Assessment of left atrial appendage function with transthoracic tissue Doppler echocardiography

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Aims A transthoracic echocardiographic (TTE) parameter that would stratify atrial fibrillation (AF) risk would be useful. Tissue Doppler imaging can quantify left atrial appendage contraction velocity (LAA A_M).

Methods and results We studied 141 patients referred for transoesophageal echocardiogram (TEE); 48 were in AF. We obtained TEE and TTE LAA A_M velocities from the LAA apex on the parasternal short-axis and apical two-chamber views. Adequate traces were obtained in 118 patients (84%). In these patients, we measured 5382 LAA A_M velocity tracings. There was a strong correlation between LAA A_M on TEE and TTE parasternal short-axis (r = 0.741; P < 0.0001) and apical two-chamber views (r = 0.729; P < 0.0001). Patients in AF had lower LAA A_M than those with sinus rhythm on parasternal short-axis (12 ± 5 vs. 23 ± 7 cm/s, P < 0.0001) and apical two-chamber (14 ± 5 vs. 23 ± 8 cm/s, P < 0.0001) views. On parasternal short axis, LAA A_M velocities were lower in patients with spontaneous echo contrast, 11 ± 4 vs. 22 ± 8 cm/s (P < 0.0001), and in those with thrombus, 8 ± 2 cm/s (P < 0.0001). On apical two-chamber, LAA A_M velocities were also lower with spontaneous echo contrast, 12 ± 4 vs. 22 ± 7 cm/s (P < 0.0001), and with thrombus, 10 ± 4 cm/s (P < 0.0001). In patients with AF and TTE LAA A_M ≤11 cm/s, we found that nearly one-third had LAA thrombus. In patients with AF and a history of stroke or transient ischaemic attack (TIA), LAA A_M velocities were lower compared with those without history of stroke or TIA in the parasternal short-axis (9 ± 3 vs. 13 ± 5 cm/s, P = 0.02) and apical two-chamber views (11 ± 3 vs. 15 ± 6 cm/s, P = 0.008).

Conclusion Acquiring and quantifying LAA A_M contraction velocity is feasible on TTE in a high percentage of patients and correlates with TEE. LAA A_M was lower in AF compared with sinus rhythm, with spontaneous echo contrast compared to without spontaneous echo contrast, and in AF patients with a history of stroke or TIA. Those with LAA thrombus had the lowest LAA A_M velocities. LAA A_M is a novel functional parameter that may prove useful for risk stratification of AF.

Introduction
Atrial fibrillation (AF) is an independent risk factor for stroke and peripheral emboli, increasing risk five-fold.1–3 In AF, cardiogenic emboli are the sources of transient ischaemic attack (TIA) and stroke in 20–40% of patients, and the left atrial appendage (LAA) is almost always the site of thrombus formation.4 Decision-making for anticoagulation in AF patients presents thorny dilemmas.5–7 Despite the benefits of anticoagulation with warfarin in preventing stroke in patients with AF,8 there is clinical ambiguity in many patients.5–7 Currently, the need for anticoagulation is assessed on the basis of clinical parameters.9–12 Transoesophageal echocardiographic (TEE) parameters such as the presence of spontaneous echocardiographic contrast and LAA emptying velocity further risk stratifies AF patients who would most benefit from anticoagulation.13–17 However, the assessment of spontaneous echo contrast and LAA emptying velocity require TEE. TTE tissue Doppler imaging, previously measured with TEE,18,19 directly characterizes LAA myocardial function and may offer risk stratification for thrombus and embolism. The advantage of tissue Doppler imaging is that it is a high amplitude signal with high signal-to-noise ratio and is relatively easily detected from the chest wall. Thus, the purpose of this study was...
to assess how often this velocity could be reliably quantified during transthoracic echocardiogram (TTE) and to correlate it with clinically relevant variables.

**Methods**

**Patients**

Eighty-two patients in sinus rhythm and 59 patients in AF referred for TEE, >18 years old and able to give informed consent, were enrolled in the study. Patient demographics and medical history were obtained by a physician or trained registered nurse. The interpreters of the TEE and TTE data were blinded to each other's results. This study was approved by the Institutional Review Board of St Luke’s-Roosevelt Hospital.

**Transthoracic echocardiographic parameters**

All TTE studies were performed on a Sequoia Acuson (Siemens, Mountain View, CA, USA) using a 3.5 MHz probe. Measurements were obtained offline. Left atrial volume was calculated using the Simpson biplane method in the four-chamber and two-chamber views. Lateral left ventricular mitral valve annulus tissue Doppler velocities were obtained in the four-chamber view.

**Transoesophageal echocardiographic parameters**

TEE studies were performed on the same machine using a 7 MHz probe. LAA area was obtained on TEE using the largest LAA diastolic area.\(^2\) LAA emptying velocity was obtained by placing pulse Doppler cursor in the LAA 2 mm from its orifice. In sinus rhythm, LAA emptying velocity was calculated as the average of the three highest velocities. In AF, LAA emptying velocity was determined by analysing an average of 20 cardiac cycles, using four different methods to assess the best concordance with spontaneous echo contrast: (i) average of the three highest diastolic velocities; (ii) average of 10 consecutive systolic and diastolic velocities; (iii) average of 10 consecutive diastolic velocities; and (iv) average of the 10 highest diastolic velocities. The duration of the LAA \(A_M\) and the left ventricular mitral annulus diastolic velocities and the time from their onset to the start of the QRS were determined. Left ventricular ejection fraction was visually estimated.

**Statistical analysis**

All analyses were carried out using standard statistical package (SPSS or Windows, Version 13.0, SPSS Inc., Chicago, IL, USA). Continuous variables were reported as mean ± SD. Patient groups were compared using Student’s t-test (for normally distributed variable) or the Wilcoxon rank-sum test (for other variables) for continuous variables, and \(\chi^2\) test or Fisher’s exact test for categorical variables. Receiver operating characteristic (ROC) curves were used to evaluate the best method of calculating LAA \(A_M\) in patients with AF with respect to concordance with spontaneous echocardiographic contrast. Correlation between the TEE-derived LAA \(A_M\) and the TTE-derived LAA \(A_M\) was calculated using Pearson’s correlation. \(P\)-values were considered significant at less than 0.05.

**Results**

LAA \(A_M\) on TTE was obtained in 118 of 141 (84%) patients (male 47%, 63 ± 15 years) referred to the echocardiography laboratory for TEE. Most common indications for TEE were stroke/TIA (30%), AF (30%), and endocarditis (13%). Baseline clinical and echocardiographic characteristics are listed in Table 1. Seventy (59%) patients were in sinus rhythm, and 48 (41%) were in AF at the time of the study. During this study, we measured 5382 LAA \(A_M\) velocity tracings. Based on ROC statistical analysis for the detection of spontaneous echo contrast, we selected the average of three highest diastolic LAA \(A_M\) velocities in AF patients [area under the curve (AUC): TEE LAA \(A_M\) = 0.964, parasternal short axis = 0.867, apical two-chamber = 0.877]. For TEE LAA emptying velocity we selected 3 highest diastolic velocities [AUC: 0.964].

**Transoesophageal echocardiogram**

Of the 70 patients in sinus rhythm, 6 (9%) patients had spontaneous echo contrast and none had LAA thrombus. Of the 48 patients in AF, 33 (69%) had spontaneous echocardiographic contrast and 7 (14%) had LAA thrombus. See Table 2 for comparisons: LAA emptying velocity and LAA \(A_M\) were lower in patients with AF compared with those with sinus rhythm. In AF, LAA \(A_M\) was lower in patients with spontaneous echocardiographic contrast than in those without spontaneous echocardiographic contrast. In sinus rhythm patients, LAA \(A_M\) was lower in patients with spontaneous echocardiographic contrast than in those without spontaneous echocardiographic contrast. In AF patients, LAA emptying velocity and LAA \(A_M\) were also lower with thrombus compared with AF without
thrombus. LAA \( V_m \) TEE \( \leq 13 \) cm/s had a sensitivity of 82% and a specificity of 100% for the detection of spontaneous echocardiographic contrast (Figure 4A). LAA \( V_m \) on TEE \( \leq 9 \) cm/s had a sensitivity of 100% and a specificity of 83% for LAA thrombus detected on TEE (Figure 5A). LAA emptying velocity had a strong correlation with LAA \( V_m \) obtained by TEE (\( r = 0.635, P < 0.0001 \)), parasternal short-axis view (\( r = 0.576, P < 0.0001 \)), and apical two-chamber view (\( r = 0.590, P < 0.0001 \)).

Transcatheter echocardiogram parasternal short-axis view
LAA \( V_m \) was obtained in the parasternal short-axis view in 112 of the 118 patients (95%) analysed. A mean angle theta of 25 ± 11° was measured during acquisition. There was a strong correlation between LAA \( V_m \) obtained on TEE and TTE parasternal short-axis view (Pearson’s \( r = 0.741, P < 0.0001 \)). Bland–Altman analysis is shown in Figure 6A. See Table 2 for comparisons: LAA \( V_m \) was lower in patients with AF compared with those with sinus rhythm. In sinus rhythm patients, LAA \( V_m \) was lower in patients with spontaneous echocardiographic contrast compared with those without spontaneous echocardiographic contrast. In AF patients, LAA \( V_m \) was lower in patients with spontaneous echocardiographic contrast than in those without spontaneous echocardiographic contrast; it was lower in those with thrombus compared with those without thrombus; and, it was lower in patients with a history of stroke or TIA compared with those without stroke or TIA (9 ± 3 vs. 13 ± 5 cm/s, \( P = 0.02 \)). LAA \( V_m \) on TTE parasternal short axis of \( \leq 13 \) cm/s had a sensitivity of 97% and a specificity
of 60% for the detection of spontaneous echocardiographic contrast (Figure 4B). LAA \( A_M \) on TTE parasternal short axis of \( \leq 8 \text{ cm/s} \) had a sensitivity of 83% and a specificity of 80% for LAA thrombus detected on TEE (Figure 5B).

### Transthoracic echocardiogram apical two-chamber view

LAA \( A_M \) was obtained in the apical two-chamber view in 110 of the 118 patients (93%) analysed. A mean angle theta of 30 \( \pm 13^\circ \) was measured during acquisition. There was a strong correlation between LAA \( A_M \) obtained on TEE and TTE apical two-chamber view (Pearson’s \( r = 0.729, P < 0.0001 \)). Bland–Altman analysis is shown in Figure 6B. See Table 2 for comparisons: LAA \( A_M \) was lower in patients with AF compared with those with sinus rhythm. In sinus rhythm, LAA \( A_M \) was lower in patients with spontaneous echocardiographic contrast compared with those without spontaneous echocardiographic contrast. In AF, LAA \( A_M \) was lower in patients with spontaneous echocardiographic contrast than in those without spontaneous echocardiographic contrast; it was lower in patients with thrombus compared with those without thrombus (Figure 5C); and, it was lower in patients with a history of stroke or TIA compared with those without stroke or TIA (11 \( \pm 3 \) vs. 15 \( \pm 6 \text{ cm/s}, P = 0.008 \)). LAA \( A_M \) on TTE apical two-chamber \( \leq 13 \text{ cm/s} \) had a sensitivity of 76% and a specificity of 79% for the detection of spontaneous echocardiographic contrast (Figure 4C).
Left atrial appendage contraction velocity $A_M$ as a predictor spontaneous echo contrast and thrombus in atrial fibrillation

In the AF patients with both TTE LAA $A_M$ velocities $\leq 11$ cm/s, there was a $5/16$ (31%) likelihood of thrombus on TEE. This was a frequency higher than that observed when velocities were $>11$ cm/s, in whom only $2/32$ (6%) had thrombus ($P = 0.03$). Similarly, in AF patients with both TTE LAA $A_M$ velocities $\leq 13$, spontaneous echocardiographic contrast was present in $26/29$ (90%) vs. $9/21$ (43%) of patients with LAA $A_M > 13$ ($P = 0.001$).
Mean LAA_A_M velocities were higher than mean left ventricular mitral annulus velocities (24 ± 7 vs. 13 ± 5 cm/s, \( P < 0.0001 \)). However, there was no difference between duration of LAA_A_M and left ventricular mitral annulus velocities (88 ± 23 vs. 86 ± 23 cm/s, \( P = 0.45 \)). There was no difference in the time interval from QRS onset to onset LAA_A_M and the time interval from QRS onset to onset left ventricular mitral annulus velocities (65 ± 33 vs. 79 ± 42 cm/s, \( P = 0.083 \)). In AF, there could be no correlation between LAA_A_M and left ventricular mitral annulus velocities because there often is no perceptible left ventricular mitral annulus \( A \) velocity.

**Left atrial appendage A_M vs. left ventricular mitral valve annulus tissue velocities**

**Left atrial volume as a predictor of spontaneous echocardiographic contrast**

Spontaneous echocardiographic contrast occurred across a wide range of left atrial volumes. Based on the ROC analysis, the AUC for LAA_A_M on TTE parasternal short axis and apical two-chamber views was significantly better than left atrial volume in predicting spontaneous echocardiographic contrast \( (P = 0.03 \) and \( 0.045, \) respectively). The addition of TTE left atrial volume to LAA_A_M offered no further discrimination in the detection of spontaneous echocardiographic contrast to that offered by LAA_A_M alone.
Inter-observer variability

Using two-way random-effects model for absolute agreement, there was strong inter-observer [inter class correlation (ICC) = 0.991] and intra-observer [ICC = 0.983; 95% confidence interval (CI) = 0.936–0.996] correlations for the measurement of TEE for single measures. Using two-way random-effects model for absolute agreement, there was strong inter-observer (ICC = 0.997) and intra-observer (ICC = 0.997; 95% CI = 0.987–0.999) correlations for the measurement of TEE parasternal short-axis LAA Am for single measures. Using two-way random-effects model for absolute agreement, there was strong inter-observer (ICC = 0.993) and intra-observer (ICC = 0.991; 95% CI = 0.956–0.998) correlations for the measurement of TTE apical two-chamber LAA Am for single measures.

Discussion

In this study, we investigated LAA Am, the LAA contraction myocardial velocity, in a wide spectrum of cardiac patients using TTE-pulsed tissue Doppler imaging. Our findings are that LAA Am velocities could be recorded and measured in 84% of the patients; it is a feasible and reproducible measurement. Also, LAA Am velocities measured on TTE correlate well with measures done on TEE in the same patient on the same day. This lends credence to the idea that useful LAA Am information might be obtained by TTE. Furthermore, we have found that TTE LAA Am velocities are lower in patients with AF than in those with sinus rhythm. Also, they are lower in patients with spontaneous echocardiographic contrast and/or thrombus compared with patients without spontaneous echocardiographic contrast and/or thrombus. We found that in patients with AF who had LAA Am velocities $\leq$ 11 cm/s, thrombus was present in nearly a third, and more frequently than when LAA velocities were $>11$ cm/s (6%). We highlight the potential usefulness of finding low LAA Am velocities, because in the literature LAA thrombus is found in just 10–18% of all AF.$^{4,21}$ It appears that LAA Am velocities may non-invasively help predict the presence of LAA thrombus in AF patients. As the presence of spontaneous echocardiographic contrast and thrombus on TEE effectively stratifies embolic risk in AF patients,$^{16,17}$ we hypothesize that low LAA Am velocity may similarly prove to be a marker for embolic risk if studied prospectively in an AF cohort. Based on our observations here, we hypothesize that as TTE LAA Am $\leq$ 13 cm/s correlates with spontaneous echocardiographic contrast and TTE LAA Am $<11$ cm/s correlates with thrombus, lower TTE values might correlate with increased embolic risk. Our finding on cross-sectional analysis that AF patients with stroke and TIA had lower LAA Am velocities lends credence to this hypothesis.

The findings in our study are in agreement with earlier studies that have investigated the tissue Doppler velocity of the LAA but using only TEE.$^{22–24}$ Recently, Yoshida et al.$^{25}$ showed that in patients with paroxysmal AF, now in sinus rhythm, posterior left atrial wall velocities could be measured on TEE and that spontaneous echocardiographic contrast in sinus rhythm was associated with lower velocities.$^{16}$ However, patients in AF at that time were not studied. In the present study, AF patients were specifically included because these are the most clinically relevant patients, and LAA velocities were measured as opposed to the left atrial wall, because thrombi are most likely to form here.

The embolic risk in patients with AF is multifactorial and depends on LAA dysfunction, atrial and appendage dilatation, pressure and haemodynamic variables, and haematological factors.$^{15}$ Moreover, atrial and appendage dilatation and dysfunction depend not only on the severity of structural heart disease but also on the duration of AF—‘AF begets more AF’ via remodelling the left atrium and left atrial appendage.$^{26,27}$ A time-line of risk, with a personal slope, may be discernable for each individual patient. At present, risk is assessed through clinical variables that impact atrial function, i.e. heart failure, hypertension, and diabetes. However, the effects of these variables on atrial appendage function are continuous, not dichotomous. For example, hypertension may be mild, moderate, or severe. Moreover, the effect of time is continuous. Hence, the attraction of a direct measurement of LAA function.

It is common to encounter a patient in whom there is ambiguity about the appropriateness of long-term
anticoagulation. Both the pathophysiology of AF and clinical need support the import of developing a non-invasive method to risk stratify AF patients. It is uncertain how this parameter will be used in echocardiography, after continued study. In the AF patients with both TTE LAA velocities ≤11 cm/s, we found that nearly a third had LAA thrombus. If low LAA $A_M$ is confirmed to predict a high likelihood of LA thrombus, it may actually point to a need for early TEE in some AF patients. This is because when LAA thrombus is found, even with conventional anticoagulation, there is a high risk of embolism and death which may mandate more aggressive anticoagulation strategies. In others, quantification of LAA $A_M$ might be incorporated into clinical risk stratification schemes.

Technical issues

Echocardiographers may have noticed tissue Doppler LAA $A_M$ velocities during TEE acquisition of the LAA emptying velocities, as these tissue Doppler signals can appear under the LAA emptying velocities, especially in patients with small LAAAs. During acquisition of LAA $A_M$ on TTE, care must be taken to avoid obtaining the late diastolic left ventricular mitral valve annulus velocities, particularly in the apical two-chamber view. The main method to differentiate these two is careful positioning of the pulsed cursor (Figure 1). In addition, LAA $A_M$ velocities are, on average, twice as high. This is less of an issue in AF as these left ventricular velocities are attenuated or absent. Minimizing Doppler gain is important, to avoid overmeasuring LAA $A_M$ velocities. We recommend acquiring LAA $A_M$ in both the parasternal short-axis and apical two-chamber views.

Study limitations

There are several limitations of our study that should be acknowledged. Although TTE LAA $A_M$ velocities correlated with spontaneous echocardiographic contrast and thrombi, in our study, we have not yet correlated prospectively acquired LAA $A_M$ velocities and clinical events. Thus LAA $A_M$ velocities cannot yet impact clinical decisions. There is a learning curve for acquiring LAA $A_M$ from the chest wall, but we were able to obtain LAA $A_M$ measurement in 84% of the patients. In this study, 69% of the patients had swirling spontaneous echocardiographic contrast and thrombi, as determined by two blinded readers. This is a somewhat higher proportion than is usually seen in AF patients (50%). However, this does not detract from the fact that low LAA $A_M$ predicted spontaneous echocardiographic contrast in the AF cohort. Tissue Doppler imaging velocities acquired using echocardiographs that measure mean velocities will be lower.

Conclusions

The LAA $A_M$ velocity is a novel TTE parameter that allows non-invasive interrogation of the LAA myocardial function. Patients in AF with spontaneous echocardiographic contrast, thrombus, or a history of stroke or TIA have lower LAA $A_M$ velocities. This novel TTE functional parameter may prove useful for risk stratification of AF.

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References

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