Left ventricular fluid dynamics in heart failure: echocardiographic measurement and utilities of vortex formation time

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Background
In clinical heart failure (HF), inefficient propagation of blood through the left ventricle (LV) may result from suboptimal vortex formation (VF) ability of the LV during early diastole. We aim to (i) validate echocardiographic-derived vortex formation time (adapted) (VFTa) in control subjects and (ii) examine its utility in both systolic and diastolic HF.

Methods
Transthoracic echocardiography was performed in 32 normal subjects and in 130 patients who were hospitalized with HF [91, reduced ejection fraction (rEF) and 39, preserved ejection fraction (pEF)]. In addition to bipline left ventricular ejection fraction (LVEF) and conventional parameters, the Tei index and tissue Doppler (TD) indices were measured. VFTa was obtained using the formula: 4 × (1 − β/π × α² × LVEF), where β is the fraction of total transmitral diastolic stroke volume contributed by atrial contraction (assessed by time velocity integral of the mitral E- and A-waves) and α is the bipline end-diastolic volume (EDV)¹⁄³ divided by mitral annular diameter during early diastole. VFTa was correlated with demographic, cardiac parameters, and a composite clinical endpoint comprising cardiac death and repeat hospitalization for HF.

Results
Mean VFTa was 2.67 ± 0.8 in control subjects; reduced in HF, preserved EF HF, 2.21 ± 0.8; HF with reduced EF, 1.25 ± 0.6 (P < 0.001). It was not affected by age, gender, body surface area but was correlated positively with TD early diastolic myocardial velocities (E′, septal, r = 0.46; lateral, r = 0.43), systolic myocardial velocities (S′, septal, r = 0.47; lateral, r = 0.41), and inversely with the Tei index (r = − 0.41); all Ps < 0.001. Sixty-two HF patients (49%) met the composite endpoint. VFTa of < 1.32 was associated with significantly reduced event-free survival (Kaplan Meier log rank = 16.3, P = 0.0001) and predicted the endpoint with a sensitivity and specificity of 65 and 72%, respectively.

Conclusion
VFTa, a dimensionless index, incorporating LV geometry, systolic and diastolic parameters, may be useful in the diagnosis and prognosis of HF.

Keywords
Vortex formation time • Heart failure • Systolic • Preserved ejection fraction • Diastolic dysfunction • Myocardial performance index • Echocardiography • Tissue Doppler • Prognostic significance

Introduction
Asymmetric streaming of blood through the atrial and ventricular cavities appears to confer potential fluidic and dynamic advantages.¹ In normal heart, flow of blood from the left atrium (LA) into the left ventricle (LV) during early diastole results in an intraventricular rotational body of fluid.² This form of fluid transportation by vortex ring formation appears more efficient than by a steady straight jet.³,4 Left ventricular blood flow patterns have been described using three-dimensional magnetic resonance velocity mapping⁵ and recently using echocardiographic particle image velocimetry.⁶,⁷ These studies show that during early diastole, a large vortex is created behind the anterior mitral valve leaflet. This has a counterclockwise rotation in the four-chamber view...
and clockwise in the three-chamber view. The vortex results in the mitral inflow vector to be angled more towards the posterior ventricular wall. With atrial systole, late mitral inflow is directed more laterally and generates a second smaller vortex. At early systole, the rotating blood is redirected towards the outflow tract. The systolic outflow is unidirectional and laminar.5,6 The presence of vortices is also demonstrated by high frame rate Doppler echocardiography8 and digital processing of colour Doppler echocardiographic images.9

Previously, Gharib et al.4 have successfully quantified the process of vortex ring formation using a dimensionless index. In addition, the authors have shown that in a small subpopulation of patients with dilated cardiomyopathy and impaired LV ejection fraction (EF), vortex formation time (VFT) is consistently below the optimal range.6 The entire derivation has been published (simplified in Appendix).3 This simple index may be useful as it is dimensionless and may allow comparisons across patient groups without needing patient-specific parameters.4

We aim to (i) use non-invasive transthoracic echocardiography to derive vortex formation time (adapted) (VFTa) from the full formula, \( 4 \times (1 - \beta)/\pi \times a^3 \times LVEF \), (ii) validate VFTa in normal subjects, and (iii) examine its utility in clinical heart failure (HF) patients, both systolic HF (HF with reduced EF, HFrEF) and diastolic HF (HF with preserved EF, HFpEF). We hypothesize that VFTa is lower in patients, both systolic HF and diastolic HF, and may correlate with early diastolic tissue Doppler echocardiographic (TDE)-derived indices of myocardial function and myocardial performance index (Tei Index). VFTa may also have prognostic significance in HF.

**Methods**

**Subjects**

We analysed 32 control subjects (aged > 40 years) with structurally normal hearts on echocardiogram and 130 patients admitted for clinical HF; 91 demonstrated reduced LVEF (< 50%), whereas 39 had preserved EF. The controls were selected from our imaging database with normal echocardiograms. None of them had HF. All HF patients presented acutely and were diagnosed, in accordance to published guidelines.10 The aetiology of HF, prevalence of coronary artery disease, risk factors, and renal insufficiency were recorded. Exclusion criteria were suboptimal echocardiographic images, irregular heart rhythm, and concomitant significant primary valvular heart diseases. Approval was obtained from the Institutional Ethics Review Board.

**Echocardiography and computation of VFTa**

All subjects underwent a comprehensive echocardiographic examination (two-dimensional, pulsed, and continuous Doppler) as well as myocardial tissue Doppler studies. Those with HF had their echocardiographies performed during their primary admission for HF. We measured the mitral annulus diameter (D, mm) in early diastole from the four-chamber view (Figure 1A). The LVEF and the EDV were quantified using the biplane method of disks (Figure 1B and C). \( a \) was determined by \( EDV^{1/3} \) divided by \( D \). Transmural mitral inflow flows were assessed using pulsed Doppler at the apical four-chamber view. Velocity time integrals (VTIs) of early (E) and late (A) diastole were measured (Figure 1D) to calculate \( \beta \) which was the fraction of total transmural diastolic filling contributed by atrial contraction. VFTa was then computed using the formula \( 4 \times (1 - \beta)/\pi \times a^3 \times LVEF \). Diastolic function was categorized into four grades: normal for age, prolonged relaxation (grade I dysfunction), pseudonormal (grade II), and restrictive (grade III) by integrating transmural and pulmonary venous Doppler findings.11 Tei index was determined as the sum of isovolumic contraction time and isovolumic relaxation time divided by the ejection time.12 Peak systolic (S’), early (E’), and late (A’) diastolic TDE velocities were measured at the septal and lateral mitral annulus in the apical four-chamber view and the respective mitral E/E’ ratios were derived.13 Each parameter value was obtained as an average of three measurements.

**Clinical endpoints**

Follow-up clinical information was obtained from chart reviews by an investigator blinded to VFTa values and echocardiographic findings. The endpoint of interest was a composite of adverse events comprising cardiovascular death and repeat hospitalization for HF.

**Statistical analysis**

Continuous variables were expressed as mean value ± SD. One-way analysis of variance was performed for comparisons between three groups after satisfying the homogeneity assumption. Correlation coefficients (rho) were obtained between relevant parameters and VFTa. \( \chi^2 \) analyses were performed for comparisons of categorical variables between groups. We constructed ROC curves to compare areas under curves (AUCs) of VFTa with E’ and E/E’ in the diagnosis of HF in the entire cohort and between controls and subjects with HFpEF. Multivariate linear regression analyses were performed to determine independent predictors of VFTa. Septal and lateral TDE parameters were averaged for these analyses. Event-free survival curves were generated using the Kaplan–Meier method and differences between groups analysed using the log rank test. The association of echocardiographic and clinical variables with outcome was assessed using Cox models to estimate the univariable hazard ratio of event for each variable. Multivariable analysis was performed for variables with \( P < 0.2 \). The incremental value of VFTa was assessed in a series of Cox models. Statistical significance was attributed when \( P < 0.05 \). SPSS for Windows (version 14.0, SPSS, Inc., Chicago, IL, USA) was used for all analyses except in the comparison of pairs of ROC curves which was performed using MedCalc (version 8.0.1.1, MedCalc Software, Mariakerke, Belgium).

The data sets from 10 randomly selected patients were analysed by the first operator 3 months after the first analyses and also by the second operator who was blinded to the results of the first operator. Intra- and inter-observer variability was assessed by intra-class correlation coefficients14 with 95% confidence intervals using SPSS reliability analyses.

**Results**

Baseline demographics and echocardiographic parameters are listed in Tables 1 and 2. In HFrEF and HFpEF patients, echocardiography was performed 4 ± 7 and 4 ± 6 days, respectively, after hospital admission. The control subjects were younger than the HF groups. There was a higher proportion of females in the HFpEF group. Among patients with the HFpEF, 59 and 31% had grade II and III diastolic dysfunction, respectively; 9, 34, and 49% of patients in the HFrEF group had grade II, III, and IV diastolic dysfunction, respectively. Most patients (92%) in the HFrEF group had HF secondary to ischaemic heart disease. In contrast,
Hypertensive heart disease was the most common aetiology in the HFpEF group, with ischaemic heart accounting for only 15% of patients in this group.

LV volume was the lowest in subjects with the HFpEF and the highest in the HFrEF. In contrast, there were incremental increases in LA volume and LV mass indexed to body surface area, from normal subjects to HFpEF to HFrEF groups. Similarly, LV E/E’ increased, whereas E’ and S’ decreased across the three groups. Mean A’ velocity was lowest in the HFrEF group.

We were able to quantitate VFTa using the full formula of $4 \times \left(1 - \beta\right)/\pi \times \alpha^3 \times \text{LVEF}$ from transthoracic echocardiography in all our subjects. VFTa was $2.67 \pm 0.8$ in normal subjects. This dimensionless index was reduced in HF: HFpEF, $2.21 \pm 0.8$ (P = 0.019); HFrEF, $1.25 \pm 0.6$ (P < 0.001) (Figure 2, Table 2).

VFTa correlated positively with the LVEF, modestly with mitral annular S’ and E’ (septal, $r = 0.46$; lateral, $r = 0.43$), and inversely with the Tei index ($r = -0.41$) and LA volume (Table 3). In contrast, there were weak correlations of VFI with mitral inflow E velocities, LV filling pressure (E/E’ septal, $r = -0.24$; lateral, $r = -0.20$), and TD-derived A’ velocities. VFTa correlated best with the LV geometric parameter $\alpha$ in the control subjects and in the HFpEF group but this relationship appeared to be weaker and altered in patients with the HFrEF (Figure 3). In multivariate analyses, including LVMi, LA volume, and TDE parameters but excluding parameters used in the derivation of VFTa, we found only $E’$ ($x^2 = 8.20$, 95% CI: 5.41–16.9, P < 0.001) and LA volume to be significant independent determinants of VFTa.
Table 2  Selected echocardiographic variables in 32 control subjects and 130 patients with heart failure

<table>
<thead>
<tr>
<th></th>
<th>Control subjects (n = 32)</th>
<th>HFP EF (n = 39)</th>
<th>HFR EF (n = 91)</th>
<th>P-value (between three groups)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV ejection fraction (%)</td>
<td>70 ± 5.7</td>
<td>69 ± 6.6</td>
<td>27 ± 8.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-diastolic volume (mL)</td>
<td>97 ± 22</td>
<td>86 ± 25</td>
<td>149 ± 45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass indexed to BSA (g/m²)</td>
<td>77 ± 12</td>
<td>113 ± 31</td>
<td>128 ± 37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV RWT</td>
<td>0.35 ± 0.07</td>
<td>0.51 ± 0.13</td>
<td>0.32 ± 0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA volume (mL)</td>
<td>36 ± 11</td>
<td>47 ± 20</td>
<td>58 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVSP (mmHg)</td>
<td>31 ± 4</td>
<td>36 ± 9</td>
<td>45 ± 15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tei index</td>
<td>0.41 ± 0.09</td>
<td>0.49 ± 0.15</td>
<td>0.67 ± 0.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VFTa</td>
<td>2.67 ± 0.80</td>
<td>2.21 ± 0.80</td>
<td>1.25 ± 0.55</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Mitral inflow Doppler
- Peak E velocity (cm/s) | 74 ± 11 | 73 ± 24 | 74 ± 22 | NS |
- Peak A velocity (cm/s) | 68 ± 18 | 89 ± 26 | 64 ± 24 | <0.001 |
- E/A ratio              | 1.17 ± 0.4 | 0.86 ± 0.3 | 1.43 ± 1.0 | 0.001 |

Septal annular TDE
- Peak S’ velocity (cm/s) | 8.6 ± 1.8 | 8.5 ± 2.8 | 5.7 ± 2.2 | <0.001 |
- Peak E’ velocity (cm/s) | 9.5 ± 2.4 | 7.9 ± 4.0 | 5.8 ± 1.7 | <0.001 |
- Peak A’ velocity (cm/s) | 11.1 ± 2.0 | 10.9 ± 3.4 | 8.1 ± 2.3 | <0.001 |
- E/E’ ratio              | 8.3 ± 2.3 | 10.3 ± 4.0 | 13.6 ± 5.5 | <0.001 |

Lateral annular TDE
- Peak S’ velocity (cm/s) | 10.8 ± 3.2 | 9.7 ± 3.5 | 6.9 ± 3.1 | <0.001 |
- Peak E’ velocity (cm/s) | 12.0 ± 3.2 | 9.1 ± 3.5 | 7.7 ± 2.2 | <0.001 |
- Peak A’ velocity (cm/s) | 12.2 ± 3.6 | 12.5 ± 3.3 | 8.5 ± 2.7 | <0.001 |
- E/E’ ratio              | 6.5 ± 1.7 | 8.8 ± 3.4 | 9.8 ± 4.2 | <0.001 |

BSA: body surface area; LA: left atrium; LV: left ventricle; pEF: preserved ejection fraction; rEF: reduced ejection fraction; HF: heart failure; RVSP: right ventricular systolic pressure; RWT, relative wall thickness; TDE, tissue Doppler echocardiography; VFTa, vortex formation time (adapted). Other abbreviations as in Table 3.

ROC curves were constructed to provide head-to-head comparisons of VFTa with E’, E/E’, and the LVEF. We found that in the diagnosis of HF, the AUCs for E’, E/E’, the LVEF, and VFTa were 0.85 (95% CI: 0.78–0.92), 0.77 (95% CI: 0.70–0.85), 0.86 (95% CI: 0.80–0.91), and 0.87 (95% CI: 0.81–0.92), respectively, all Ps < 0.001 (Figure 4). The areas under the ROC curves were not statistically different between each of the paired parameters (z-statistic = 0.39–1.88; P = 0.06–0.70). Similarly, in comparison between the HFP EF vs. controls, the AUCs for E’, E/E’, and VFTa were 0.73 (95% CI: 0.61–0.85, P < 0.001), 0.64 (95% CI: 0.51–0.77, P = 0.040), and 0.68 (95% CI: 0.55–0.80, P = 0.011), respectively. Direct comparisons of each pair of ROC curves showed no significant difference between the AUCs (z-statistic = 0.35–0.92; P = 0.36–0.73). An optimized threshold VFTa of <2.06 discriminated HFP EF from controls with a sensitivity of 59% and a specificity of 78%.

Figure 2 Box plot showing a gradient of vortex formation time (adapted) across the three categories. There is a decrease of vortex formation time (adapted) with heart failure and preserved ejection fraction compared with control. The lowest vortex formation time (adapted) occurs in the heart failure with reduced ejection fraction.

During a median follow-up period of 741 days (inter-quartile range, 89–1668 days), four patients were lost to follow-up and the composite endpoint occurred in 62 patients (49%). Higher proportion of patients in the HFR EF (61%) had an adverse event, compared with 23% of the HFP EF (χ² = 15.4, P < 0.001). Fifteen patients died of cardiovascular causes: 10 from progressive HF, 3 suddenly, 1 with documented ventricular fibrillation and another from non-ST elevation myocardial infarction. In Cox regression models, univariate predictors of adverse events were listed in
Table 4. Multivariable analysis showed VFTa to be the only independent predictor of the endpoint (HR = 0.63, 95% CI: 0.42–0.94, P = 0.02). A model using limited clinical variables gave an overall $\chi^2$ of 4.26. The addition of selected echocardiographic parameters, including VFTa, increased the power of this model (Figure 5). Patients with an endpoint had lower VFTa (1.32 ± 0.70 vs. 1.73 ± 0.80, P = 0.003). ROC curve for prediction of adverse events had an AUC of 0.67 (P = 0.58–0.77, P = 0.001). The most optimal cut-off for VFTa was 1.32 cm/s with a sensitivity of 65% and a specificity of 72%. Kaplan–Meier analyses for patient groups dichotomized by VFTa of less than and greater than or equal to 1.32 showed significantly lower event-free survival in the group with reduced VFTa (log rank 16.3, P = 0.0001) (Figure 6).

The intra-observer and inter-observer variabilities for the computation of VFTa as assessed by the intraclass correlation coefficients ($r$) were 0.96 (95% CI: 0.84–0.99, P < 0.0001) and 0.87 (95% CI: 0.58–0.97, P = 0.0002), respectively.

**Discussion**

We employ echocardiography to derive VFTa from its full formula and use it in clinical HF. We find that VFTa, a dimensionless index which reflect efficiency of fluid propagation through the LV and thus heart health, is diminished in HF. VFTa is also significantly impaired in the HFP EF. In addition, we demonstrate that VFTa predicts a composite of adverse events, comprising cardiovascular death, and rehospitalization for HF.

In contrast to the previous article that used a simplified formulae to calculate VFT, this formula of $4 \times (1 - \beta) / \pi \times a^3 \times LVEF$ takes into consideration, LV geometry, diastolic and systolic components. We find that the mean VFTa in subjects with structurally normal hearts on echocardiography is 2.67 ± 0.8. This is lower than the previous derived the simplified index of 4. In the landmark paper by Gharib et al., time-velocity integral divided by the diameter of the mitral annulus is used in their analysis of vortex formation time (adapted) are illustrated in this figure. The relationships of $\alpha$ and vortex formation time (adapted) are similar between controls and subjects with the heart failure preserved ejection fraction. However, this is distinctly different in the heart failure with reduced ejection fraction.
formation in healthy subjects and in patients with dilated cardiomyopathy. Recently, several authors have calculated VFT differently.15 – 18 Some estimated $V_T$ from peak transmitral Doppler A-wave divided by the sum of the A- and E-wave peak magnitudes.15 – 18 For simplification and improved practicality, mean mitral valve diameter was measured from maximum opening diameters obtained in two apical projections rather than taking a time-averaged diameter. The largest mitral orifice diameter obtained in the two, three, and four-chamber apical views may also be used.15,18 We have used this method for calculating VFT but found that, it is challenging to consistently image the mitral leaflets tips, especially in the apical two-chamber view. Furthermore, in the HFrEF, conflicting contribution of diastolic tethering of the mitral valve leaflets and reduced LVEF, result in low, high, and intermediate values. Overall, this parameter was not able to differentiate our three groups of subjects (data not shown). Thus, the VFTa values are lower than the original VFT, published in the literature. This may be secondary to how we have measured the parameters. The mitral annular diameter was measured instead of the smaller mitral orifice, resulting in lower values. This is more practical, more consistent and as discussed in the following, has diagnostic and prognostic utilities in HF.

We show that VFTa is markedly diminished in reduced EF HF. It is also diminished in the HFpEF, albeit not as low as in the HFrEF. In contrast the Tei index is higher in the HFpEF. Though the Tei index has been suggested to be used for diagnosis of HF, it may be limited by preload, fluctuating cardiac cycle length and of the considerable overlap between control subjects and HF.19,20 VFTa may also be affected by preload as the formula include VTI of transmitral E and A to calculate $\beta$, which was the fraction of total transmitral diastolic filling contributed by atrial contraction. Therefore, if preload is increased, $\beta$ may be correspondingly lower and VFTa higher, provided the rest of the parameters remain the same.

Our HFpEF cohort appears similar in demographics compared with patients from epidemiological studies where the patients consist of more women, smaller LV, and concentric remodelling.21 – 23 Our study suggests that there is primarily LV dysfunction in these patients and the propagation of fluid through the LV may

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### Table 4 Prediction of adverse events by univariate analysis of selected echocardiographic and clinical variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01 (0.98–1.01)</td>
<td>0.62</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.75 (0.19–3.04)</td>
<td>0.69</td>
</tr>
<tr>
<td>Left ventricular mass index</td>
<td>1.00 (1.00–1.01)</td>
<td>0.45</td>
</tr>
<tr>
<td>Left atrial volume</td>
<td>1.01 (1.00–1.03)</td>
<td>0.01</td>
</tr>
<tr>
<td>Tei index</td>
<td>1.66 (0.55–5.02)</td>
<td>0.37</td>
</tr>
<tr>
<td>Averaged annular TDE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak S’ velocity</td>
<td>0.97 (0.88–1.07)</td>
<td>0.51</td>
</tr>
<tr>
<td>Peak E’ velocity</td>
<td>0.93 (0.83–1.05)</td>
<td>0.27</td>
</tr>
<tr>
<td>Peak A’ velocity</td>
<td>0.89 (0.81–0.98)</td>
<td>0.01</td>
</tr>
<tr>
<td>E/E'</td>
<td>1.01 (0.96–1.07)</td>
<td>0.67</td>
</tr>
<tr>
<td>Vortex formation time (adapted)</td>
<td>0.56 (0.38–0.84)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>0.98 (0.96–0.99)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

$A'$, late diastolic annular velocity; $E'$, early diastolic annular velocity; $E/E'$, ratio of transmitral to annular early diastolic velocities; $S'$, systolic annular velocity; TDE, tissue Doppler echocardiography.
be impaired. This is consistent with other studies which showed diastolic and even systolic dysfunction in the HFrEF.\textsuperscript{22,24,25} In a small study by Takeda et al.,\textsuperscript{26} LV diastolic dysfunction in the HFrEF may have been clinically underestimated by the transmitral flow velocity curves. We find that VFTa is comparable with tissue Doppler indices ($E'$ and $E/E'$) in diagnosing HF. VFTa may also be useful in the HFrEF. However, patients with the HFrEF, in this study, may be sicker and have more severe HF, in comparison with the HFrEF and this may affect VFTa values.

We find a significant correlation between LVEF and VFTa but this is not surprising as the LVEF is used in the calculation of VFTa. Correlations with TDE and the myocardial performance index (Tei index) are moderate at best. The inverse relationship between VFTm and the Tei index suggests that efficiency and propagation of fluid may be significantly reduced with worsening LV function. However, fluid dynamics may not be affected by heart function alone (which explained the only modest correlation) as other factors including LV geometry may be important. Thus, it is interesting to demonstrate the different relationships between VFTa and LV geometry ($\alpha$) between HFrEF patients and those with preserved EF. In normal controls and HFrEF patients, fluid propagation appeared to be related more strongly to and predicted by LV geometry. In the HFrEF, other factors especially LVEF influence the relationship between $\alpha$ and VFTa. Conventional Doppler using transmitral flow velocities to assess LV diastolic function suffers from known phenomenon of pseudonormalization.\textsuperscript{27} Regional tissue Doppler imaging has been shown to be a useful contribution in the evaluation of heart function, overcoming the pattern of pseudonormalization,\textsuperscript{28} though not without limitations.\textsuperscript{29} We demonstrate reasonable correlations of VFTa with mitral annular $S'$ and $E'$ velocities, but not with mitral inflow parameters and TD-derived $A'$ velocities. This may be because, unlike transmitral velocities, VFTa, as a dimensionless index and the index of cardiac health is less subjected to pseudonormalization.\textsuperscript{4} The process of vortex ring formation occurs during early LV diastole.\textsuperscript{4,5} Therefore, late diastolic annular $A'$ may not contribute as much to diastolic fluid propagation through the LV, compared with $E'$. In our multivariate analyses, only $E'$ and LA volume are significant independent determinants of VFTa. This is consistent with previous studies showing that mitral annular recoil is related to VFT.\textsuperscript{30} LV filling pressure as determined by $E/E'$ ratios\textsuperscript{13,31} appears also to correlate modestly with vortex formation. Other LV characteristics, not analysed in this study, include torsion/untwisting which may also contribute to fluid propagation through the LV.

We show that VFTa is important in predicting adverse events among the HF patients. It is possible that differences in clinical management of the HF groups may account for differences in clinical events at follow-up and confound this study. However, many studies have demonstrated prognostic significance of echocardiographic parameters of LV systolic and diastolic functions.\textsuperscript{22,33} These include the LVEF, mitral inflow Doppler, TDE, and flow propagation parameters.\textsuperscript{34} LA volume and LV mass are also established indices.\textsuperscript{35} As a composite index integrating LV geometry, systolic and diastolic components of cardiac functions, it is not surprising that VFTa correlate with adverse events. Inefficient vortex formation result in suboptimal transfer of energy from diastole to systole. Low VFTa portends a grim prognosis. Indeed, VFTa may be complementary to other echocardiographic parameters because of its predictive ability, if confirmed in future studies.

**Limitations**

We did not systematically image fluid propagation and vortices in the LV in normal and HF hearts. This may be performed with aid of digital particle image velocimetry (PIV).\textsuperscript{5,7,36,37} However, PIV is not widely available, unlike computation of VFTa using readily obtainable transthoracic echocardiographic parameters, thus precluding the need for highly sophisticated imaging technology. In addition, VFT has been extensively verified in controlled models and shown to be robust, although a simplified formula was used.\textsuperscript{6} Some patients with arrhythmias such as atrial fibrillation were excluded. In this setting, atrial contribution of LV filling could not be determined accurately. We also excluded subjects with primary valvular heart disease as LV vortices may be affected by the regurgitant or stenotic lesions per se.\textsuperscript{18,38} We did not assess the effects of ischaemic/functional mitral regurgitation, which may be present in HF.\textsuperscript{39} on VFTa. Though all control subjects have normal echocardiograms, some of them have cardiovascular risk factors and coronary artery disease. However, the derived VFTa are not, as a result, excessively low. In fact, these values are similar to that in healthy young non-athletes and Olympian athletics (unpublished). Since we used the biplane method of disks to obtain LV volumes and EF, we relied on proper visualization of the LV endocardial borders, which may not be well defined. LV opacification using contrast agents may be used to enhance LV borders\textsuperscript{40} and hence obtain more accurate VFTa computation. However, this contrast technique is associated with higher costs and is not yet routinely employed in most echocardiographic laboratories.\textsuperscript{41,42} Similarly, three-dimensional echocardiography may also provide better quantification, especially in LV with distorted geometry in HF.\textsuperscript{43,44} As discussed above, another source of discrepancy can be the way the mitral valve diameter is calculated. If possible, an integrated average diameter over the cardiac cycle should be obtained. However, we have standardized the methodology to produce consistent results.

In comparing the HFrEF and the HFrEF, there remains a possibility of selection bias with a heterogenous response to therapy between the HF patients. A prospective study with comparable severity in disease between the two groups is warranted.

**Conclusions**

In this clinical study, VFTa, a dimensionless index incorporating LV geometry, systolic and diastolic parameters derived from transthoracic echocardiography, may be able to aid in the diagnosis of HF. In addition, it appears to be a predictor of adverse cardiovascular events in HF. Larger studies are warranted.

**Conflict of interest:** none declared.
Appendix

Simplified mathematical derivation of VFT⁴

We know that (i) LVEF = [(end-diastolic volume (EDV) − end-systolic volume (ESV))/EDV]; stroke volume (SV)/EDV and that (ii) SV = Vt + Vw (where Vt and Vw were contributions of E- and A-waves during LV filling, respectively) = U(t(E))/πD⁴/4 + U(t(A))/πD⁴/4 (where t = mitral filling period, U average velocity for the filling period and D diameter of mitral valve annulus).

Multiplying both sides of the second equation by 4/(πD⁴) and replacing the SV with the first equation, we obtain:

$$\frac{4}{\pi D^4} \times (EF \times EDV) = \frac{U(t(E))}{D} + \frac{4}{(\pi D^4)} \times V_A.$$ 

Since VFT = U(t)/D,

$$VFT = \frac{4}{(\pi D^4)} \times [(EF \times EDV) - V_A].$$

Substituting β as the fraction of SV contributed by atrial contraction and α as LV geometric parameter of (EDV)¹/³/D,

$$VFT = 4 \times \frac{1 - \beta}{\pi \times \alpha^3 \times LVEF}.$$ 

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Bouncing ball myxoma in the left atrial cavity

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A left atrial (LA) free-floating myxoma is a rare disorder, which has an embolic potential and may also cause sudden death because of the occlusion of the mitral orifice. A 77-year-old female patient presented with an episode of dizziness and syncope on exertion. For the last 2 months prior to the admission, she was suffering from progressive exertional dyspnoea. The transthoracic echocardiogram revealed a mobile mass in the LA cavity (Panel A; see Supplementary data online, Video S1). A transoesophageal echocardiogram demonstrated a giant mass with a broken stalk (35 × 35 mm sized), spherical shaped, and floating freely in the LA. Another semi-mobile mass (15 × 21 mm) considered to be connected to the fossa ovalis with a stalk was also detected. It was thought that the mobile mass was split off from the semi-mobile mass, and as we observed, the mobile mass was bouncing in the manner of a ball on the semi-mobile one (Panels B–D; see Supplementary data online, Videos S2–S4). The surgery confirmed the existence of the free-floating mass with a stalk fragment in the LA and another mass on the side of the fossa ovalis. Initially, the mobile mass was excised from the LA, followed by the excision of the semi-mobile mass which was attached to the interatrial septum tissue, and the resulting defect was repaired with an epicardial patch (Panel E). The mass was histologically proven to be a myxoma (Panel F).

Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

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