Proximal aortic stiffness is related to left ventricular function and exercise capacity in patients with dilated cardiomyopathy

Alexandros P. Patrianakos*, Fragiskos I. Parthenakis, Dimitrios Karakitsos, Eva Nyktari, and Panos E. Vardas

Cardiology Department, Heraklion University Hospital, PO Box 1352 Stavrakia, Heraklion, Crete, Greece

Received 12 August 2008; accepted after revision 26 October 2008; online publish-ahead-of-print 28 November 2008

Aims Patients with heart failure (HF) show abnormal arterial stiffening.

Methods and results We examined 60 patients (52.1 ± 12, 8 years) with non-ischaemic dilated cardiomyopathy (NIDC), New York Heart Association II–III, in sinus rhythm, left ventricular ejection fraction 30.1 ± 8.6%, and 44 normals. All subjects underwent an echocardiographic study and a cardiopulmonary exercise test. We evaluated the segmental proximal aorta (AO) pulse wave velocity (PWV) in the region of aortic arch with a new echo-method: from the suprasternal view, the distance between ascending and descending AO was measured with two-dimensional ultrasound, and the aortic flow wave transit time (TT) was measured with pulsed-wave Doppler. Pulse wave velocity was calculated as aortic distance/TT. Patients showed increased PWV (7.4 ± 2.9 vs. 4.8 ± 1.1 m/s, \( P < 0.001 \)), compared with controls. Patients with advanced left ventricular (LV) (restrictive or pseudo-normal filling pattern) diastolic dysfunction showed increased PWV (8.6 ± 2.6 vs. 6.6 ± 2.9 m/s, \( P = 0.01 \)) and reduced peak and predicted (for age, sex, and body mass) VO2 (both \( P < 0.001 \)), compared with those with mild diastolic dysfunction (delayed relaxation filling pattern). Pulse wave velocity was significantly correlated with the LV mass (\( r = 0.32, P = 0.01 \)), the peak spectral tissue Doppler imaging systolic wave (\( r = -0.34, P = 0.006 \)), the LV diastolic filling pattern (\( r = 0.42, P = 0.001 \)), and the peak (\( r = -0.47, P < 0.001 \)) and predicted VO2 (\( r = -0.579, P < 0.001 \)).

Conclusion Patients with NIDC showed increased proximal aortic stiffness, which relates to LV systolic and diastolic function and exercise capacity. The echocardiographic assessment of the regional aorta PWV seems to be clinically important.

Introduction

The interaction of the heart with the systemic vasculature is a major determinant of net cardiovascular performance.

It has been shown that progression of myocardial systolic function impairment leads to reduced left ventricular (LV) end-systolic elastance and increased effective arterial elastance.\(^1\)\(^-\)\(^3\) Thus, the effective arterial elastance/end-systolic elastance ratio, representing the ventriculo-arterial coupling, is progressively increased in the heart failure (HF) syndrome and is far from the optimal value, while it further impairs during exercise or high heart rates.\(^4\)\(^,\)\(^5\)

Previous studies showing abnormal cardiovascular stiffening in patients with HF syndrome support the concept that the cardiac muscle disease is also accompanied by impairment of the central aorta function.\(^6\)\(^-\)\(^8\)

The three- and four-element Windkessel model introduced by Westerhof et al.\(^9\) provided insight into the contribution of different arterial properties to the load of the heart. Based on this model, which in turn is based on wave transmission theory, the characteristic aortic impedance is a major determinant of the left ventricular (LV) load and accounts for the local inertia and local compliance of the proximal ascending aorta. Furthermore, experimental data showed that about half of the total arterial compliance is located in the proximal thoracic aorta.\(^10\)

However, there is no extensive information about the proximal elastic aorta stiffening, which determines the ability of the aorta to perform its cushioning function and may correspond to the cardiac load in patients with HF.\(^5\)\(^,\)\(^11\)
Arterial stiffness can be assessed non-invasively by indirect measurements of pulse wave velocity (PWV), based on the time the pulse wave takes to travel a specific distance along the vasculature. According to the Moens–Koerwew equation, PWV travels faster in stiffer arteries.\(^\text{12}\)

The aim of this study was to evaluate the proximal aorta stiffness, a major determinant of the cardiac load, using a new echocardiographic application and its relationship with LV function and exercise capacity in patients with HF due to non-ischaemic dilated cardiomyopathy (NIDC).

Methods

Study group

The study population comprised 67 consecutive patients enrolled from the Heart Failure Clinic of our hospital, aged <75 years of whom 15 were women. The patients had an echocardiographic diagnosis of dilated cardiomyopathy defined as LV end-diastolic dimensions >55 mm with LV ejection fraction (LVEF) <40%, chronic mild-to-moderate HF (NYHA functional class II–III), and a clinical history >6 months. All patients were in sinus rhythm and underwent cardiac catheterization before their inclusion in the study.

Exclusion criteria were the presence of significant coronary artery disease (lumen stenosis >50% of any coronary artery or prior myocardial infarction), severe cardiac valve disease, atrial fibrillation, long-standing diabetes mellitus (>1 year) or arterial hypertension (>180/90 mmHg, more than 1 year), chronic liver or renal insufficiency (creatinine plasma levels >1.5 mg/dL), and chronic obstructive pulmonary disease.

All patients were in a stable condition for at least 4 weeks, with the medication individually optimized without modification in the last month.

Seven (10.4%) of them were excluded due to inadequate images of the aortic arch (two because of aortic arch imaging failure and the rest due to non-accurate recording of the onset of the flow at the ascending or descending aorta due to velocity turbulence). Forty-four healthy persons, aged 49.7 ± 8.5 years, nine women, without any history of cardiovascular disease served as the control group. The study conformed to the principles outlined in the Declaration of Helsinki\(^\text{13}\) and was approved by the Institutional Ethics Committee. All patients gave written, informed consent.

Echocardiography study

Standard M-mode two-dimensional (2D) echocardiography and Doppler measurements of LV function were performed using a Vivid 7 (General Electric, Horten, Norway) ultrasound device with a 1.5–3.6 MHz wide angle phased-array transducer (Matrix), according to the recommendations of the American Society of Echocardiography,\(^\text{14}\) and all examinations were digitally stored for off-line analysis as the mean of three cardiac cycles.

Spectral Doppler recordings from the mitral inflow were obtained from the apical four-chamber view to assess LV filling dynamics, and the (a) peak early (E) wave and late (A wave) transmitral filling velocities in centimetres per second; (b) E/A ratio; and (c) deceleration time of the E (DTE) velocity in milliseconds (from peak E velocity to baseline) were measured.

Spectral tissue Doppler imaging (TDI) was performed in the apical four-chamber view, the sample volume was set at 5 × 5 mm and placed at the junction of the LV septal and lateral wall with the mitral annulus, and three consecutive cardiac cycles were transferred to a workstation and analysed (Echopac, GE). Peak velocities during systole (Sm), early diastole (e'), and late diastole (a') were measured. The final value represented the average of both sites.

The patients were divided into mild (group A, with delayed relaxation LV filling pattern) and advanced (group B, pseudo-normal or restrictive filling pattern) LV diastolic dysfunction on the basis of the E/A ratio, E-wave deceleration time, and spectral tissue Doppler velocities of the mitral annulus.

Delayed relaxation pattern was defined by E/A ratio <1 and DTE >220 ms and the e' wave <8 cm, pseudo-normal pattern by E/A ratio between 1 and 2 with DTE >140 ms and the e' <8 cm/s, and a restrictive filling pattern was defined either by E/A ratio >2 or E/A ratio between 1 and 2 with DTE <140 ms.\(^\text{15}\)

Regional PWV of the proximal aorta (PWv \(_\text{R}\)) was estimated as described previously with some modifications.\(^\text{16}\) From the suprasternal view, pulsed wave (PW)-Doppler tracings of the ascending (just above the right pulmonary artery as the standard reference point) and descending aorta (as far as possible) were recorded and averaged over 10 cycles at a sweep speed of 200 mm/s. From the R wave of the QRS complex to the onset of the PW-Doppler aortic flow, time 1 (T1) in the ascending and time 2 (T2) in the descending aorta were then measured accordingly. The distance from the PW-Doppler sample volume in the ascending to the descending aorta was measured on two-dimensional echo as aortic length (AOL), using the open trace method of measurement (Echopac, GE) (Figure 1).

Cardiopulmonary exercise testing

All patients underwent an exercise test (mean time ± 48 h) after echocardiography study using a Marquette treadmill device (Max-1), typically during the morning and after at least 3 h without food, coffee, or cigarettes. A graded, symptom-limited test was performed using a Naughton protocol. A 12-lead ECG was monitored continuously, with recordings every 2 min at the end of each stage.

Gas exchange data were collected continuously with an automated breath-by-breath system (Oxycon A, version 3.1, Jaeger). Maximal oxygen consumption at peak exercise (PVO\(_2\)) was calculated as the average oxygen consumption value over the final 30 s of exercise. Peak oxygen pulse was also measured in mL/beat as the ratio of maximal oxygen consumption at peak exercise to peak exercise heart rate.

Statistical analysis

Summary data are expressed as mean ± standard deviation. Correlations between continuous variables were assessed using the Pearson correlation coefficient. For ordinal data, the Spearman rank correlation was used.

Diastolic dysfunction was categorized on a semi-quantitative scale as: normal, 0; delayed relaxation filling pattern, 1; pseudo-normal, 2; restrictive filling pattern, 3.

Group comparisons were made using the unpaired Student's t-test or the Mann–Whitney U-test, as appropriate.

Agreement between repeated intra- and inter-observer measurements was evaluated by the agreement analysis method of Bland–Altman, and 95% confidence intervals were also calculated as described by Bland–Altman.

A two-tailed significance level of 0.05 was considered statistically significant. All analyses were performed using a commercially available statistical package (SPSS for Windows 15.0).

Results

Study population characteristics are shown in Table 1.

There were no age, sex, or body surface area (BSA) differences between patients and controls.

Patients were primarily under treatment with angiotensin-converting enzyme inhibitors (85%), diuretics (76%), β-blockers (89%), statins (22%), and digoxin (16%), and they did not show increased systolic or diastolic blood pressure compared with controls.
Echocardiographic parameters

Patients showed increased PWV compared with controls (7.48 ± 2.96 vs. 4.85 ± 1.11 m/s, P < 0.001, Figure 2A).

Differences between the patients with delayed relaxation filling pattern (group A) or advanced stages of diastolic dysfunction (pseudo-normal or restrictive filling pattern, group B) are shown in Table 2. Group B patients showed increased values of PWV (8.6 ± 2.6 vs. 6.6 ± 2.9 m/s, P = 0.01) compared with group A patients (Figure 2B).

Furthermore, PWV showed a relationship with age (r = 0.36, P = 0.007), pulse pressure (r = 0.38, P = 0.003), LVEF (r = 0.31, P = 0.02), the Sm wave (r = −0.34, P = 0.006) (Figure 3A), LV mass (r = 0.32, P = 0.01) (Figure 3B), DTE (r = −0.29, P = 0.02), the e’ (r = −0.32, P = 0.01), and the E/e’ ratio (r = 0.30, P = 0.02), an index that has been proposed to reflect the LV end-diastolic filling pressures.

Non-parametric Spearman correlation coefficient showed that PWV was also associated with the diastolic LV filling pattern (r = 0.42, P = 0.001).

Aortic stiffness and cardiopulmonary exercise test

Non-ischaemic dilated cardiomyopathy patients showed reduced exercise capacity and reduced PVO₂ compared with controls (both P < 0.001) (Table 1). Furthermore, group B patients showed decreased PVO₂ and predicted for age, sex, and BSA PVO₂ compared with group A patients (both P < 0.001) (Table 2).

Aortic PWV showed an inverse relationship with PVO₂ (r = −0.47, P < 0.001) (Figure 4A), predicted PVO₂ (r = −0.579, P < 0.001), and maximal oxygen pulse (r = −0.50, P < 0.001) (Figure 4B), which is a crude non-invasive measure of stroke volume at peak effort.

Reproducibility

The mean values of repeated intra-observer PWV measurements performed initially and 1 h later in 73 patients of the whole study population (18 controls) were 6.8 ± 2.8 and 6.6 ± 2.7 m/s (r = 0.97, P < 0.001), respectively. The Bland–Altman analysis showed that 95% limits of agreement of intra-observer variation were (−1.45) – 1.05 (Figure 5). The mean values for inter-observer PWV measurements performed by observers A and B were 6.8 ± 2.8 vs. 7.1 ± 2.8 m/s (r = 0.95, P < 0.001). The Bland–Altman analysis showed that 95% limits of agreement of inter-observer variation were (−2.28) – 1.49.
Table 1  Study population characteristics

<table>
<thead>
<tr>
<th></th>
<th>NIDC (n = 60)</th>
<th>Control (n = 44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.1 ± 12.8</td>
<td>49.7 ± 8.5</td>
<td>0.28</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>46/14</td>
<td>39/9</td>
<td>0.9</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.2 ± 0.4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>125 ± 13.3</td>
<td>122 ± 7.5</td>
<td>0.29</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>75.4 ± 7</td>
<td>75.5 ± 5.6</td>
<td>0.95</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>50.2 ± 14.5</td>
<td>46.6 ± 6.6</td>
<td>0.31</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>69.4 ± 12.1</td>
<td>73.6 ± 4.7</td>
<td>0.15</td>
</tr>
<tr>
<td>LBBB</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.86 ± 0.15</td>
<td>1.81 ± 0.13</td>
<td>0.27</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>57.8 ± 5.9</td>
<td>47.2 ± 2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LA (mm)</td>
<td>40.6 ± 5.9</td>
<td>36.2 ± 1.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>294.6 ± 78.7</td>
<td>165.5 ± 32.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shortening fraction (%)</td>
<td>22.1 ± 7.4</td>
<td>33.8 ± 22.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>34.6 ± 7.2</td>
<td>65.7 ± 4.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Em (m/s)</td>
<td>0.67 ± 0.23</td>
<td>0.64 ± 0.04</td>
<td>0.67</td>
</tr>
<tr>
<td>Am (m/s)</td>
<td>0.57 ± 0.21</td>
<td>0.49 ± 0.03</td>
<td>0.11</td>
</tr>
<tr>
<td>Em/Am ratio</td>
<td>1.39 ± 0.88</td>
<td>1.31 ± 0.09</td>
<td>0.70</td>
</tr>
<tr>
<td>DTE (ms)</td>
<td>196.4 ± 54.1</td>
<td>182 ± 6.6</td>
<td>0.28</td>
</tr>
<tr>
<td>sm (cm/s)</td>
<td>5.2 ± 1.7</td>
<td>10.5 ± 1.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E’ (cm/s)</td>
<td>6.1 ± 3.05</td>
<td>11 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Em/e’</td>
<td>12.2 ± 6.7</td>
<td>5.6 ± 0.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exercise duration (min)</td>
<td>1073 ± 339</td>
<td>1683 ± 359</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exercise HR (bpm)</td>
<td>139.5 ± 17.1</td>
<td>160 ± 8.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVO2 (mL/kg/min)</td>
<td>21.1 ± 3.9</td>
<td>31.8 ± 3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pred PVO2 (%)</td>
<td>84.2 ± 10</td>
<td>99.2 ± 9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AQL (mm)</td>
<td>10.46 ± 1.1</td>
<td>10.75 ± 1.31</td>
<td>0.24</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>7.46 ± 2.96</td>
<td>4.88 ± 1.11</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SBP, systolic arterial blood pressure; DBP, diastolic blood pressure; HR, heart rate; LBBB, left bundle branch block; BSA, body surface area; LVDD, left ventricular end-diastolic diameter; LA, left atrial; LVEF, left ventricular ejection fraction; Em and Am, early and late pulsed wave doppler transmural wave; DTE, deceleration time of Em wave; Sm and e’, average peak systolic and early diastolic PW-TDI wave of the basal septal and lateral LV wall; PVO2, oxygen consumption at peak exercise; pred., predicted for age, sex, and BSA; PWV, pulse wave velocity of the proximal aorta; AQL, aortic distance for PWV.

Discussion

The evaluation of the elastic proximal aorta properties, a major determinant of the load that impedes on the LV, is of great interest. Until now, the proximal aorta could be evaluated non-invasively by MRI and using M-mode echocardiography, which has the disadvantage that it examines the ascending aorta properties at a specific point.

We used a new echocardiographic method that allows us to evaluate the PWV, a non-invasive index that reflects the stiffness of an artery, at the proximal elastic aorta and at the site of maximal delay of the blood flow due to bell-shaped curve of the aortic arch. An analogous method has previously been used in a paediatric population to evaluate the local aorta proximal stiffness.17

We found that in patients with HF due to NIDC, the PWV at this region correlates with LV systolic and diastolic function and is also correlated with crucial parameters of cardiopulmonary exercise test.

Aorta stiffness and left ventricular function in heart failure

The elastic proximal aorta is the main region that is affected by ageing, hypertension, diabetes and also contents the summation of the peripheral reflected waves. Previous trials supported the presence of increased aortic stiffness in diastolic HF, independent of age and/or hypertension.6

In HF patients, it has been proposed that large arteries, through evaluation of abdominal aorta and carotid artery, are stiffer and their distensibility correlates with LV diastolic function indices, such as E/A ratio, whereas no difference was found in the radial artery, suggesting that after cardiac pump failure, there might be a non-uniform progression of arterial stiffening in smaller and larger arteries.7

In accordance to our results, Mitchell et al.8 also found abnormalities in the proximal aortic pressure flow and pressure area relationships, indicating increased functional stiffness of the central conduits in CHF, whereas in contrast, distal (muscular) conduit vessels tended to be less stiff.

Figure 2  Pulse wave velocity as measured in control (CRL) and in patients with non-ischaemic dilated cardiomyopathy patients (NIDC) (A). The left panel (B) illustrates the pulse wave velocity in non-ischaemic dilated cardiomyopathy patients according to their left ventricular diastolic filling pattern. NL, normal; DLR, delayed relaxation; PSN, pseudo-normal; RESTR, restrictive filling pattern.
In the present study for the first time, to the best of our knowledge, we found that proximal elastic aortic stiffness is increased in patients with NIDC, who are used as a model of non-atherosclerotic cause of HF, and that this reduced distensibility is correlated with the LV diastolic and systolic function.

With increased PWV, the wave reflections impact on the aorta during systole, rather than diastole, increasing systolic pressures, pulse pressure, and myocardial oxygen consumption and decreasing diastolic BP and coronary perfusion gradient.

Although the present study cannot establish a definite causal relation, we found that increased proximal aortic stiffness is related to both LV systolic and diastolic function indices and reduced exercise tolerance.

Although it is well established the interrelation of LV systolic performance and LV afterload, rather explaining our finding about the relation of PWV and Sm wave, the association between cardiac afterload and LV diastolic function is less clear. Experimental studies have shown that LV afterload (particularly that related to arterial resistance and wave reflections) more consistently affects myocardial relaxation; however, the responsible mechanisms and the significance of this interaction in vivo remain unclear. Studies in intact hearts using abrupt occlusion of the central aorta have imposed loads during late systole at the identical pre-load and found a non-linear relationship between end-systolic pressure and myocardial relaxation rate.

Table 2 Differences between non-ischaemic dilated cardiomyopathy patients with mild (delayed relaxation filling pattern, group A) or advanced (pseudo-normal or restrictive filling pattern, group B) left ventricular diastolic dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 34)</th>
<th>Group B (n = 26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.5 ± 13.7</td>
<td>54.9 ± 13</td>
<td>0.52</td>
</tr>
<tr>
<td>NYHA</td>
<td>2.1 ± 0.37</td>
<td>2.25 ± 0.44</td>
<td>0.45</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.5 ± 12.4</td>
<td>127.1 ± 14.5</td>
<td>0.48</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>47 ± 13.6</td>
<td>54.4 ± 14.8</td>
<td>0.058</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>70.6 ± 9.3</td>
<td>71.5 ± 15</td>
<td>0.22</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>56.8 ± 4.5</td>
<td>59.2 ± 7.1</td>
<td>0.12</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>297 ± 86.2</td>
<td>290 ± 69.4</td>
<td>0.73</td>
</tr>
<tr>
<td>LVHF (%)</td>
<td>35.5 ± 5.7</td>
<td>32.9 ± 8.8</td>
<td>0.19</td>
</tr>
<tr>
<td>LA (mm)</td>
<td>42 ± 3.1</td>
<td>43.1 ± 3.5</td>
<td>0.26</td>
</tr>
<tr>
<td>Em/Am</td>
<td>0.93 ± 0.33</td>
<td>1.98 ± 1.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DTE (ms)</td>
<td>233 ± 35.5</td>
<td>149.3 ± 33.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>e’ (cm/s)</td>
<td>6.3 ± 2.8</td>
<td>5.8 ± 3.3</td>
<td>0.52</td>
</tr>
<tr>
<td>E/e’</td>
<td>9.2 ± 3.7</td>
<td>15.6 ± 7.8</td>
<td>0.002</td>
</tr>
<tr>
<td>Sm(cm/s)</td>
<td>5.6 ± 1.8</td>
<td>4.7 ± 1.4</td>
<td>0.052</td>
</tr>
<tr>
<td>AOL (mm)</td>
<td>10.92 ± 1.26</td>
<td>10.52 ± 1.37</td>
<td>0.25</td>
</tr>
<tr>
<td>PWV (m/s)</td>
<td>6.6 ± 2.9</td>
<td>8.6 ± 2.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Ex. Dur (s)</td>
<td>1113 ± 390</td>
<td>969 ± 264</td>
<td>0.06</td>
</tr>
<tr>
<td>PVO2 (mL/kg/min)</td>
<td>23 ± 4.3</td>
<td>19 ± 2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pred PVO2 (%)</td>
<td>88.6 ± 9.5</td>
<td>77.6 ± 8.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oxygen pulse</td>
<td>7.6 ± 1.6</td>
<td>5.9 ± 2.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

SBP, systolic arterial blood pressure; PP, pulse pressure; HR, heart rate; LVDD, left ventricular end-diastolic volume; LA, left atrial; LVHF, left ventricular ejection fraction; Em, early pulsed wave Doppler transmural wave; Am, late pulsed wave Doppler transmural wave; DTE, deceleration time of Em wave; Sm, average peak systolic PW-TDI wave of the basal septal and lateral LV wall; e’, average peak early diastolic PW-TDI wave of the basal septal and lateral LV wall; Ex., exercise; Dur, duration; PVO2, oxygen consumption at peak exercise; Pred., predicted for age, BSA, and sex; PWV, pulse wave velocity of the proximal aorta.

Figure 3 Relationship of pulse wave velocity with the averaged (septal and lateral mitral annulus) systolic pulse wave-tissue Doppler imaging wave and left ventricular mass in patients with non-ischaemic dilated cardiomyopathy.
proposed in an attempt to explain the reduced arterial distensibility in HF.

Recently, we have also reported that the proximal aorta stiffness as evaluated with the present method relates with LV mass and diastolic function in end-stage renal failure patients, further supporting our concept that the proximal aorta stiffness through the rise of LV afterload affects the LV function.

Arterial stiffness and exercise capacity in non-ischaemic dilated cardiomyopathy patients

The alterations of ventriculo-aortic coupling seem to further exacerbate during exercise, and our findings suggest that increased aortic stiffness is related to reduced PVO₂ and peak exercise oxygen pulse, an index of cardiac stroke volume.

Previous study in accordance with our results, assessing the aortic distensibility with MRI, also concludes that in patients with systolic HF, aortic stiffness relates with the exercise capacity.

Bonapace et al. reported that a higher PWV measured by foot-to-foot method was associated with a more restrictive filling pattern and reduced PVO₂.

Stiffening of the aorta may contribute to exercise capacity in several ways. Reduced aortic distensibility affects the proximal aorta-cushioning effect, thus increasing the LV afterload with further compromising the ability to generate adequate cardiac output during exercise in patients with HF. The relationship found in the present study between PWV and peak oxygen pulse, an indicator of

Figure 4 Relationship of pulse wave velocity with the peak exercise oxygen consumption (PVO₂) (A) and peak exercise oxygen pulse (B) in patients with non-ischaemic dilated cardiomyopathy.

Figure 5 Bland–Atman analysis showing the 95% limits of agreement of intra- (A) and inter (B)-observer variation.
stroke volume and arteriovenous O₂ difference, rather suggests the above mechanism as a possible reason for the reduced exercise tolerance. Secondly, combined ventricular–aorta stiffness could potentially reduce the cardiovascular reserve. As a consequence, the ability of the heart to accommodate the peripheral demands and the increased pre-load during exercise may be reduced, further increasing the left atrial pressure, thus producing further increase in pulmonary capillary wedge pressure and the appearance of shortness of breath eliminating the exercise capacity.

Thirdly, during exercise, the combination of a reduced diastolic period due to high heart rates and a further increment of LV afterload due to the declined cushioning properties of the stiffer aorta leads to the reduction in coronary perfusion gradient, thus affecting coronary perfusion.

Finally, we found that a stiffer aorta is related to more advanced LV diastolic dysfunction. The latter is associated with increased LV end-diastolic pressures at rest, which further increase during increased heart rate and reduced diastolic period. This lead to pulmonary capillary wedge pressure increase, thus eliminating the exercise capacity. Thus we can postulate that LV dysfunction and aortic stiffness create a vicious circle with each other causing deterioration of the other with further impairment during exercise.

Technical considerations and concept

We made two important modifications to the method, which we have already reported, measuring the PWV in the aortic arch segment of the proximal aorta.

First, we digitally stored the cardiac cycles and the recording for measuring the time interval was made at 200 mm/s sweep speed, resulting in measuring time intervals with a difference of 2.5 ms. Such a measurement makes the time difference measurement in such small portion more accurate. Secondly, we measured the AOL with the open trace method using a continuous line to calculate the bell-shaped aortic arch distance instead of separate straight distances that could not follow the shape of the aortic arch.

Both modifications result in measuring increased PWV in control subjects than previously reported; values that are more close to previous invasive measurements in that region.

Our method includes an elastic proximal aorta region of great interest due to

1. the neighbouring of the LV, thus affecting the ventriculararterial coupling,
2. its unique shape resulting in a maximum flow propagation delay,
3. the origin of three large crucial body vessels (innominate, common carotid, and left subclavian artery) that may be affected by increased aorta stiffness → increased flow velocities → increased shear stress to the origin of the vessels.

However, besides the theoretical advantages of our proposed method for the assessment of the PWV in the proximal aorta, its clinical value must be confirmed with large trials which can prove its prognostic value.

Conclusion

Patients with NIDC have increased aortic stiffness compared with controls, which is correlated with impaired LV systolic and diastolic function as well as with the reduced exercise capacity commonly observed in these patients. Thus, a stiffer proximal aorta with decreased cushioning ability may further increase the LV afterload and affect the cardiovascular performance of patients with HF.

Conflict of interest: none declared.

References


