Using mitral ‘annulus reversus’ to diagnose constrictive pericarditis

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Aims To characterize mitral medial and lateral annular velocities in constrictive pericarditis or restrictive cardiomyopathy compared with normal subjects.

Methods and results Tissue Doppler imaging peak systolic velocity (S'), peak early diastolic annular velocity (e'), and timing difference between mitral early flow and early annular movement were measured in 14 patients with constrictive pericarditis, 10 with restrictive cardiomyopathy, and 17 normal subjects using the apical four-chamber view lateral and medial mitral annulus. In controls, mitral lateral e' velocity was 25% higher than medial e' velocity (13.0 ± 3.1 vs. 10.7 ± 2.8 cm/s; P = 0.02), whereas with constrictive pericarditis, averaged lateral e' velocity was 2% lower than medial e' velocity (10.7 ± 2.5 vs. 11.2 ± 3.1 cm/s; P > 0.05). This relationship represented a reversal of lateral and medial e' velocities compared with normal subjects (P = 0.004). Differences in S', E/e', and timing intervals between normal subjects and patients with constrictive pericarditis were not statistically significant; however, restrictive cardiomyopathy could be distinguished from constrictive pericarditis and controls with all other parameters (S', E/e', medial and lateral e' velocities, and timing interval differences; all P < 0.05).

Conclusion Practical applications of tissue Doppler imaging for evaluation of possible constrictive pericarditis include reversal of the relationship between lateral and medial e' velocities (i.e. ‘annulus reversus’).

Introduction

Constrictive pericarditis and restrictive cardiomyopathy are challenging entities for echocardiographers to differentiate; however, advances in tissue Doppler imaging technology have led to more sophisticated methods to distinguish these cardiac conditions.1,2 Specifically, tissue Doppler imaging has allowed the determination of discrete amplitude cut points at the lateral mitral annulus to distinguish constrictive pericarditis from restrictive cardiomyopathy without overlap.3 Tissue Doppler imaging of the interventricular septum can also be used to distinguish constrictive pericarditis from abnormal septal motion due to other causes.4 We have reported the observation of annulus paradoxus in patients with constrictive pericarditis when there is an inverse relationship between the pulmonary capillary occlusion pressure and the ratio of transmitral velocity to mitral lateral annulus early diastolic velocity (E/e') compared with high left ventricular filling pressure in patients without pericardial disease.5 Our continued research into this entity has led to another observation unique to patients with constrictive pericarditis and is added to the echocardiographic armamentarium to identify this condition.

We hypothesized that the relationship of amplitude differences in the mitral lateral (lat) and medial (med) annulus may be useful in differentiating those patients with constrictive pericarditis from normal subjects as well as from those patients with restrictive cardiomyopathy. Thus, we sought to characterize and compare mitral annular velocities and timing intervals among these three groups.

Methods

Study group

We searched the Echocardiography Information Management Systems database of Mayo Clinic, Scottsdale, Arizona, for records that listed any of the following search terms as a final
diagnosis: normal echocardiogram, constriction, constrictive pericarditis, cardiac amyloidosis, amyloid, amyloidosis, and restrictive cardiomyopathy. All patients (age range, 27–88 years) who underwent transthoracic echocardiography between 2004 and 2006 at Mayo Clinic, Scottsdale, Arizona, were included in this study. Patients were excluded if atrial fibrillation was noted at the time of the study or if inadequate Doppler signals precluded offline analysis. After exclusion criteria were applied, 41 patients remained for analysis (17 normal controls, 14 with constrictive pericarditis, and 10 with cardiac amyloidosis).

Echocardiographic examination

From stored digital transthoracic echocardiographic still frames, we independently remeasured all parameters using electronic calipers on the ProSolv CV Analyzer 3.0 viewing program (ProSolv CardioVascular, Indianapolis, Indiana). Peak mitral inflow velocity was measured in early (E) and late (A) diastole in cm/s using pulsed-wave Doppler. Peak annular velocities were measured from the apical four-chamber view at peak annular systole (S), early (e), and late (a') diastole in cm/s from the mitral lateral and medial annulus. Timings of annular movement and mitral flow were determined by measuring the duration (ms) from the onset of the QRS to the onset of annular motion and the onset of the E-wave, respectively. Pulsed-wave Doppler was performed in patients with constrictive pericarditis using simultaneous nasal respirometer recordings. Varying sweep speeds of 25-100 mm/s were used. Analysis of Doppler velocities was performed on the first beat immediately after the onset of inspiration and expiration. Additionally, in patients with constrictive pericarditis, we averaged data over 5 to 10 beats throughout the respiratory cycle and reported it as the averaged parameter. The averaged e' velocity throughout the respiratory cycle was used to minimize the potential respirophasic impact of load on e' velocity in patients with constriction.

Statistical analysis

Data are presented as mean ± SD. One-way analysis of variance was used to test for statistically significant differences in the echocardiographic variables among the normal controls, the constrictive pericarditis patients (on inspiration), and the restrictive cardiomyopathy patients. If the overall F-test was significant (P < 0.05), then pairwise comparisons among the three groups were conducted.

Results

Patient characteristics

Of the 41 patients, 17 were normal subjects (mean age 44 years; range 27–66 years). Fourteen patients had constrictive pericarditis (71% idiopathic and 29% with a history of coronary artery bypass grafting). The mean age of this group was 63 years (range 25–75 years), and 85% of them were men. Of the 10 patients with restrictive cardiomyopathy, all had cardiac amyloidosis (60% with positive endomyocardial biopsy, 40% with a positive fat pad aspirate). Their mean age was 69 years (range 47–88 years).

Amplitude variables

Doppler echo findings among the three groups showed no statistically significant difference in mitral E velocity (P > 0.05; Table 1). The E/A ratio was higher in normal controls and in patients with constrictive pericarditis compared with patients with restrictive cardiomyopathy (1.54 ± 0.41 and 1.48 ± 0.45 vs. 2.63 ± 1.45; P = 0.003). The e' velocities were significantly higher in patients with constrictive pericarditis compared with patients with restrictive cardiomyopathy.

### Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls (n=17)</th>
<th>CP (n=14)</th>
<th>RCM (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>E, cm/s</td>
<td>71 ± 12†</td>
<td>67 ± 28</td>
<td>83 ± 38</td>
<td>81 ± 22†</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.54 ± 0.41</td>
<td>1.48 ± 0.45</td>
<td>1.67 ± 0.75</td>
<td>2.63 ± 1.45</td>
</tr>
<tr>
<td>T_E, ms</td>
<td>474 ± 36†</td>
<td>423 ± 54</td>
<td>399 ± 33</td>
<td>447 ± 75</td>
</tr>
<tr>
<td>E/E'?</td>
<td>6 ± 2</td>
<td>6 ± 4</td>
<td>9 ± 6</td>
<td>22 ± 8†</td>
</tr>
<tr>
<td>E/E'?med</td>
<td>7 ± 2</td>
<td>6 ± 3</td>
<td>10 ± 7</td>
<td>28 ± 17†</td>
</tr>
<tr>
<td>S_E(lat), cm/s</td>
<td>7.2 ± 1.3†</td>
<td>8.2 ± 1.7</td>
<td>7.8 ± 1.9</td>
<td>3.3 ± 1.3†</td>
</tr>
<tr>
<td>E_E(lat), cm/s</td>
<td>13.0 ± 3.1†</td>
<td>10.7 ± 2.8</td>
<td>7.8 ± 0.8</td>
<td>3.8 ± 1.9†</td>
</tr>
<tr>
<td>∆T_E–E'? lat, ms</td>
<td>-43 ± 12</td>
<td>-44 ± 31</td>
<td>-40 ± 95</td>
<td>+36 ± 38†</td>
</tr>
<tr>
<td>S_Eimed, cm/s</td>
<td>7.2 ± 1.4</td>
<td>8.1 ± 0.7</td>
<td>7.8 ± 0.8</td>
<td>3.8 ± 1.9†</td>
</tr>
<tr>
<td>E_Eimed, cm/s</td>
<td>10.7 ± 2.8</td>
<td>12.7 ± 2.8</td>
<td>10.0 ± 3.7</td>
<td>3.8 ± 2.4†</td>
</tr>
<tr>
<td>∆T_E–E'? Eimed, ms</td>
<td>-35 ± 26</td>
<td>-27 ± 41</td>
<td>-3 ± 37</td>
<td>+37 ± 40†</td>
</tr>
</tbody>
</table>

CP, constrictive pericarditis; E, mitral early diastolic velocity; E', mitral annulus early diastolic annular velocity; E/A ratio, ratio of early to late diastolic velocity; E/E', ratio of mitral early diastolic velocity to mitral annulus early diastolic velocity; lat, lateral mitral annulus location; med, medial mitral annulus location; RCM, restrictive cardiomyopathy; ∆T_E–E', difference in time between mitral early flow and early annular relaxation.  
*Values are mean ± SD unless indicated otherwise.  
†P-value is from the ANOVA testing for any differences among the groups.  
‡P < 0.05 compared with inspiration in patients with constrictive pericarditis.  
§P < 0.05 compared with controls.  
*P < 0.05 compared with averaged constrictive pericarditis.
cardiomyopathy [averaged \( e'_{\text{lat}} \) 10.7 \( \pm \) 2.5 vs. 3.7 \( \pm \) 1.7 cm/s (\( P < 0.001 \)) and averaged \( e'_{\text{med}} \) 11.2 \( \pm \) 3.1 vs. 3.8 \( \pm \) 2.4 cm/s (\( P < 0.001 \))]. These values were not statistically significantly different from the normal controls. The E/\( e' \) ratio was significantly lower in patients with constrictive pericarditis compared with patients with restrictive cardiomyopathy [\( E/e'_{\text{lat}} \) 6 \( \pm \) 4 vs. 22 \( \pm \) 8 (\( P = 0.001 \)) and \( E/e'_{\text{med}} \) 6 \( \pm \) 3 vs. 28 \( \pm \) 17 (\( P = 0.001 \))]. The \( S' \) velocity was significantly higher in patients with constrictive pericarditis compared with patients with restrictive cardiomyopathy [\( S_{\text{lat}} \) 8.2 \( \pm \) 1.7 vs. 3.3 \( \pm \) 1.3 cm/s (\( P < 0.001 \)); \( S_{\text{med}} \) 8.1 \( \pm \) 0.7 vs. 3.8 \( \pm \) 1.9 cm/s (\( P < 0.001 \))].

Annulus reversus

In normal subjects, mitral lateral \( e' \) velocity was higher than the medial \( e' \) velocity by 25% (13.0 \( \pm \) 3.1 vs. 10.7 \( \pm \) 2.8 cm/s; \( P = 0.02 \)), whereas in patients with constrictive pericarditis the averaged lateral \( e' \) velocity was lower than the medial \( e' \) velocity by 2% (10.7 \( \pm \) 2.5 vs. 11.2 \( \pm \) 3.1 cm/s; \( P > 0.05 \)). The absolute difference of the averaged lateral and medial \( e' \) velocities for constrictive pericarditis was \(-0.55 \pm 2.57 \) and \(2.27 \pm 2.79 \) cm/s in controls. This relationship represents a reversal of the typical lateral and medial \( e' \) velocities observed in controls, hence termed ‘annulus reversus’ (\( P = 0.004 \); Figure 1).

Timing intervals

The time difference between the onset of mitral flow and the onset of \( e' \) (\( \Delta T_{E-e'} \)) in normal subjects at the lateral and medial annuli was \(-43 \pm 12 \) and \(-35 \pm 26 \) ms, respectively. This finding remains in those patients with constrictive pericarditis, in whom the \( \Delta T_{E-e'} \) at the lateral and medial sites is \(-44 \pm 31 \) and \(-27 \pm 41 \) ms, respectively (\( P > 0.05 \) compared with patients with normal function). In contrast, restrictive cardiomyopathy showed a prolonged time difference with the \( e' \) motion occurring after E flow (\( \Delta T_{E-e'}_{\text{lat}} \) +36 \( \pm \) 38 ms; \( \Delta T_{E-e'}_{\text{med}} \) +37 \( \pm \) 40 ms; \( P < 0.001 \)) compared with patients with constrictive pericarditis or with controls.

Discussion

The principal finding of this study is the identification of the reversal of the normal relationship of mitral lateral \( e' \) and medial \( e' \) velocities. In constrictive pericarditis, the lateral \( e' \) velocity is lower than the medial \( e' \) velocity, resulting in annulus reversus. This novel finding has not been reported previously. We noted annulus reversus in patients with constrictive pericarditis despite normal \( e' \) velocities (>8 cm/s). Because of respirophasic differences in \( e' \) velocities at both annuli in patients with constrictive pericarditis, we recommend taking an average of all absolute values throughout one respiratory cycle. Doing so obviates the need to define discrete dichotomous values for the inspiration and expiration. We hypothesize that the finding of annulus reversus is likely due to the tethering of the adjacent fibrotic and scarred pericardium, which influences the lateral mitral annulus of patients with constrictive pericarditis. Therefore, in a patient with preserved mitral \( e' \) velocities (>8 cm/s) and a low E/\( e' \) ratio (<8; annulus paradoxus), the recognition of annulus reversus should alert the interpreting echocardiographer to the diagnosis of constrictive pericarditis.

Patients with restrictive cardiomyopathy did not exhibit annulus reversus; however, we found that absolute cut points of lateral \( e' \) velocity >6.5 cm/s and a medial \( e' \) velocity of >8 cm/s exhibited high sensitivity and specificity for distinguishing this group of patients from those with constrictive pericarditis (lateral sensitivity and specificity 100%; medial sensitivity 100%; specificity 90%), which is consistent with prior reports.\(^3 \)\(^6 \) Additionally, restrictive cardiomyopathy can be distinguished from constrictive pericarditis using absolute velocity values of the medial and lateral \( S' \) and \( e' \) (\( P < 0.001 \)).

Another finding of this study emphasizes the importance of maximizing the high temporal resolution that echocardiography provides to quantify timing variables that are less likely to be influenced by angle dependency.\(^7 \) The comparison of patients with constrictive pericarditis to those with restrictive cardiomyopathy showed that annular motion occurs before E flow at both sites (\( P < 0.05 \)). In restrictive cardiomyopathy, annular motion occurs after E flow. This timing delay has been previously noted during acute myocardial ischaemia and has been shown to correlate well with impaired left ventricular relaxation (tau) in dogs (\( r = 0.85 \); \( P < 0.05 \)).\(^8 \) Recently published data show that incrementally adding the timing difference to septal mitral \( e' \) and \( S' \) velocities facilitates the differentiation of constrictive pericarditis from restrictive cardiomyopathy with 94% sensitivity.\(^9 \)

Conclusion

A comprehensive echocardiographic evaluation should include the detailed tissue Doppler imaging analysis of both medial and lateral mitral annular velocities and their relationship. Constrictive pericarditis is characterized by preserved tissue Doppler imaging (both \( e' \) and \( S' \)) and by

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**Figure 1** Doppler representation of annulus reversus. The normal relationship (top panel) between lateral mitral \( e' \) and medial mitral \( e' \) is reversed in constrictive pericarditis (middle panel) but not in restrictive cardiomyopathy (bottom panel).
the presence of annulus paradoxus, to which we now add the observation of annulus reversus.

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**References**