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Editorial

Echocardiography for left atrial appendage structure and function

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For long, it was believed that the left atrial appendage (LAA) was a vestigial structure – a structure which apparently did not have any meaningful function in normal life and could be easily obliterated during cardiac surgery without producing any ill effects. Studying the function of LAA could therefore be of hardly any interest. However, with the advancements of echocardiographic techniques, it has now become apparent that the LAA is an actively contracting structure which likely plays an important role in cardiac hemodynamics. More importantly, dysfunction of LAA is the substrate for thrombus formation which can lead to potentially devastating embolic complications.^{1–5} Accordingly, a comprehensive assessment of LAA structure and function is now regularly sought to guide therapeutic decision-making in a number of cardiac illnesses.

Echocardiography, particularly transesophageal echocardiography (TEE), is currently the modality of choice for evaluation of the LAA. It allows complete delineation of the LAA anatomy in almost all patients and, at the same time, also permits a detailed assessment of its function.

1. Echocardiographic assessment of LAA structure

The LAA is a small, pyramidal structure, which is situated on the lateral aspect of the left atrium (LA), extending between the pulmonary artery above and the left ventricle (LV) below. It is usually a multilobed structure. In an autopsy study of 500 normal human hearts, the LAA was bilobed in 54% and multilobed (≥ 2 lobes) in 80% of hearts.⁶ From inside, the LAA is trabeculated with the trabeculations, known as pectinate muscles, running largely parallel to each other, giving it a comb-like structure.

Although the LAA can be visualized on transthoracic echocardiography also, in most patients a detailed assessment is not possible due to the posterior location of the LAA. In contrast, TEE, with the close proximity of the transducer to the LAA, allows excellent imaging of the LAA and is therefore mandatory whenever an assessment of LAA is sought. On TEE, the LAA is best visualized in the mid-esophageal two-chamber view (80–100°) and the mid-esophageal aortic valve short-axis view (30–60°). In most patients, these two views allow satisfactory imaging of the LAA and are therefore the recommended views for this purpose.⁷ However, as the LAA has complex, multilobed configuration, imaging in one or two planes may not be sufficient to exclude thrombus with certainty. Therefore, to exclude thrombus, it is essential to image the LAA from multiple imaging planes. This can be easily accomplished by first developing the mid-esophageal aortic valve short-axis view (30–60°) and then anteflexing the transducer and rotating the multiplane angle from 0° to 180°. This approach allows complete delineation of LAA anatomy, its different lobes and the pectinate muscles (Fig. 1). The recent availability of live-three dimensional TEE should render imaging of the complex LAA anatomy much easier now.⁸

The primary indication for performing assessment of the LAA is to rule out presence of a thrombus. TEE is highly accurate for this purpose with some studies reporting sensitivity and specificity of TEE to be as high as 100% and 99% respectively.⁹ However, in real practice, the diagnostic accuracy may not be that high and both false-positives (pectinate muscles labeled as thrombi) and false-negatives (thrombi hidden in one of the lobes missed) may occur.^{10,11} A meticulous scanning of the LAA from multiple imaging planes, as described above, is essential to minimize

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Fig. 1 – Transesophageal echocardiography for visualization of the left atrial appendage (LAA) in two orthogonal planes (A & B). Please note, the multilobed configuration of the appendage is not apparent in (A) but is well seen in (B) (arrows). Dense spontaneous echocardiographic contrast is also seen in the left atrium and the LAA.

misdiagnosis. Still, in some cases, it may be almost impossible to differentiate a thrombus from the pectinate muscles or artifacts. The administration of ultrasound contrast can be of great help in such situations.^{12–14}

In addition to delineation of thrombus, TEE is also helpful in detection of LAA spontaneous echo contrast (SEC). SEC is a smoke-like swirling pattern seen on two-dimensional imaging and is thought to reflect rouleaux formation resulting from stasis of the blood. Understandably, SEC has been shown

to be the harbinger of thrombus formation and therefore, a predictor of thromboembolic risk.^{15–17} A scheme has been proposed for semi-quantitative grading of the severity of SEC on echocardiography (Table 1).¹⁸

2. Echocardiographic assessment of left atrial function

Until recently, echocardiographic examination of LAA has focused primarily on evaluation of its anatomy and looking for the presence of thrombus or SEC. However, it has become increasingly apparent that an estimate of LAA function can provide incremental information about the risk of clot formation, embolic events, success of cardioversion etc. Therefore, evaluation of the LAA function is now often undertaken as part of the standard echocardiographic examination of the appendage.

Although LAA fractional area change and ejection fraction on two-dimensional imaging have been tried as measures of LAA function, they are inherently complex, time-consuming and have unacceptable inter-observer variability.^{19,20} Consequently, they are not preferred for routine use. In contrast, Doppler assessment of LAA function is easy to perform, reproducible and the most validated. Accordingly, Doppler measurement of LAA flow velocities is currently the preferred method of assessment of LAA function.²¹ Recently, tissue velocity and strain imaging have also been evaluated for this purpose and have shown promise.^{5,22–27}

2.1. LAA flow velocity patterns

The LAA flow velocities by pulsed-wave Doppler can be obtained from any of the standard imaging planes on TEE, provided the direction of blood flow is parallel to the ultrasound beam. Though there is no consensus on the sampling site, the most reproducible waveforms can be obtained by placing the pulsed-wave sample-volume in the proximal one-third segment (toward LA) of the LAA.^{21,28} While recording the flow velocities, the gain should be kept low and care must be taken to avoid artifacts produced by inadvertent sampling of the LAA wall.

2.1.1. Normal flow pattern (Fig. 2)

In patients with sinus rhythm, a typical quadriphasic flow pattern can be seen as described below^{21,28}:

Table 1 – Grading of spontaneous echo contrast on echocardiography.

Grade	Description
0	Absence of echogenicity
1+	Mild (minimal echogenicity, only transiently detectable with optimal gain settings during the cardiac cycle)
2+	Mild to moderate (transient spontaneous echo contrast without increased gain settings and more dense pattern than 1+)
3+	Moderate (dense swirling pattern throughout the cardiac cycle)
4+	Severe (intense echo density and very slow swirling patterns in the LA appendage, usually with similar density in the main cavity)

Adapted from the Ref.¹⁸

Fig. 2 – Left atrial appendage (LAA) flow pattern. A. Schematic diagram showing different flow waves during sinus rhythm. B. Pulsed-wave Doppler tracing of LAA flow in sinus rhythm. C. Pulsed-wave Doppler tracing of LAA flow in atrial fibrillation.

- **Early diastolic emptying velocity** – this is a low-velocity outflow (toward the transducer) signal seen immediately after mitral inflow E wave, during the early part of ventricular diastole. The proposed mechanisms underlying this early diastolic wave include a fall in the LA pressure following opening of the mitral valve and also the external compression of LAA due to distension of the LV. The average early diastolic emptying velocity is in the range of 20–40 cm/s and correlates with mitral E and pulmonary vein diastolic velocities.^{2,29,30}
- **Late diastolic emptying velocity or LAA contraction flow** – is the most important wave during the sinus rhythm and occurs

immediately after the P wave on the ECG. The late diastolic emptying velocity is believed to result from active LAA contraction and is thus a marker of LAA contractile function. It correlates with LAA ejection fraction, LA size and pressure and is a significant predictor of thromboembolic risk.³¹ The average LAA contraction velocity is 50–60 cm/s.^{2,29,30}

- **LAA filling velocity** – This is a negative wave (away from the transducer) that occurs immediately following the LAA contraction and is a result of the combined effects of LAA relaxation and elastic recoil. The average LAA filling velocity is 40–50 cm/s and correlates well with the LAA contraction velocity.^{2,29,30}
- **Systolic reflection waves** – these low-velocity, multiple, alternate inflow–outflow waves follow the more prominent filling wave described above and are usually seen in patients with slow heart rate. Although the amplitude of these waves correlates with the LAA contraction and filling waves, their functional significance is not clear.³²

The quadriphasic wave pattern described above is easier to identify in presence of slow heart rate. When tachycardia occurs, early and late diastolic emptying waves usually merge and the reflection waves disappear.³⁰

The emptying velocities (both early and late) decrease progressively with age.³¹ Women tend to have lower emptying velocities as compared to men.³¹

2.1.2. Atrial fibrillation and flutter (Fig. 2)

The flow pattern and amplitude during atrial fibrillation (AF) is quite variable. Mostly, saw-tooth waves of varying amplitude and regularity, resulting from active LAA contraction, are seen. The amplitude of these waves may vary from being normal (or even supra-normal in some patients) to markedly reduced or nearly absent.^{33,34} The velocity of saw-tooth waves is higher during ventricular diastole than systole as ventricular diastole facilitates LA and LAA emptying. For the same reason, the velocity of these waves is also higher during slow ventricular rate.³⁵ The approach to quantification of these waves remains debatable with both the peak and mean velocities used by different investigators. Nevertheless, irrespective of what is measured, the values need to be averaged over 5–10 cardiac cycles.^{21,28}

Interspersed with the above-mentioned saw-tooth waves are early diastolic LAA emptying waves resulting from passive emptying of LAA as described above. The exact significance of these waves is not clearly known.

In contrast to AF, atrial flutter is characterized by more regular, saw-tooth waves. The amplitude of these waves is greater than that seen in AF but is still reduced compared to sinus rhythm.³⁶

2.2. Tissue velocity and strain (Fig. 3)

In contrast to LAA flow velocity, which is an indirect measure of LAA function, measurement of tissue velocity has the potential to provide direct estimate of the LAA contractility. On tissue velocity imaging, a similar wave pattern is seen as in the corresponding flow velocity. In a study involving 141 patients undergoing TEE, tissue velocity imaging was found to

Fig. 3 – Color tissue velocity imaging (A) and strain imaging for the assessment of left atrial appendage (LAA) function. On tissue velocity imaging, positive waves (toward the transducer) corresponding to the LAA emptying are seen during diastole and negative wave (due to LAA filling) is seen during systole. On strain imaging, LAA contraction during diastole produces negative wave whereas its stretch during systole produces a positive wave.

have good feasibility and correlated with the presence of LAA SEC or thrombus and with the history of thromboembolic events.³⁷ In other studies, LAA tissue velocity has been successfully used for quantifying LAA contractile dysfunction in mitral stenosis, to track the effect of balloon mitral valvotomy (BMV) and to detect impairment of LAA contractility in patients with hypertension and hypertrophic cardiomyopathy even in absence of AF.^{5,22–25}

The major limitation of tissue velocity imaging is that it is subject to the tethering and the translation effects of the heart and is therefore not a true measure of myocardial contractility. Strain imaging overcomes these limitations and is hence superior to tissue velocity imaging for this purpose. Initial studies with LAA strain imaging have shown good correlation of various LAA strain parameters with the emptying and filling velocities as well as with the LA strain parameters.²⁶ The LAA strain imaging has also been shown to be helpful in quantifying LAA contractile dysfunction in patients with AF and in monitoring recovery following cardioversion.²⁷

3. Role of assessment of LAA structure and function in clinical practice

Assessment of LAA anatomy and function plays an important role in the diagnostic work-up and management of many clinical conditions. While it is a mandatory investigation prior to performance of intervention procedures such as BMV, it is also routinely sought when the cause of ischemic stroke is not apparent and a cardiac source needs to be ruled out. In addition, more recent studies have disclosed newer indications for which LAA function assessment may be warranted.

3.1. Presence of thrombus or SEC

It is known that cardioembolic strokes account for $\geq 15\%$ of all ischemic strokes.³⁸ In a substantial proportion of such cases, LAA is the source of embolus. Approximately, 90% of intracardiac thrombi in non-rheumatic AF and 60% in patients with rheumatic mitral valve disease form within the LAA.³⁹ In patients with recent embolic event and AF, LAA thrombus is found in roughly 14% patients with short duration AF (started <3 days before) and in roughly 27% patients with longer duration of AF.⁹ In another study involving 262 patients with non-rheumatic AF, TEE revealed intracardiac thrombi in 8% patients, all of which were within the LAA.⁴⁰ Accordingly, imaging of the LAA to rule out thrombus is an important indication of performing TEE in patients suspected to be having cardioembolic stroke. TEE will also reveal SEC in many such patients. The presence of SEC alone in this setting, even in absence of a clot, may be enough to label it a cardioembolic stroke.^{16,17}

In addition, as mentioned above, exclusion of LA/LAA thrombi is mandatory when planning intervention procedures such as BMV, radiofrequency ablation of atrial arrhythmias and also prior to cardioversion for AF of >48 h duration in patients who have not been on adequate anticoagulation.

3.2. Prediction of thromboembolism

Presence of LAA dysfunction has been shown to be a strong predictor of thrombus formation and the risk of embolic events, even if no clot is found at the time of initial examination.^{1–3,41} In the SPAF III (Stroke Prevention in Atrial Fibrillation III) TEE substudy that included patients with AF, 17% patients with LAA contraction velocities ≤ 20 cm/s had thrombi as compared to 5% of the patients with higher velocities.¹ The prevalence of SEC was also much higher in patients with LAA dysfunction (75% versus 58%). Furthermore, the risk of ischemic stroke in patients with lower velocities was 2.6 times greater than in those with higher velocities. Similar findings have been noted in many other studies as well.^{2,3,41} For the same degree of LAA dysfunction, the thromboembolic risk is greater with AF than with flutter.^{36,42} Even in AF, the severity of LAA dysfunction is more marked in patients with rheumatic mitral stenosis, who typically have very low or even absent LAA velocities.⁴³

LAA dysfunction is a predictor of stroke risk in sinus rhythm also. Any condition which is associated with significant increase in LA pressure can result in LAA dysfunction. Accordingly, LAA dysfunction is common, even in absence of AF, in patients with significant mitral stenosis, severe LV systolic dysfunction, hypertrophic cardiomyopathy, etc.^{4,25,43–45} In patients with mitral stenosis, the LAA dysfunction is a strong predictor of development of SEC and thrombi. Successful BMV leads to improvement in the appendage function within 24–72 h and may also lead to resolution of the stroke risk. A study published by Reddy et al in this issue of the journal reports the effect of BMV on LAA function in patients with symptomatic mitral stenosis in sinus rhythm. Significant improvement was seen in LAA flow and tissue velocities on TEE performed on 3rd day after BMV. The improvement in LAA function was accompanied by complete disappearance or reduction of SEC in all the patients who had SEC prior to the procedure.⁴⁶ This study underscores the value of TEE in assessment of LAA function and emphasizes the ease and the feasibility of performing such assessment. Given the strong association between LAA dysfunction and the risk of thromboembolic events, an evaluation of the LAA function soon after BMV may become an important diagnostic goal with significant therapeutic implications, at least in patients with sinus rhythm who would otherwise not need anticoagulation. However, the findings of this study need to be correlated with long-term outcome in these patients to determine whether a repeat TEE examination for assessment of LAA function is really helpful in guiding management. A similar study by Vijayvergiya et al had followed up the patients for 6 months after BMV and had shown continued improvement in LAA function over this period. However, this period was too short to determine the effect of improvement in LAA function on the stroke risk.²⁴

LAA dysfunction is common in dilated cardiomyopathy also and may be a substrate for thrombus formation.⁴⁵ About 15% of patients with severe dilated cardiomyopathy in sinus rhythm have atrial thrombi, majority of which form within the LAA.⁴⁷ In the SPAF study also, clinical heart failure and LV systolic dysfunction were found to be independent predictors of thromboembolic risk.⁴⁸ Markedly impaired LAA velocities during sinus rhythm have been documented in patients with hypertrophic cardiomyopathy also.²⁵ These patients also demonstrated significantly reduced LAA myocardial velocities on tissue Doppler imaging, suggesting underlying atrial myopathy to be the cause of LAA contractile dysfunction.

3.3. Immediate and short-term outcome of cardioversion

Numerous studies have shown that in AF, preserved LAA function (LAA emptying velocities >20 cm/s) is associated with higher probability of conversion to sinus rhythm.^{49–52} In addition, preserved LAA function is also a predictor of greater probability of maintenance of sinus rhythm.⁵³ A multicenter study involving 408 patients undergoing cardioversion of AF showed that duration of AF <2 weeks, LA diameter <47 mm and mean LAA velocity >31 cm/s were the only independent predictors of success of cardioversion.⁵⁴

A number of studies have demonstrated temporary worsening of LAA function following restoration of sinus rhythm in patients with AF.^{55–58} This temporary worsening of LAA function, known as LAA stunning, occurs irrespective of the mode of cardioversion and is also seen after radiofrequency or surgical ablation of AF or flutter.^{55–59} Although the mechanisms underlying the post-cardioversion stunning are not clear, it has definite therapeutic implications. The stunning is commonly associated with new or worsening SEC and may thus predispose to thromboembolism.^{57,58,60} The time course of recovery of stunning varies but significant improvement in LAA function is known to occur within 7–30 days after cardioversion.^{55,58,59} The stunning occurs after cardioversion of atrial flutter also but, compared to AF, the absolute severity of LAA dysfunction is less marked given the relatively preserved LAA function prior to cardioversion in patients with flutter.^{42,59}

3.4. Role in normal health

Contrary to earlier belief, the LAA is now thought to play an important role in normal cardiac hemodynamics. The appendage, being more compliant than LA, acts as a reservoir to attenuate the rise in intra-atrial pressure in response to various hemodynamic factors.⁶¹ The surgical clamping or removal of LAA has been shown to result in immediate increase in mean LA pressure, LA size and pulmonary and mitral inflow velocities.^{62,63} Furthermore, the LAA myocardium has the highest density of atrial natriuretic peptide granules in the heart.⁶⁴ The release of atrial natriuretic peptide with consequent diuresis is an important compensatory mechanism involved in maintenance of normal fluid homeostasis. Thus, routine obliteration of LAA during mitral valve surgery may not be an entirely benign process as earlier thought. However, the long-term hemodynamic effects of such a procedure are currently not known.

Conflicts of interest

All authors have none to declare.

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