Effects of the reduction of preload on left and right ventricular myocardial velocities analyzed by Doppler tissue echocardiography in healthy subjects

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Received 3 June 2003; received in revised form 23 September 2003; accepted 6 October 2003

Abstract Aims Previous studies using Doppler Tissue Echocardiography (DTE) have suggested that the early-diastolic myocardial velocity behaves as a relatively load-independent index of left ventricular relaxation in patients with cardiac diseases; it is not ascertained if this holds true also in normal human hearts.

Methods and results We assessed the influence of a progressive reduction of preload, obtained by Lower Body Negative Pressure (LBNP), on the diastolic and systolic myocardial waves compared to the inflow patterns estimated in left and right ventricles in nine healthy subjects. LBNP caused a significant decrease in end-diastolic volume, stroke volume and systolic arterial pressure, whilst heart rate increased only at maximum preload reduction; meridional end-systolic stress did not change significantly. The early (Ė) and late (Ȧ) myocardial velocities, at mitral and tricuspid annulus, decreased similarly during lower body suction, so that Ė/Ȧ ratio did not change. However, due to reduced early (E) but unchanged late (A) diastolic velocities, the E/A ratio of inflow patterns decreased. Systolic (Ṡ) myocardial velocities also decreased during LBNP. LBNP induced greater changes of myocardial diastolic and systolic velocities in the right than in the left ventricle.

Conclusion In this study, myocardial Ė, Ȧ and Ṡ velocities, in both the left and the right ventricle, were significantly affected by preload in healthy subjects. Our results support the usefulness of the Ė/Ȧ ratio as a relatively load-independent index of diastolic function.

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KEYWORDS
Doppler tissue imaging;
Lower body negative pressure;
Preload;
Volunteers.
Introduction

Recent studies have shown that the early-diastolic myocardial (E') wave velocity, measured by Doppler Tissue Echocardiography (DTE), is useful in the study of left ventricular relaxation in patients with diastolic dysfunction caused by different cardiac diseases.\(^1\)\(^-\)\(^5\) It has also been suggested that, unlike the mitral E wave, the E' tissue wave may be less dependent on loading conditions and may distinguish pseudonormal from normal filling patterns.\(^1\)\(^-\)\(^6\) Furthermore, it has been proposed that the early-diastolic tissue velocity behaves as a relatively load-independent index of left ventricular relaxation and therefore can be used to correct for the influence of relaxation on transmitral E velocity in the evaluation of filling pressures.\(^7\),\(^8\) Specifically, it has been shown that the ratio of mitral E velocity to myocardial E' velocity (E/E') correlates with pulmonary capillary wedge pressure (PCWP) and left ventricular diastolic pressure in patients with underlying cardiac disease.\(^7\),\(^8\) However, it is not yet defined if these indices, as validated in patients with cardiovascular diseases, may be applied also in healthy subjects.\(^9\),\(^10\)

Therefore, the current pilot investigation was designed to develop a method for assessing whether diastolic myocardial velocities, as evaluated by DTE, are influenced by loading changes.

In this study early and late diastolic (E' and A' waves) tissue velocities were measured at mitral and tricuspid annulus during a progressive reduction of preload, induced by Lower Body Negative Pressure (LBNP), in healthy volunteers. Also, the systolic myocardial velocities (S' wave) were measured during this experimental protocol.

The primary goal was to define the effects of reduced preload on physiological tissue waves. Furthermore, we were also interested in exploring potential differences in the response of the right (RV) and the left (LV) ventricle to LBNP.

Myocardial diastolic parameters, as derived by DTE, were compared to those obtained with conventional pulsed Doppler assessment of the transmitral and tricuspid flow patterns.

Methods

Subjects

Nine healthy male volunteers (mean age 28 ± 4) were enrolled. All volunteers were normotensive and were not taking any medications. All subjects were fully informed of the aims of the investigation and accepted to be enrolled. Approval of the Ethic Committee of University of Parma was obtained.

Experimental protocol

Isolated preload reduction was obtained by means of graded LBNP. The device for lower body suction has been described in detail elsewhere.\(^11\) Briefly, it consists of a plexiglas cylinder whose bottom end is latched close with a tight-fitting cover; the top end carries a rubber seal which is fitted around the subject’s waist just above the iliac crest and ensures airtight closure. Vacuum is produced by means of an electrically powered annular pump, and a valve allows sensitive adjustments of the level of negative pressure within the chamber.

Basal echocardiographic and Doppler measurements were performed after 15 min of rest in the recumbent position; negative pressure was subsequently applied in a scalar fashion with -10 mmHg steps down to -40 mmHg, to avoid abrupt volume decentralization. All subjects were able to tolerate this protocol without any adverse effects. Measurements were repeated 3 min after the maximum level of negative pressure had been reached.

Systolic (SAP) and diastolic (DAP) blood pressures and heart rate (HR) were continuously recorded from the dominant arm at 1 min intervals by means of an automatic device (Takeda TM2420; A&D Co. Ltd., Tokyo, Japan).

Standard echocardiographic study

All echocardiographic examinations were performed by one experienced operator (G.P.) using a commercially available equipment (Acuson Aspen, Mountain View, California) and a multi-Hertz sector probe (2.5–4 Hz) in basal condition and at each step of LBNP (-10, -20, -30 and -40 mmHg).

With the subject in the left lateral decubitus position, images were obtained from the standard projections. Systolic and diastolic thickness of interventricular septum (IVSs, IVSd) and posterior wall (PWs, PWd), and systolic and diastolic LV dimensions (LVDs and LVDd) were measured according to the Penn convention in the parasternal view.\(^12\),\(^13\)

Relative wall thickness (RWT) was computed at end diastole as the ratio of IVS + PW and LVDd. Meridional end-systolic stress (ESS) was calculated with the formula of Devereux and colleagues.\(^14\)

Left ventricular mass (LVM) was calculated using the Penn convention and indexed to Body Surface Area (LVMi).\(^12\),\(^13\) LV end-diastolic (EDV) and endsystolic (ESV) volume as well as ejection fraction
(EF) and stroke volume (SV) were calculated from measurements taken in the apical two-chamber view according to the Simpson’s single-plane rule.

The mitral and the tricuspid flows were recorded with pulsed-wave Doppler technique from the apical four-chamber view placing the sample volume at the leaflet tips of the open atrioventricular valves; the peak velocities, time—velocity integrals of E and A waves and the E/A ratios were evaluated.

Each measurement from recorded data was performed by two investigators on a sequence of five cycles. The intra-observer and inter-observer coefficients of variation were 5.1% and 7.2% for peak velocities and 11.0% and 13.3% for integrals, respectively, in the LV. The intra-observer and inter-observer coefficients of variation were 5.5% and 7.7% for peak velocities and 11.4% and 13.5% for integrals, respectively, in the RV.

Pulsed Doppler tissue echocardiography

The myocardial velocities of the LV and RV were measured sampling the mitral and tricuspid annulus excursion at lateral sites in the four-chamber view. Care was taken to keep the ultrasound beam perpendicular to the plane of the annulus in order to minimize the angle between the beam and the direction of annular motion.

The width of the sample volume was 3–5 mm. Measurements were focused on the systolic myocardial wave (S’), the early-diastolic (E’) and end-diastolic myocardial (A’) waves. From each site, DTE images were stored in digital format; measurements of peak velocities and calculation of time—velocity integrals of each wave were performed off-line using the software package implemented in the ultrasound machine. Usually, several cardiac cycles were acquired, and the best two consecutive ones were analyzed and averaged. In the text and figures below, peak velocities and time—velocity integrals are abbreviated with the pv and tvi subscripts, respectively (e.g. $S'_{pv}$, $E'_{tvi}$).

The intra-observer and inter-observer coefficients of variation were 5.3% and 8.2% for peak velocities, compared with 9.5% and 14.2% for integrals in the LV. The intra-observer and inter-observer coefficients of variation were 5.0% and 8.3% for peak velocities, compared with 9.5% and 14.5% for integrals in the RV.

Statistics

Values are expressed as mean ± standard deviation. Preliminary data exploration by Kolmogorov—Smirnov test showed no significant deviation from normality. Analysis of variance for repeated measures and paired Student’s t test were therefore used to assess differences before and after alteration of loading condition. Linear regression was used to evaluate whether the Doppler parameters were correlated with preload parameters during LBNP. For all statistics, a two-sided p value < 0.05 was considered statistically significant.

Results

Table 1 summarizes the hemodynamic data obtained during LBNP: the volume decentralization resulted in a significant decrease in EDV and SV and a lesser, non-significant, decrease in ESV and EF. HR increased at maximum preload reduction (−40 mmHg), whilst SAP progressively decreased. No significant changes were observed in DAP.

RWT increased at −40 mmHg LBNP (from baseline = 0.38 ± 0.06 to 0.50 ± 0.07, P < 0.01) as a result of a decrease in LV diameter (from 48 ± 3 to 42 ± 4 mm, P < 0.01) and increased parietal thickness (IVSd: from 10.1 ± 1.5 to 11.3 ± 1.5 mm, P < 0.05; PWd: from 8.3 ± 1.3 to 9.7 ± 1.4 mm, P < 0.01). Consequently, a slight non-significant decrease in ESS

### Table 1  Hemodynamic effects induced by lower body negative pressure

<table>
<thead>
<tr>
<th></th>
<th>EDV (ml)</th>
<th>ESV (ml)</th>
<th>SV (ml)</th>
<th>EF (%)</th>
<th>HR (bpm)</th>
<th>SAP (mmHg)</th>
<th>DAP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>105 ± 19</td>
<td>30 ± 10</td>
<td>74 ± 14</td>
<td>71 ± 6</td>
<td>67 ± 6</td>
<td>124 ± 7</td>
<td>76 ± 5</td>
</tr>
<tr>
<td>−10</td>
<td>90 ± 15*</td>
<td>32 ± 7</td>
<td>59 ± 11</td>
<td>65 ± 5</td>
<td>67 ± 4</td>
<td>120 ± 9*</td>
<td>73 ± 7</td>
</tr>
<tr>
<td>−20</td>
<td>86 ± 17†</td>
<td>28 ± 5</td>
<td>58 ± 13</td>
<td>68 ± 4</td>
<td>70 ± 10</td>
<td>117 ± 10†</td>
<td>74 ± 4</td>
</tr>
<tr>
<td>−30</td>
<td>74 ± 12†</td>
<td>29 ± 6</td>
<td>45 ± 9†</td>
<td>60 ± 6</td>
<td>68 ± 10</td>
<td>117 ± 10*</td>
<td>77 ± 5</td>
</tr>
<tr>
<td>−40</td>
<td>63 ± 6†</td>
<td>25 ± 4</td>
<td>38 ± 9†</td>
<td>60 ± 10</td>
<td>74 ± 7†</td>
<td>116 ± 8†</td>
<td>76 ± 5</td>
</tr>
</tbody>
</table>

Data are means ± SD. EDV = end-diastolic volume; ESV = end-systolic volume; SV = stroke volume; EF = ejection fraction; HR = heart rate; SAP = systolic arterial pressure; DAP = diastolic arterial pressure.

* $p<0.05$.
† $p<0.01$.
‡ $p<0.001$. 

was observed (baseline = $61.2 \pm 21.8 \times 10^3$ dynes/cm$^2$; LBNP $-40$ mmHg = $43.7 \pm 4.8 \times 10^3$ dynes/cm$^2$, $P = NS$).

Fig. 1 shows an example of the changes induced by LBNP at $-40$ mmHg on the mitral inflow pattern and the mitral annulus velocity pattern; during volume decentralization the $E/A$ ratio of the mitral flow significantly decreased whilst the $E'/A'$ ratio of tissue motion did not change. Similar changes were observed for the tricuspid flow and myocardial velocities (Fig. 2). It can be observed that $E'_{pv}$ and $A'_{pv}$ decreased similarly both at the mitral and tricuspid annulus (Tables 2 and 3, respectively) during lower body suction, so that $E_{pv}/A_{pv}$ ratios were unchanged. Similar variations were observed for $E'_{tvi}$ and $A'_{tvi}$ in LV and RV (Tables 2 and 3). Conversely, the mitral and tricuspid flow patterns showed a significant decrease of $E_{pv}$ and $E_{tvi}$ but no changes in $A_{pv}$ and $A_{tvi}$. Hence, the $E/A$ ratio of inflow patterns decreased, although statistical significance was not reached for mitral $E_{tvi}/A_{tvi}$ (Tables 2 and 3). Furthermore, a stepwise decrease in $E/A$ ratio of the inflow patterns was observed during gradual LBNP, whilst myocardial $E'/A'$ ratio remained constant (Fig. 3).

The $S_{tvi}$ decreased in LV and RV during LBNP, as well as the RV $S_{pv}$; no changes were observed in the LV $S_{pv}$ (LV: $S_{pv}$ from $17.4 \pm 4.7$ to $17.5 \pm 3.8$ cm/s, $P = NS$; $S_{tvi}$ from $2.9 \pm 0.5$ to $2.3 \pm 0.5$ cm, $P < 0.01$; RV: $S_{pv}$ from $17.2 \pm 2.5$ to $12.9 \pm 2.1$ cm/s, $P < 0.001$; $S_{tvi}$ from $3.2 \pm 0.4$ to $2.0 \pm 0.4$ cm, $P < 0.001$).

Somewhat greater variations in RV as compared with LV myocardial velocities were detected by DTE during LBNP (RV $\Delta E'_{pv} = -38\%$ vs LV $\Delta E'_{pv} = -24\%$; RV $\Delta E'_{tvi} = -37\%$ vs LV $\Delta E'_{tvi} = -26\%$; RV $\Delta A'_{pv} = -37\%$ vs LV $\Delta A'_{pv} = -17\%$; RV $\Delta A'_{tvi} = -35\%$ vs LV $\Delta A'_{tvi} = -14\%$; RV $\Delta S'_{pv} = -25\%$ vs LV $\Delta S'_{pv} = -19\%$).
Peak mitral early-to-late diastolic flow velocity ratio ($E/ A$) was strongly related to left ventricular EDV during volume decentralization ($r = 0.76$, $P < 0.001$), whereas a weaker though significant correlation was apparent between peak tricuspid $E/ A$ velocity ratio and left ventricular EDV ($r = 0.29$, $P < 0.05$). This was due to the fact that peak $E$ velocity, but not peak $A$ velocity, decreased significantly during LBNP (Tables 2 and 3). On the contrary, no significant correlations were detected between peak myocardial early-to-late diastolic velocity ratio ($E'/ A'$) and left ventricular EDV at either the mitral ($r = 0.25$, $p = NS$) or the tricuspid ($r = -0.12$, $p = NS$) annulus, due to the fact that both velocities decreased during LBNP (Tables 2 and 3). Similar relations were found between the same flow and myocardial Doppler indices and left ventricular SV (data not shown). Interestingly, no correlation was observed between peak flow/myocardial early velocity ratio ($E_{pv}/ E'_{pv}$) and left ventricular EDV during volume decentralization at either the mitral or tricuspid site (Fig. 4).

**Discussion**

Doppler Tissue Echocardiography (DTE) is a technique which allows recording of myocardial ventricular wall motion during both systole ($S'$ wave) and diastole ($E'$ and $A'$ waves). $^{15-18}$ Many studies have supported the usefulness of DTE indices in the study of LV systolic $^{19,20}$ and diastolic function. $^{1-6,21}$ Specifically, the velocity of the early-diastolic tissue motion may reflect the rate of
Table 2  Left ventricular diastolic parameters

<table>
<thead>
<tr>
<th></th>
<th>Mitral flow</th>
<th>DTE</th>
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<tbody>
<tr>
<td></td>
<td>$E_{pv}$ (cm/s)</td>
<td>$E_{tvi}$ (cm)</td>
</tr>
<tr>
<td>Baseline</td>
<td>77.1 ± 9.4</td>
<td>13.1 ± 2.6</td>
</tr>
<tr>
<td>LBNP –40 mmHg</td>
<td>50.8 ± 5.0</td>
<td>10.8 ± 2.5</td>
</tr>
<tr>
<td>$P$</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data are means ± SD. $E_{pv}$ and $E_{tvi}$ = peak velocity and time–velocity integral of early diastolic mitral flow wave, respectively; $A_{pv}$ and $A_{tvi}$ = peak velocity and time–velocity integral of late diastolic mitral flow wave, respectively; $E'_{pv}$ and $E'_{tvi}$ = peak velocity and time–velocity integral of early diastolic tissue wave, respectively; $A'_{pv}$ and $A'_{tvi}$ = peak velocity and time–velocity integral of late diastolic tissue wave, respectively; LBNP = lower body negative pressure.

Table 3  Right ventricular diastolic parameters

<table>
<thead>
<tr>
<th></th>
<th>Tricuspid flow</th>
<th>DTE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E_{pv}$ (cm/s)</td>
<td>$E_{tvi}$ (cm)</td>
</tr>
<tr>
<td>Baseline</td>
<td>51.1 ± 8.5</td>
<td>10.7 ± 2.1</td>
</tr>
<tr>
<td>LBNP –40 mmHg</td>
<td>38.9 ± 6.6</td>
<td>8.9 ± 1.4</td>
</tr>
<tr>
<td>$P$</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data are means ± SD. $E_{pv}$ and $E_{tvi}$ = peak velocity and time–velocity integral of early diastolic tricuspid flow wave, respectively; $A_{pv}$ and $A_{tvi}$ = peak velocity and time–velocity integral of late diastolic tricuspid flow wave, respectively; $E'_{pv}$ and $E'_{tvi}$ = peak velocity and time–velocity integral of early diastolic tissue wave, respectively; $A'_{pv}$ and $A'_{tvi}$ = peak velocity and time–velocity integral of late diastolic tissue wave, respectively; LBNP = lower body negative pressure.
myocardial relaxation and may not be as dependent on pressure gradients as is the mitral flow. Based on some observations suggesting a relative independence of loading conditions, the early-diastolic mitral annulus excursion has been used to correct for the influence of relaxation on the transmitral E velocity and to predict filling pressures. Nagueh et al., in patients who underwent right heart catheterization, have shown that the ratio of mitral E velocity to the mitral annulus E’ velocity (E/E’) is the most accurate index in determining pulmonary capillary wedge pressure. More

Figure 3  Peak early-to-late diastolic flow velocity ratio (left) (● — ●, mitral inflow; ▲ — ▲, tricuspid flow) and peak early-to-late diastolic myocardial velocity ratio (right) (○ — ○, mitral annulus; △ — △, tricuspid annulus) during graded LBNP in normal subjects (see text for details). *P<0.05 and **P<0.01 compared to baseline.

Figure 4  Relationship between peak flow velocity/peak myocardial velocity ratio in early diastole (E/E’) and left ventricular end-diastolic volume (LVEDV). ○, Peak transmitral flow/peak mitral annulus velocity ratio and ▲, peak transtricuspid flow/peak tricuspid annulus velocity ratio. Separate regression lines and equations are also shown. Note the absence of correlation of E/E’ to LVEDV in either ventricle (left ventricle: r= 0.09, P = NS; right ventricle: r= −0.22, P = NS).
recently Ommen et al.\textsuperscript{8} have shown that this ratio is the best parameter for predicting mean left ventricular diastolic pressure.

The $E_{\text{flow}}/E_{\text{annulus}}$ has been also applied to evaluate right filling pressures.\textsuperscript{22} The ratio of tricuspid inflow $E$ to the tricuspid annulus $E'$ velocities has been found to correlate significantly with mean right atrial pressure, whilst the correlations worsen when DTE or conventional Doppler echocardiography indices are studied separately.\textsuperscript{23} However, all of these data were obtained in patients with underlying cardiac diseases, and it is not yet ascertained if these DTE indices can be applied also in normal human hearts.

Therefore, this preliminary study aimed at developing a method for assessing the effects of LBNP-induced preload reduction on diastolic and systolic myocardial velocities, as measured in both the LV and the RV, in healthy subjects. The excursions of the mitral and tricuspid annulus at the lateral corner were analyzed, as they reflect the longitudinal dynamics of the free wall in both ventricles. In a previous report\textsuperscript{21} on the effects of LBNP on the mitral flow pattern we had documented, in a subgroup of healthy subjects, a significant reduction in the peak velocity of the early-diastolic flow wave with reversal of the normal $E/ A$ ratio at the maximum depression attained, thus confirming the preload dependence of the transmural flow pattern. Conversely, in the present study we were able to show that the myocardial $E'/ A'$ ratio displays no significant changes through all steps of graded LBNP, either in the LV or in the RV. Sohn et al.,\textsuperscript{3} modifying cardiac preload by nitroglycerine infusion, had obtained qualitatively similar results in subjects with normal diastolic function.

In our healthy volunteers the $E'/ A'$ ratio did not change during suction because of a balanced reduction in both diastolic myocardial velocity waves ($E'$ and $A'$), which were in fact significantly affected by the reduction in the venous return to the heart. Thus, our data suggest that, in contrast with what has been reported in patients with various cardiac diseases,\textsuperscript{1–6} in the normal heart neither of the diastolic myocardial velocities waves is completely independent of filling pressure when analyzed separately.

Two recent experimental studies in dogs have demonstrated a decrease in the early-diastolic myocardial velocity, as measured at the mitral annulus during preload reduction by transient caval occlusion.\textsuperscript{24,25} Moreover, in the same studies, a significant correlation was observed between peak myocardial early-diastolic velocity and filling pressure, albeit only in the presence of normal relaxation.\textsuperscript{24,25} Furthermore, recent data obtained with strain rate imaging\textsuperscript{26} indicate that the propagation velocities of left ventricular lengthening in both early and late diastole are dependent on preload changes in healthy human subjects. Thus, in the physiologic state, the early-diastolic tissue velocity seems to reflect both components, i.e. that due to active relaxation and that related to actual flow volume, whilst the late diastolic tissue velocity may be affected only by ventricular filling during atrial contraction.

It is known that the myocardial $E'$ wave precedes flow $E$ wave. The ventricular elongation taking place with atrioventricular valves still closed is due to an active distension which is not affected by flow volume, but depends on the energy stored by myocardial elastic components during ventricular systole.\textsuperscript{27} The release of this energy in the early-diastolic phase produces a longitudinal movement of the ventricle which, in turn, causes the endoventricular pressure to fall and the atrioventricular pressure gradient to increase.\textsuperscript{27} When the atrioventricular valves open, the normal ventricles are passively distended by the blood volume that flows from the atria. This passive phenomenon may thus justify the reduction of the myocardial early-diastolic velocities that we and others observed during preload reduction with LBNP. The late diastolic $A'$ wave, being due to a passive ventricular distension mainly affected by the force of atrial systole,\textsuperscript{25} hence by atrial filling, is also reduced during lower body suction. Therefore, if changes in preload affect peak velocities and time–velocity integrals of both the $E'$ and the $A'$ waves, conceivably the $E'/A'$ ratio is less dependent on filling pressures compared to the single waves, and may be of importance as an index of diastolic function. Our results are in partial agreement with those of Firstenberg et al.,\textsuperscript{28} these authors recently demonstrated, in subjects without evidence of cardiac diseases submitted to preload alteration by either LBNP or saline infusion, a positive correlation between PCWP and $E'$ wave velocity sampled at the mitral annulus. However, they did not analyze $A'$ wave, nor did they measure right ventricular myocardial velocities. On the other hand, our data are at variance with those obtained in diseased hearts,\textsuperscript{1–8} such differences may be interpreted in the light of recent experimental observations\textsuperscript{24,25} showing that the preload influence on the myocardial $E'$ wave gradually decreases as diastolic dysfunction worsens. This may explain the validity of $E_{\text{flow}}/E_{\text{annulus}}$ to estimate filling pressure in cardiac patients\textsuperscript{7,8,22} whilst we (Fig. 4) and others\textsuperscript{28} were not able to detect any correlations between $E_{\text{flow}}/E_{\text{annulus}}$ and preload indices in healthy subjects.
We also observed a reduction in systolic myocardial velocities during LBNP. Myocardial shortening, as analyzed by DTE, results from the interplay of contractility, preload and afterload. Oki et al., by infusing angiotensin II in healthy subjects, were able to prove a dependence of myocardial S' and E' velocities on afterload. However, in the present study, end-systolic stress, an index of afterload, was not significantly altered during graded lower body suction; thus, the reduction of preload seems to be entirely responsible for the observed changes in systolic myocardial velocities in our volunteers.

A comparison between the data obtained at mitral and tricuspid annulus during LBNP in our study shows greater changes of myocardial diastolic and systolic velocities in the right as opposed to the left ventricle. Conceivably, this result can be explained in the light of the greater preload dependence of the right ventricular function.

In conclusion, we developed a method for exploring the effects of preload reduction on systolic and diastolic velocities of the ventricular myocardium; in a small series of healthy subjects, myocardial E', A' and S' velocities as measured by DTE in both the left and the right ventricle were significantly affected by preload changes. Therefore, these preliminary results suggest that the $E'/A'$ myocardial velocity ratio is a relatively preload-independent index which may add to the evaluation of diastolic function.

A few limitations of the present investigation should be clearly acknowledged. First, this pilot study was carried out on a small number of subjects free of cardiac diseases to assess the feasibility of the measurement of myocardial velocities during graded, non-pharmacological reduction of preload; thus, further studies enrolling larger series of both healthy subjects and cardiac patients are needed to confirm the usefulness of the $E'/A'$ ratio in the evaluation of diastolic function. Second, due to the young age of the volunteers participating in this study, caution should be exerted before extending our observations to the general population. Third, invasive hemodynamic measures of filling pressures (e.g. PWCP) and relaxation indices (e.g. tau constant) were not available for direct correlation with tissue Doppler parameters due to ethical concerns in performing cardiac catheterization in subjects without known cardiac diseases; moreover, we did not perform color M-mode interrogation of mitral inflow and thus could not attempt an estimation of PCWP with the formula proposed by Garcia and coworkers. However, lack of correlation between mitral $E/E'$ ratio and LVEDV in this study (Fig. 4) is in good agreement with the lack of correlation between mitral $E/E'$ ratio and PCWP reported by Firstenberg et al. in healthy volunteers, supporting the adequacy of LVEDV as a surrogate index of preload.

Acknowledgements

We are very grateful to Maria Antonietta Pianini for secretarial and technical assistance.

References


