Assessment of early diastolic left ventricular function by two-dimensional echocardiographic speckle tracking

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Aims To determine whether the degree of untwisting of the apex in early diastole is related to established parameters of diastolic function.

Methods and results Data from 71 hospital inpatients with preserved left ventricular systolic function who underwent standard two-dimensional echocardiography was analysed using an off-line speckle tracking software package. Early diastolic mitral inflow velocity (e'), mitral septal annular tissue Doppler velocity (e0), and the rate of early diastolic apical untwist in degrees per second (rotR) from a parasternal short-axis view of the apex were all measured. Of the 71 patients, 14 had normal diastolic function, 25 had an abnormal relaxation pattern, 27 had a pseudonormalized pattern, and 5 had a restrictive pattern as defined by standard echocardiography criteria. Both e' and the ratio of e'/e0 correlated with the rate (speed) of early diastolic apical untwist (rotR) (P < 0.001 for both).

Conclusion This non-invasive assessment of apical diastolic untwist is related to established echocardiographic measures of diastolic function and may illustrate the importance of a ventricular suction effect in varying left ventricular filling states.

KEYWORDS Echocardiography; Speckle tracking; Diastolic function

Introduction

Diastolic filling of the left ventricle (LV) is an important component of normal LV function. From the Frank–Starling law of the heart, we know that increased LV filling and consequent myocardial stretch result in increased contractility.1 Early diastolic filling is directly related to the active process of LV relaxation leading to a 'suction' effect causing blood to flow from the left atrium (LA) into the LV across a pressure gradient. This 'suction' effect is thought to be caused by rapid untwisting of the LV apex in early diastole.2–5 Animal models have shown that LV twist at end systole and end diastole is linearly related to volume and that this relationship is independent of variations in contractility, afterload, and heart rate.6,7 Moreover, the amplitude of apical twist and untwist has been found to be independent of changes in preload.6

Currently the gold standard for the non-invasive assessment of diastolic function is using echocardiography by comparing the early mitral inflow velocity (e) to the mitral inflow wave velocity after atrial contraction (a) to give a ratio (e:a). In addition, the e velocity to tissue velocity of the mitral annulus in early diastole (e') to give a ratio (e:e') is used to estimate LV filling pressures.7 However, these measurements are all made after the mitral valve has opened and have a degree of load dependence. Apical untwisting usually occurs during isovolumic relaxation and may be less dependent on LA pressure or preload. In fact, the rate of LV untwist as measured by magnetic resonance imaging (MRI) has been proposed as a load independent measure of diastolic suction and tau.2 LV systolic rotation has also been assessed using MRI8–11 which is proving a valuable tool for analysis of LV mechanics; however, MRI is only available in a larger hospital environment and involves bulky and expensive equipment. Echocardiography has superior temporal resolution when assessing LV mechanics and is more available and accessible than MRI.

Recent advances in echocardiographic software have led to the development of two-dimensional (2D) speckle tracking,12–16 which allows for automated tracking of left LV endocardial borders over time. When used on a parasternal short-axis view, the speckle 'fingerprint' may be tracked for circumferential rotational changes over the cardiac cycle ('twist' and 'untwist'). Furthermore, 2D speckle tracking has been shown to correlate closely with MRI17 results when analysing systolic apical rotation.

We aimed to determine (i) whether the speed of LV apical untwist as measured by 2D echocardiographic speckle tracking is related to established measures of diastolic function and (ii) whether the timing of mitral valve opening (MVO) is influenced by this untwisting.
Methods

This study was approved by the Flinders Research Ethics Committee.

Echocardiographic data collected from consecutive hospital inpatients with preserved LV ejection fraction (>50% by Simpson’s biplane method) and without regional wall motion abnormalities who underwent standard 2D echocardiography in a 6 month period were analysed using an off-line speckle tracking software package (Echo Pac, GE Healthcare, Horton, Norway). Parasternal short-axis images at the apical level were selected this being defined as a circular section below the level of the papillary muscles. The operator manually defined the endocardial border in end systole and set the region of interest from the epicardial border to the endocardial border to ensure that the entire myocardium was tracked. The software automatically tracks six segments within the image and each segment is given a tracking grade. Images with frame rates below 40 Hz and above 80 Hz were excluded from analysis to ensure adequate temporal and spatial resolution as well as accurate frame to frame tracking.

The timings of mitral and aortic valve opening and closure were defined by pulse wave (PW) Doppler tracing of mitral inflow (taken at the mitral leaflet tips) and the left ventricular outflow. The tissue Doppler analysis was performed by placing a PW sample volume on the mitral septal annulus and the early diastolic velocity (e’) was measured. Diastolic function was classified as normal, abnormal relaxation, pseudonormal, or restrictive according to standard criteria.18 Briefly, normal diastolic function was classified as an e’:a >1 (no reversal with Valsalva), e’:e < 10, and mitral deceleration time >150 ms; abnormal relaxation if the mitral e’:a < 1; pseudonormalized if e’:a > 1 (with reversal during Valsalva), the deceleration time greater than 150 ms, and the e’:e ratio greater than 10; and restrictive filling if e:a > 1 with a shortened mitral deceleration time (<150 ms) and e’e ratio greater than 10. Further classification of diastolic function was made into low filling pressures (normal and abnormal relaxation pattern subjects) and high filling pressures (pseudonormal and restrictive pattern subjects).

On the speckle tracking graph, the maximum early diastolic rotation rate was defined as the first negative deflection after aortic valve closure (rotR) (Figure 1). The timing from MVO to rotR was also measured (t). Timing (t) was considered positive if rotR occurred before MVO and negative if rotR occurred after MVO.

Statistical analysis

RotR was compared to e’ and e’e’ using Spearman’s correlation. A Kruskal–Wallis test was used to calculate difference in rotR, age, and t over the diastolic category, and then a Mann–Whitney U-test was used to calculate difference in rotR, age, and t between each of the diastolic categories of normal, abnormal relaxation, pseudonormal, and restrictive. Significance was assumed at $P < 0.05$. Bonferroni’s correction was used for repeated measures.

Results

One hundred echocardiographic studies were analysed for this study. Of these, 71 were deemed to have adequate images for the speckle tracking analysis software. Images were rejected if the speckle tracking software was unable to analyse one or more of the six segments. All 100 images used were reanalysed by the same operator and a different operator on separate days to determine inter- and intra-operator variability.

Of the 71 patients, the mean age was 64 ± 14 years and ejection fraction was 60 ± 9%. Fourteen subjects had normal diastolic function, 25 an abnormal relaxation pattern, 27 a pseudonormalized pattern, and 5 a restrictive pattern as defined by standard echocardiography criteria. Subjects with normal diastolic function were younger ($P < 0.001$ for all other subgroups); however, there was no significant difference in age between the other diastolic categories. There was no difference between the diastolic groups in the presence of hypertension, coronary artery disease, diabetes mellitus, LV wall thickness, or end-diastolic dimension. Subject characteristics are listed in Table 1.

The intra- and inter-operator variability of the speckle tracking was $r = 0.8$ ($P < 0.001$) and $r = 0.7$ ($P < 0.001$), respectively.

Both e’ (Figure 2) and the ratio of e:e’ (Figure 3) correlated with the rate (speed) of early diastolic apical untwist (rotR) ($r = 0.7$ and $r = -0.5$ respectively, $P < 0.001$ for both).

Subjects classified as normal and abnormal relaxation (low filling pressure group) had increased rotR compared with those with pseudonormal or restrictive patterns (high filling pressure group) ($P < 0.001$) (Figure 4). There was increased rotR in subjects with normal diastology compared to subjects with abnormal relaxation ($P = 0.003$), pseudonormal ($P < 0.001$), and restrictive patterns ($P < 0.001$). There was also an increased rotR in subjects with abnormal relaxation compared to those with pseudonormal and restrictive pattern ($P < 0.001$ for both). However, there

Figure 1  (A) The speckle tracking rotation rate graph of a subject with a normal diastolic profile. (B) The speckle tracking rotation rate graph of a subject with a pseudonormal diastolic profile. White line represents mitral valve opening, arrow represents peak early diastolic apical untwist (rotR).
was no difference in rotR between subjects with pseudonormal and restrictive filling \((P = 0.36)\) (Figure 4).

Subjects classified as normal and abnormal relaxation (low filling pressure group) had a longer time period between rotR and MVO \((t)\) compared with those with pseudonormal or restrictive patterns (high filling pressure group) \((P < 0.001)\) (Figure 5). In fact, the majority patients in the high filling group had their peak of apical untwist occurring on or after MVO giving a negative value for \(t\). There was longer \(t\) in subjects with normal diastology compared to subjects with pseudonormal \((P < 0.001)\) and restrictive patterns \((P = 0.001)\). There was also a longer \(t\) in subjects with abnormal relaxation compared to those with pseudonormal filling \((P = 0.002)\) (Figure 5). Age was found to have a negative correlation with rotR, \(r = -0.4, P = 0.001\).

### Table 1: Subject characteristics split into diastolic categories of normal, abnormal relaxation, pseudonormal, and restrictive patterns

<table>
<thead>
<tr>
<th>Category</th>
<th>Normal (Age ± SD)</th>
<th>Abnormal relaxation (Age ± SD)</th>
<th>Pseudonormal (Age ± SD)</th>
<th>Restrictive (Age ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48 ± 8</td>
<td>67 ± 12*</td>
<td>67 ± 14*</td>
<td>75 ± 6*</td>
</tr>
<tr>
<td>EF (%)</td>
<td>67 ± 6</td>
<td>60 ± 9*</td>
<td>57 ± 9*</td>
<td>61 ± 11</td>
</tr>
<tr>
<td>Mitral e/a ratio</td>
<td>1.43 ± 0.26</td>
<td>0.74 ± 0.14*</td>
<td>1.79 ± 1.6**</td>
<td>3.51 ± 1.2**</td>
</tr>
<tr>
<td>IVS (cm)</td>
<td>0.99 ± 0.18</td>
<td>1.11 ± 0.15</td>
<td>1.10 ± 0.18</td>
<td>1.03 ± 0.33</td>
</tr>
<tr>
<td>PW (cm)</td>
<td>1.0 ± 0.17</td>
<td>1.06 ± 0.15</td>
<td>1.13 ± 0.2</td>
<td>1.18 ± 0.41</td>
</tr>
<tr>
<td>LVD (cm)</td>
<td>5.29 ± 0.47</td>
<td>5.15 ± 0.64</td>
<td>5.17 ± 0.39</td>
<td>5.4 ± 1.76</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (14%)</td>
<td>7 (28%)</td>
<td>3 (11%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>CAD</td>
<td>1 (7%)</td>
<td>5 (20%)</td>
<td>8 (30%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0 (0%)</td>
<td>2 (8%)</td>
<td>3 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>67 ± 6</td>
<td>60 ± 9*</td>
<td>57 ± 9*</td>
<td>61 ± 11</td>
</tr>
</tbody>
</table>

Continuous data are displayed as mean ± SD, discrete variables are displayed as number (%). EF, ejection fraction; CAD, coronary artery disease; IVS, interventricular wall thickness; PW, posterior left ventricular wall thickness; LVD, left ventricular diastolic diameter.

*\(P < 0.05\) c/w normal.

**\(P < 0.05\) c/w abnormal relaxation.

***\(P < 0.05\) c/w pseudonormal.
Discussion

Diastolic dysfunction is important to assess for many reasons. Heart failure with preserved LV systolic function is common, increasingly recognized, and will continue to grow in prevalence as western society ages. Although it does not appear to have the same mortality rate as systolic heart failure, the morbidity is similar. Echocardiography remains the key investigatory modality in the assessment of diastolic dysfunction but is not without limitation. Hence, improved echocardiographic detection of diastolic dysfunction may be of significant clinical importance.

We have demonstrated that the speed of diastolic untwist is related to established echocardiographic parameters of diastolic function. This rapid early diastolic untwist in normal people may be an important component of the phenomenon known as diastolic suction where blood is actively ‘sucked’ into the LV from the LA. It is this suction effect that is diminished in the earliest stages of diastolic dysfunction and hence this may be reflected in decreased apical diastolic untwist with increasing age demonstrating this phenomenon known as diastolic suction where blood is actively ‘sucked’ into the LV from the LA.2 It is this suction effect that is diminished in the earliest stages of diastolic dysfunction and hence this may be reflected in decreased apical diastolic untwist with increasing age (Figure 1). This may explain the moderate correlation between the traditional diastolic criteria and the untwist parameters since the former reflects pressure and flow differences between the atria and ventricle while the latter is more likely the precursor and reflects intrinsic LV myocardial mechanics. It is possible that a more load-independent measure of diastolic function would correlate better with rotR, particularly in the lower filling pressure group.

The timing between the peak of early diastolic untwisting and MVO reflects important diastolic haemodynamic mechanics. In those subjects with normal filling pressures, the peak of this rapid diastolic untwisting occurred during the isovolumic relaxation phase suggesting that the suction effect resulting from diastolic untwisting may be responsible for MVO. Conversely, in those subjects with high-filling pressures, the peak of rotR more often occurred on or after MVO, suggesting that it is the higher LA pressure that contributes more to MVO rather than a strong ‘suction’ effect.

In the majority of subjects, the peak of apical untwist occurred during isovolumic relaxation indicating that this may be a less load-dependent measure of non-invasively measured diastolic function.

Age has been found to influence diastolic function,21 with diastolic function decreasing with increasing age. Similarly, we found our normal diastolic group to be younger than the other three groups and there was a reduction in the speed of diastolic untwist with increasing age demonstrating this phenomenon.

Further longitudinal studies will be required to determine whether the finding of reduced apical diastolic untwist with preserved diastolic parameters may actually be a sign of subclinical diastolic dysfunction.

Limitations

The major limitation using echocardiographic speckle tracking is its dependence on high-quality images. In our study population, consisting of 100 consecutive hospital inpatients, we found adequate image quality for analysis in 71%. This is a similar rate to other studies using speckle tracking.12–16 Speckle tracking works optimally when there are adequate speckles in the echocardiographic image for it to track in each frame. Reduction in image quality (e.g., poor quality parasternal window, significant lung disease, and respiratory motion artefacts) significantly impacts on the ability of the technique to provide meaningful data. Further advances in ultrasound technology should reduce this limitation. Moreover, because this study is retrospective, we were unable to control the cut slices taken of the apex, however, using specific guideline of what constitutes an apical parasternal short-axis view minimized this limitation.

Using a two-dimensional slice at the apical level makes an assumption that the longitudinal motion of the heart is not causing translation of the speckle finger print in and out of the scanning plane. This possible limitation is minimized, however, due to the fact that most of the longitudinal motion of the heart comes from the base descending to the apex in systole and then recoiling back in diastole with the apex remaining relatively fixed. The advancement of three-dimensional speckle tracking would assist in overcoming this issue.

We had a large number of subjects who demonstrated a pseudonormalized filling pattern which may be higher than expected in consecutive patients. However, these subjects were recruited from patients in a large acute cardiac hospital setting. These patients had echocardiography conducted from a standard referral basis (Table 2) and were not specifically targeted because of heart failure. Using preserved systolic function, heart failure patients may have more clinical relevance for further studies.

LV torsion (rotation differences between apex and base) though an important component of myocardial function was not measured and it may be a more complete assessment of myocardial mechanics. However, we felt that the greater complexity in measuring rotation in different planes would decrease its reliability and usability. Furthermore, we were more interested in the contribution of apical function and its relationship to myocardial suction.

Table 2 Clinical indication for echocardiographic referral split into diastolic categories

<table>
<thead>
<tr>
<th>Clinical indication</th>
<th>Normal</th>
<th>Abnormal</th>
<th>Pseudonormal</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>4 (29%)</td>
<td>8 (32%)</td>
<td>5 (19%)</td>
<td>2 (40%)</td>
</tr>
<tr>
<td>SOB</td>
<td>0 (0%)</td>
<td>3 (12%)</td>
<td>5 (19%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>CVA</td>
<td>1 (7%)</td>
<td>1 (4%)</td>
<td>3 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Murmur</td>
<td>2 (14%)</td>
<td>2 (8%)</td>
<td>3 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (50%)</td>
<td>11 (44%)</td>
<td>11 (41%)</td>
<td>2 (40%)</td>
</tr>
</tbody>
</table>

Other refers to indications including: palpitations, pre-operative assessment, pre-chemotherapy, and syncope/ pre syncope. SOB, shortness of breath; CVA, cerebrovascular accident.

Conclusion

The non-invasive assessment of apical diastolic untwist using speckle tracking is related to established echocardiographic measures of diastolic function and warrants further investigation as a potentially useful measure of diastolic function.
The timing of apical untwisting to MVO in different filling states, as demonstrated by our study, supports the theory of a ventricular suction effect.

Conflict of interest: none declared.

References