been generally favorable across studies. Reported areas under the curve have typically ranged from 0.80 to 0.90, indicating good to excellent discriminatory ability. These performance characteristics compare favorably to those of clinical risk scores and conventional echocardiographic parameters, supporting the potential utility of strain assessment in clinical practice. (60)

It is important to note that optimal cut-off values may need to be adjusted based on clinical context and the specific question being addressed. For screening purposes where high sensitivity is prioritized to avoid missing high-risk patients, higher threshold values that maximize sensitivity at some cost to specificity may be appropriate. Conversely, for decisions regarding anticoagulation de-escalation where specificity is paramount, lower thresholds might be preferred. (61)

Technical factors affecting strain measurement must also be considered when interpreting results and applying cut-off values. Different echocarography vendors and analysis software packages may yield somewhat different absolute strain values due to variations in algorithms and tracking approaches, though rank ordering of patients generally remains consistent. Some investigators have advocated for vendor-specific reference ranges and cut-offs, while others have found that relative differences between patients are preserved across platforms. (62)

The reproducibility of LA strain measurements has been evaluated in several studies, generally showing good inter-observer and intra-observer agreement with correlation coefficients typically exceeding 0.80-0.90. However, reproducibility may be somewhat lower in AF patients compared to those in sinus rhythm due to beat-to-beat variability and the need to average measurements over multiple cardiac cycles. Guidelines recommend averaging strain values over 3-5 consecutive beats in AF to improve measurement stability. (63)

**Conclusion**

Left atrial longitudinal strain assessed by speckle-tracking echocardiography has emerged as a valuable functional biomarker that provides important insights into atrial mechanics in patients with atrial fibrillation. Accumulating evidence demonstrates robust inverse associations between reduced LA strain parameters, particularly reservoir strain, and the presence and severity of left atrial appendage spontaneous echo contrast, a validated surrogate marker of thrombogenic risk. These associations persist after adjustment for clinical risk scores and conventional echocardiographic parameters, suggesting that strain captures unique information about atrial pathophysiology not reflected in traditional assessment tools. The diagnostic performance of LA strain for predicting high-grade SEC or thrombus appears favorable, with optimal cut-off values in the range of 8-15% yielding sensitivities and specificities of 80-90% in most studies. While important limitations remain, including technical challenges, lack of standardization across platforms, and absence of large-scale outcome trials, LA strain represents a promising non-invasive approach to enhance thromboembolic risk stratification in AF patients. Future research should focus on prospective validation, standardization of methodology, integration with other biomarkers, and demonstration of clinical utility in improving patient outcomes. As evidence continues to accumulate, LA strain assessment may become an important component of comprehensive atrial function evaluation and personalized management strategies in atrial fibrillation.

**References**

1. 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 for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2021;42(5):373-498.
2. Vinciguerra M, Dobrev D, Nattel S. Atrial fibrillation: pathophysiology, genetic and epigenetic mechanisms. Lancet Reg Health Eur. 2024;37:100835.
3. Lip GYH, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest. 2010;137(2):263-272.
4. Fatkin D, Kelly RP, Feneley MP. Relations between left atrial appendage blood flow velocity, spontaneous echo contrast and thromboembolic risk in vivo. J Am Coll Cardiol. 1994;23(4):961-969.
5. Voigt JU, Mălăescu GG, Haugaa K, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging. 2021;16(1):1-11.
6. Ma CS, Sun SK, Wang L, et al. The value of left atrial longitudinal strain in evaluating left atrial appendage spontaneous echo contrast in non-valvular atrial fibrillation. Front Cardiovasc Med. 2023;10:1090139.
7. Elliott AD, Middeldorp ME, Van Gelder IC, et al. Epidemiology and modifiable risk factors for atrial fibrillation. Nat Rev Cardiol. 2023;20(6):404-417.
8. Sagris M, Vardas EP, Theofilis P, et al. Atrial fibrillation: pathogenesis, predisposing factors, and genetics. Int J Mol Sci. 2021;23(1):6.
9. Bizhanov KA, Abzaliyev KB, Baimbetov AK, et al. Atrial fibrillation: epidemiology, pathophysiology, and clinical complications (literature review). J Cardiovasc Electrophysiol. 2023;34(1):153-165.
10. Essien UR, Kornej J, Johnson AE, et al. Social determinants of atrial fibrillation. Nat Rev Cardiol. 2021;18(11):763-773.
11. Zhang Z, Zhou J, Lin Q, et al. Overcoming barriers for left atrial appendage thrombus: a systematic review of left atrial appendage closure. BMC Cardiovasc Disord. 2024;24(1):1-17.
12. Goldberg YH, Gordon SC, Spevack DM, et al. Disparities in emptying velocity within the left atrial appendage. Eur J Echocardiogr. 2010;11(3):290-295.
13. Lip GYH, Tse HF, Lane DA. Atrial fibrillation. Lancet. 2012;379(9816):648-661.
14. Goldberger JJ, Arora R, Green D, et al. Evaluating the atrial myopathy underlying atrial fibrillation: identifying the arrhythmogenic and thrombogenic substrate. Circulation. 2015;132(4):278-291.

15. Linz D, Gawalko M, Betz K, et al. Atrial fibrillation: epidemiology, screening and digital health. Lancet Reg Health Eur. 2024;37:100798.
16. Karakasis P, Theofilis P, Vlachakis PK, et al. Atrial cardiomyopathy in atrial fibrillation: mechanistic pathways and emerging treatment concepts. J Clin Med. 2025;14(9):3250.
17. Beneki E, Dimitriadis K, Theofilis P, et al. Intracardiac or transesophageal echocardiography for left atrial appendage occlusion: an updated systematic review and meta-analysis. Int J Cardiovasc Imaging. 2025;41:1-17.
18. Anwar AM. Morphological and functional assessment of the left atrial appendage in daily practice: a comprehensive approach using basic and advanced echocardiography with practical tips. J Cardiovasc Imaging. 2024;32(1):12.
19. Tan CD, Liu JZ, Zheng YP, et al. Left atrial enlargement and high uric acid level are risk factors for left atrial thrombus or dense spontaneous echo contrast in atrial fibrillation patients with low to moderate embolic risk assessed by CHA2DS2-VASc score. Front Cardiovasc Med. 2023;10:937770.
20. Ven PM. Atrial fibrillation: insights on mechanisms, mapping and catheter ablation. Eur Heart J. 2023;110:60.
21. Wang B, Wang Z, Fu G, et al. Left atrial spontaneous echo contrast and ischemic stroke in patients undergoing percutaneous left atrial appendage closure. Front Cardiovasc Med. 2021;8:723280.
22. Sun S, Su B, Lin J, et al. A nomogram to predict left atrial appendage thrombus and spontaneous echo contrast in non-valvular atrial fibrillation patients. BMC Cardiovasc Disord. 2022;22:311.
23. Traub J, Hettesheimer D, Pinter J, et al. Spontaneous echo contrast in the left atrial appendage is linked to a higher risk of thromboembolic events and mortality in patients with atrial fibrillation. IJC Heart Vasc. 2025;56:101590.
24. Gedikli O, Yilmaz F, Kaya H, et al. Left atrial spontaneous echo contrast and ischemic stroke in patients undergoing percutaneous left atrial appendage closure. Front Cardiovasc Med. 2021;8:723280.
25. Lee JM, Cha MJ, Nam GB, et al. Incidence and predictors of left atrial thrombus in patients with atrial fibrillation under anticoagulation therapy. Clin Res Cardiol. 2024;113:1-9.
26. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2024;83(1):109-279.
27. Chao TF, Liu CJ, Wang KL, et al. Using the CHA2DS2-VASc score for refining stroke risk stratification in 'low-risk' Asian patients with atrial fibrillation. J Am Coll Cardiol. 2020;64(16):1658-1665.
28. Potpara T, Romiti GF, Sohns C. The 2024 European Society of Cardiology guidelines for diagnosis and management of atrial fibrillation: a viewpoint from a practicing clinician's perspective. Thromb Haemost. 2024;124(12):1087-1094.
29. Rachieru C, Luca CT, Văcărescu C, et al. Future perspectives to improve CHA2DS2VASc score: the role of left atrium remodelling, inflammation and genetics in anticoagulation of atrial fibrillation. Clin Interv Aging. 2023;18:1737-1748.
30. Inan D, Genc D, Şimsek B, et al. Relationship between $CHA_2DS_2$-VASc score on admission and in-hospital major adverse cardiovascular events in patients diagnosed with ST-elevation myocardial infarction. Angiology. 2025;76(4):330-339.
31. Romiti GF, Pastori D, Rivera-Caravaca JM, et al. Adherence to the 'atrial fibrillation better care' pathway in patients with atrial fibrillation: impact on clinical outcomes—a systematic review and meta-analysis of 285,000 patients. Thromb Haemost. 2022;122(03):406-414.
32. Cameli M, Lisi M, Righini FM, et al. Left atrial deformation analysis by speckle tracking echocardiography for prediction of cardiovascular outcomes. Am J Cardiol. 2009;104(4):556-560.
33. Hoit BD. Left atrial size and function: role in prognosis. J Am Coll Cardiol. 2014;63:493-505.
34. Mandoli GE, Pastore MC, Procopio MC, et al. Unveiling the reliability of left atrial strain measurement: a dedicated speckle tracking software perspective in controls and cases. Eur Heart J Imaging Methods Pract. 2024;2(1):qyae061.

35. Hagendorff A, Stöbe S, Helfen A, et al. Echocardiographic assessment of left atrial appendage morphology and function—an expert proposal by the German Working Group of Cardiovascular Ultrasound. Clin Res Cardiol. 2025;114(1):25-40.
36. Gan GCH, Bhat A, Chen HHL, et al. Left atrial reservoir strain by speckle tracking echocardiography: association with exercise capacity in chronic kidney disease. J Am Heart Assoc. 2021;10(1):e017840.
37. Li R, Sun F, Piao S, et al. Left atrial strain and compliance correlate with diastolic dysfunction grades and complications during pre-eclampsia: a speckle-tracking echocardiography study. Ultrasound Med Biol. 2021;47(12):3411-3419.
38. Krishan S, Hashim L, Javed L, et al. Comparison of intracardiac echocardiography with transesophageal echocardiography for left atrial appendage occlusion: an updated systematic review and meta-analysis. J Interv Card Electrophysiol. 2023;66(6):1337-1340.
39. Zhong XF, Liu DS, Zheng YQ, et al. Left atrial reservoir and pump function after catheter ablation with persistent atrial fibrillation: a two-dimensional speckle tracking imaging study. Acta Cardiol. 2023;78(3):331-340.
40. Katic J, Borovac JA. Treatment of persistent left atrial appendage thrombus in patients with atrial fibrillation on adequate oral anticoagulation: pathways of care for all-comers and heart failure patients. Card Fail Rev. 2023;9:e05.
41. Duus LS, Lindberg S, Olsen FJ, et al. Left atrial strain predicts heart failure and cardiovascular death in patients undergoing coronary artery bypass grafting. Cardiovasc Imaging. 2021;14(1):295-296.
42. Beyls C, Abou-Arab O, Mahjoub Y. Left atrial strain: an operator and software-dependent tool. Ann Intensive Care. 2024;14(1):95.
43. Fan JL, Wang HP, Lu Y, et al. Correlation between anterior mitral annular plane systolic excursion and left atrial appendage stasis in patients with nonvalvular atrial fibrillation. Rev Cardiovasc Med. 2024;25(7):236.
44. Fang R, Li Y, Wang J, et al. Stroke risk evaluation for patients with atrial fibrillation: insights from left atrial appendage. Front Cardiovasc Med. 2022;9:968630.
45. Su B, Sun SK, Dai XJ, et al. The novel left atrial appendage strain parameters are associated with thrombosis risk in patients with non-valvular atrial fibrillation. Echocardiography. 2023;40(6):483-493.
46. Sonaglioni A, Lombardo M, Nicolosi GL, et al. Incremental diagnostic role of left atrial strain analysis in thrombotic risk assessment of nonvalvular atrial fibrillation patients planned for electrical cardioversion. Int J Cardiovasc Imaging. 2021;37:1539-1550.
47. Yamada A, Hashimoto N, Fujito H, et al. Comprehensive assessment of left atrial and ventricular remodeling in paroxysmal atrial fibrillation by the cardiovascular magnetic resonance myocardial extracellular volume fraction and feature tracking strain. Sci Rep. 2021;11(1):10941.
48. Mao Y, Yu C, Yang Y, et al. Comparison of left atrial and left atrial appendage mechanics in the risk stratification of stroke in patients with atrial fibrillation. Cardiovasc Ultrasound. 2021;19:1-12.
49. Cameli M, Lunghetti S, Mandoli GE, et al. Left atrial strain predicts pro-thrombotic state in patients with non-valvular atrial fibrillation. J Atr Fibrillation. 2017;10(4):1641.
50. Sonaglioni A, Lombardo M, Schiavone L, et al. Predictive value of left atrial reservoir strain for thromboembolic risk in patients with non-valvular atrial fibrillation. BMC Cardiovasc Disord. 2022;22:213.
51. Ma CS, Sun SK, Wang L, et al. The value of left atrial longitudinal strain in evaluating left atrial appendage spontaneous echo contrast in non-valvular atrial fibrillation. Front Cardiovasc Med. 2023;10:1090139.
52. Sonaglioni A, Lombardo M, Nicolosi GL, et al. Mechanical concordance between left atrium and left atrial appendage in nonvalvular atrial fibrillation: can it be exploited to avoid transesophageal echocardiography prior to electrical cardioversion during Covid-19 pandemic? Int J Cardiovasc Imaging. 2022;38(2):351-362.

53. Deferm S, Bertrand PB, Churchill TW, et al. Left atrial mechanics assessed early during hospitalization for cryptogenic stroke are associated with occult atrial fibrillation: a speckle-tracking strain echocardiography study. J Am Soc Echocardiogr. 2021;34(2):156-165.
54. Mao Y, Zhao H, Yu C, et al. Left atrial appendage mechanical dispersion assessed by speckle-tracking echocardiography as a determinant of left atrial appendage blood stasis in patients with atrial fibrillation. Front Cardiovasc Med. 2022;9:905293.
55. Sun SK, Ma CS, Li Y, et al. Development and validation of a nomogram superior to CHADS2 and CHA2DS2-VASc models for predicting left atrial appendage dense spontaneous echo contrast/thrombus. J Thorac Dis. 2024;16:288.
56. Zeng D, Zhang X, Chang S, et al. A nomogram for predicting left atrial thrombus or spontaneous echo contrast in non valvular atrial fibrillation patients using hemodynamic parameters from transthoracic echocardiography. Front Cardiovasc Med. 2024;11:1337853.
57. Puwanant S, Assad TH, Zimmerman TU, et al. Incremental diagnostic role of left atrial strain analysis in thrombotic risk assessment of non valvular atrial fibrillation. Int J Cardiovasc Imaging. 2020;36:2127-2136.
58. Hsu PC, Lee WH, Chu CY, et al. Prognostic role of left atrial strain and its combination index with transmitral E-wave velocity in patients with atrial fibrillation. Sci Rep. 2016;6:17318.
59. Sasaki S, Watanabe T, Tamura H, et al. Left atrial strain as evaluated by two-dimensional speckle tracking predicts left atrial appendage dysfunction in patients with acute ischemic stroke. BBA Clin. 2014;2:40-47.
60. Gofus J, Zacek P, Shahin Y, et al. Left atrial appendage occlusion: percutaneous and surgical approaches in everyday practice. Kardiol Pol. 2024;82(3):267-275.
61. Lozier MR, Sanchez AM, Mihos CG. A systematic review on the use of ultrasound enhancing agents with transesophageal echocardiography to assess the left atrial appendage prior to cardioversion. Echocardiography. 2021;38(8):1414-1421.
62. Smiseth OA, Morris DA, Cardim N, et al. Multimodality imaging in patients with heart failure and preserved ejection fraction: an expert consensus document of the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2022;23(2):e34-e61.
63. Modin D, Olsen FJ, Pedersen S, et al. Left atrial reservoir strain obtained by two-dimensional speckle tracking echocardiography is an independent predictor of incident atrial fibrillation following STEMI. Int J Cardiol. 2018;263:1-6.