Disparities in emptying velocity within the left atrial appendage

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Aims
Pulsed Doppler measurement of left atrial appendage (LAA) emptying velocity, a marker of left atrium contractile function, has been shown to predict success of cardioversion, thrombo-embolic risk, and maintenance of sinus rhythm after cardioversion and pulmonary vein isolation. However, in the published literature, emptying velocity measurement location is not uniform, and no standard currently exists. We assessed the hypothesis that emptying velocity when acquired near the LAA orifice differs from that at the LAA apex.

Methods and results
The study group comprised 44 patients (32 in sinus rhythm and 12 in atrial fibrillation) who were able to complete a non-emergent transoesophageal echocardiography. Pulsed Doppler recordings were obtained with the sample volume first positioned 1 cm from the LAA orifice, and then positioned within 1 cm of the LAA apex. At each location, we calculated the average of the peak end-diastolic LAA emptying velocity from five consecutive cardiac cycles. LAA orifice emptying velocity was higher than the apex emptying velocity in all patients. The median velocity at the orifice was 72 cm/s, which was 45% higher than the median velocity at the apex (43 cm/s, \( P < 0.001 \)). Lower LAA emptying velocity at the orifice was associated with a larger discrepancy between orifice and apex velocities. The ratio of orifice to apex velocity did not vary with orifice velocity. Multivariate analysis demonstrated that clinical patient characteristics were not significant predictors of the discrepancy between orifice and apex velocities.

Conclusion
LAA emptying velocity is greater at the LAA orifice compared with the LAA apex. Higher, more easily measured velocity and greater variability observed with orifice measurements make it the location of choice for research and clinical applications.

Keywords
Left atrial appendage • Atrial function • Transoesophageal echocardiography • Atrial fibrillation

Background
Left atrial appendage (LAA) velocities are often obtained during standard transoesophageal echocardiography as a surrogate marker for left atrium (LA) function. Pulsed Doppler measurement of LAA flow velocities has been shown to predict success of cardioversion,1 thrombo-embolic risk,2 and maintenance of sinus rhythm after both electrical cardioversion3 and pulmonary vein isolation.4 Specifically, Zabalgoitia et al.5 demonstrated an association between LAA emptying velocities <20 cm/s and increased risk of spontaneous echo contrast, LAA thrombus, and subsequent cardioembolic events. In this study, LAA emptying velocity was measured 1 cm within the LAA. While this measurement location has been used in other studies as well,6–7 there is no consensus for ideal cursor placement within the LAA.8 Different locations for pulsed-wave Doppler cursor placement have been reported in the literature, such as in the proximal one-third of the LAA,9–10 while in other studies the location was not specified.11–13 Guidelines on quantification for Doppler echocardiography from the American Society of Echocardiography do not make recommendations regarding LAA emptying velocity.14–15

We sought to determine whether LAA emptying velocity differed near the orifice compared to near the apex, and if so, which location might be more suitable for measurement.

Methods
Study sample
We visually assessed the LAA in 44 patients who underwent non-emergent TEE and were able to tolerate a complete examination.
This group included 12 patients whose indication was for assessment of atrial thrombus prior to cardioversion for atrial fibrillation (AF).

Echocardiographic methods
Transoesophageal echocardiography was performed in all patients using a 5 MHz multi-plane probe (Philips Medical Systems, Bothell, WA, USA). Visualizing the LAA from the mid-oesophageal position at multiple omni-plane angles, the angle providing the longest apex to orifice length was used for pulsed Doppler analysis, typically between 45 and 90°. A 4 mm sample volume was positioned 1 cm from the LAA orifice, and then within 1 cm of the apex. All measurements were recorded for offline analysis. The peak end-diastolic emptying velocity was calculated as an average of five consecutive cardiac cycles. LAA length was measured from the apex to the orifice in the view where the appendage was longest. LA anterior–posterior diameter was measured in the 120° three-chamber view at end systole from the aortic root perpendicular to the aorta.

Statistical analysis
All analysis was conducted using STATA version 10.0 (STATA Corp., College Station, TX, USA). As a descriptive assessment of the difference between measures, we calculated a Wilcoxon signed-rank statistic, a non-parametric test of differences in repeated measurements on the same sample. To consider the relationship between relative differences and emptying velocity more closely, we employed a ratio-intensity (RI) graph. To examine absolute differences between emptying velocities at the LAA orifice and the apex, we employed least absolute deviation (LAD) regression in the context of a scatterplot of the raw data. We also performed a simple linear multivariate regression to identify baseline predictors, if any, of the difference between the measures. Statistical significance was accepted at P < 0.05.

Results

Patient characteristics

Demographic and echocardiographic data are presented in Table 1. Among patients in sinus rhythm, evaluation for cardioembolic source of stroke and endocarditis were the most common indications for TEE. Evaluation for left atrial thrombus was the most common indication for TEE in the AF group. Mean left ventricular ejection fraction was 57% in the sinus rhythm group and 46% in the AF group. On average, LA and LAA dimensions were greater in patients in AF. Spontaneous echocardiographic contrast was present in 11 of 12 patients with AF and 1 of the 32 patients in sinus rhythm. LAA thrombus was present in two patients with AF and none in sinus rhythm.

Interobserver variability

The correlation coefficient of LAA velocity measurements between two observers was 0.98 (P < 0.001). The mean difference ± SD was 6.1 ± 6.7 cm/s.

Analysis

Table 2 displays summary statistical information for the LAA orifice and apex velocity measures, as well as for the difference between these measures and their ratio. Although the two measures are highly correlated (P = 0.85), the data indicate substantial disparities between the two measures. All patients in the sample manifested an orifice emptying velocity higher than the apex velocity. The orifice velocity was 45% higher, with a mean difference between the two measures of 23.1 cm/s. A Wilcoxon signed-rank test of the difference between the two measures revealed that difference to be statistically significant with P < 0.001. A representative example of orifice and apical LAA pulsed-wave Doppler waveforms is shown in Figure 1.

The logarithm of the ratio of the two velocity measures (a measure of disparity) against the logarithm of their geometric mean (a measure of central tendency) is represented in Figure 2. Figure 2A displays the resultant RI plot. For comparison, we also include the mean of the logged ratio (the dashed line) and its 95% confidence interval (the grey band). Patients in sinus rhythm are denoted by black circles, and those in AF by hollow circles.

Three features of this plot are noteworthy: first, the mean disparity and its confidence interval lie substantially above zero. (This is not an artefact of the log transformation; the mean untransformed ratio is statistically significantly larger than one.) Second, none of the observations lies below the horizontal (solid) line placed at zero, indicating that no patient had an orifice velocity below his or her apex velocity (though several are close). Third, there is neither a substantively nor statistically
significant relationship between the measures of relative disparity and central tendency. A regression of the former measure on the latter yielded a slope coefficient statistically indistinguishable from zero. This means that the discrepancy between orifice and apex velocities does not vary with overall LAA ejection velocity. We also conducted an analysis of the absolute differences between the measures. Figure 2B displays a scatter plot of the raw data. Superimposed on the graph is the 45° (solid) line, which represents hypothetical equality of the measures, and the LAD regression (dashed) line derived from the data, as well as its 95% confidence interval.

The fact that the estimated slope coefficient exceeds one, combined with the proximity of the estimated intercept to zero, implies that the distance between the regression line and the 45° line increases with blood flow velocity. In other words, the larger the apex velocity, the greater the disparity between that and the orifice velocity. A t-test permits us to reject the null hypothesis that the slope of the regression line is equal to one with \( p < 0.02 \).

Figure 3 plots emptying velocities at both the LAA apex and the orifice vs. LAA length and LA diameter. Both apex and orifice velocities showed a significant inverse association with LA diameter (apex \( r^2 = -0.36, \quad p = 0.02 \); orifice \( r^2 = -0.52, \quad p < 0.001 \)).
whereas their relationship with LAA length was not statistically significant (apex $r^2 = -0.20, P = 0.18$; orifice $r^2 = -0.20, P = 0.20$). On multivariate regression, however, neither LAA length nor LA diameter were independent predictors of the relative disparity between the orifice and apex velocities. Gender, ejection fraction, and indication for TEE were also not independent predictors of multivariate analysis. AF was a marginally significant negative predictor of absolute difference ($P < 0.09$); however, as is evident from Figure 2B, this is attributable to the tendency of patients with this indication to have lower emptying velocities generally.

Spontaneous echocardiographic contrast was associated with low ejection velocities at both locations. However, there was no association between the orifice–apex velocity difference and the presence of either spontaneous echocardiographic contrast or interatrial thrombus.

**Discussion**

This study used pulsed-wave Doppler to evaluate the peak emptying velocity at the LAA orifice and apex. It demonstrated a large

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**Figure 2** Ratio-intensity and scatter plots of data. (A) Dashed line is the mean of log(orifice/apex). (B) Dashed line is the least absolute deviation regression line: left atrial appendage orifice $= 5.00 (6.66) + 1.36 (0.14) \times$ LAA apex. Grey bands in both figures denote corresponding 95% confidence intervals.
and significant discrepancy between these locations. The relative difference in velocities was similar in both the sinus rhythm and the AF group.

To our knowledge, there is only one other study that compared emptying velocities at two different locations within the LAA. They found no significant difference between emptying velocities measured at the orifice vs. the mid-third of the appendage. The discrepancy between our results and theirs could be explained by our measurement being at the apex rather than at the mid-appendage. Though we did not measure emptying velocities at the mid-appendage, we would expect that these velocities decline from the orifice to the base in a continuous, though not necessarily linear, manner.

The clinical significance of lower emptying velocities at the apex vs. the orifice are unknown. One study, which compared the location of LAA thrombi for 41 patients with paroxysmal or chronic AF, found a higher incidence of occurrence at or near the orifice than at the apex. Although the sample size was
small, these findings could be interpreted to mean that there are other factors other than blood velocity that determine thrombus location, such as shear forces or local variation in endocardial expression of pro- and anti-thrombotic mediators.

One major limitation of our study is the relatively small sample size, particularly for patients in AF. Since the difference in velocities was highly significant even in the smaller AF group, a larger cohort would not likely change the outcome.

Another limitation is the lack of clinical outcomes data to determine the superiority of one location over the other for prognostic purposes. By not having follow-up data, we are unable to answer the question of whether the difference in velocity between the LAA orifice and the apex is an independent risk factor for adverse events. We did show, however, a lack of association between this difference and the presence of spontaneous echocardiographic contrast, which is itself a predictor of embolism.

Measuring emptying velocity at the LAA orifice does provide several advantages over the apex. Based on our study, which demonstrated higher overall velocities with greater variability, the discriminatory power of measurements made at the orifice should be greater. Additionally, the orifice is an easily defined landmark, and pulsed Doppler is less likely to be affected by interference from the appendage wall. Lastly, LAA orifice velocity has previously been shown to correlate with prognosis, whereas no clinical correlation data exist for the apex.

In conclusion, LAA emptying velocity is consistently greater at the LAA orifice compared with the LAA apex. If one is to measure LAA emptying velocities, it is imperative to be consistent in Doppler sample placement. Higher, more easily measured velocity and greater variability observed with orifice measurements make it the location of choice for research and clinical applications.

Conflict of interest: none declared.

References