Reduction of Left Ventricular Preload by Lower Body Negative Pressure Alters Doppler Transmitial Filling Patterns

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The objective of this study was to evaluate the effect of alterations in preload induced by lower body negative pressure on Doppler transmitial filling patterns. Echocardiograms and Doppler recordings were performed in 10 normal young men (aged 23 to 32 years) during various levels of lower body negative pressure (0, -20 and -50 mm Hg). Lower body negative pressure induced a reduction in diastolic velocity integral (from 12.17 ± 0.79 to 8.42 ± 0.71 cm, p = 0.0067) and consequently left ventricular diastolic diameter (from 5.11 ± 0.09 to 4.45 ± 0.1 cm, p < 0.0001). There was a significant reflex increase in heart rate from 59.9 ± 1.9 to 77.1 ± 2.4 beats/min (p < 0.0001), but blood pressure was unchanged.

This reduction in preload altered Doppler transmitial filling patterns as follows: 1) peak early velocity (E) decreased from 59.2 ± 3.8 to 39.1 ± 1.7 cm/s (p < 0.0001); 2) atrial filling velocity (A) was unchanged (35.58 ± 1.5 to 33.52 ± 1.4 cm/s, p = 0.517); 3) E/A ratio decreased from 1.7 ± 0.13 to 1.19 ± 0.08 (p = 0.0067); 4) mean acceleration (from 482 ± 37 to 390 ± 27 cm/s², p = 0.03) and mean deceleration (from 327 ± 31 to 169 ± 21 cm/s², p < 0.001) of the early filling wave were significantly reduced; and 5) peak acceleration (from 967 ± 42 to 829 ± 29 cm/s²) and peak deceleration (from 771 ± 94 to 547 ± 76 cm/s) also decreased, but not significantly. The reduction in deceleration induced a prolongation of the pressure half-time (from 64.3 ± 3.0 to 86.9 ± 4.9 ms, p = 0.0017).

Thus, a decrease in preload, as produced by lower body negative pressure, alters the transmitial Doppler flow pattern to one that has previously been associated with impaired diastolic relaxation. Alterations in preload must be considered when interpreting diastolic transmitial flow profiles obtained by Doppler echocardiography.

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of blood in the periphery, gradually reduces the left ventricular dimensions and volume and by inference ventricular preload in normal humans (27,28). In addition, because of the ability of lower body negative pressure to decrease venous return in a stepwise fashion, it is a convenient noninvasive technique by which to evaluate the load dependence of Doppler transmitral filling patterns. The objective of this study was, therefore, to assess the effects of alterations in preload on Doppler variables of transmitral diastolic flow.

Methods

Study subjects. The study group consisted of 18 healthy male volunteers between the ages of 23 and 32 years (mean 28), all of whom had good quality Doppler echocardiographic recordings during the intervention procedure. All subjects had normal findings on history and physical examination, electrocardiogram and two-dimensional echocardiogram: none were taking medications. Informed consent was obtained, and the study was approved by the Institutional Review Board of the University of Kentucky.

Study protocol. Each subject was placed supine on a table in a quiet, dimly lit room. The lower body from the pelvis to the toes was placed in an airtight glass chamber with a seal being placed just below the level of the iliac crest. The lower body negative pressure chamber was connected to a vacuum system that had computer-assisted rate and level controls. Increasing grades of lower body negative pressure were then applied at levels of rest and -20 and -50 mm Hg. During each stage, cuff blood pressure, heart rate, and Doppler echocardiographic recordings were performed.

Doppler echocardiographic methods. At each level of negative pressure, two-dimensional directed M-mode echocardiography with a 2.5 MHz transducer was performed from the parasternal view and pulsed Doppler recording was performed from the apical view. The transducer was oriented to obtain an apical four chamber view of the heart ensuring good visualization of the left ventricular cavity and maximal excursion of the mitral valve leaflets. Care was taken to achieve the smallest possible angle between the presumed direction of the diastolic blood flow and the orientation of the ultrasound beam. Recordings were made with the sample volume placed at the level of the mitral valve anulus and at the tips of the mitral valve leaflets within the left ventricular cavity. Data were recorded on professional videotape for all studies, as well as on paper in most instances.

Measurements and calculations. Three consecutive beats of good quality were analyzed off-line with commercially available equipment (Microsonics). Left ventricular dimensions were measured from the M-mode recordings in concordance with the recommendations of the American Society of Echocardiography. Doppler measurements were then traced with a handheld cursor, and automatic calculations of the following variables were made: peak velocity during early filling (maximal E), peak velocity during late atrial filling (maximal A), E/A ratio, diastolic velocity integral, pressure half-time and peak and mean acceleration and deceleration of the early diastolic velocity (Fig. 1).

Statistics. Results are reported as mean values ± SEM. The measurements were subjected to an analysis of variance procedure (F test). A significant result was regarded as a p value < 0.05.

Results

All studies were performed without complications or discomfort to the subjects. Adequate quality recordings were obtained in all cases.

Effect on diastolic velocity integral, ventricular dimensions, heart rate and blood pressure. The application of lower body negative pressure with subsequent decrease in venous return resulted in a reduction in transmitral diastolic velocity integral from a mean of 12.17 ± 0.79 to 8.42 ± 0.71 cm (p = 0.0067) (Fig. 2A). This reduction in mitral inflow resulted in a progressive decrease in left ventricular diastolic dimension from a mean of 5.11 ± 0.09 to 4.45 ± 0.1 cm (p < 0.0001) (Fig. 2B). With the assumption of small change in mitral anulus size, the decrease in flow velocity integral represents a significant reduction in stroke volume that resulted in a reflex increase in heart rate from 59.9 ± 1.9 to 77.1 ± 2.4 beats/min (p < 0.0001) (Fig. 3A).

Despite these changes in hemodynamics, systolic arterial blood pressure was unchanged: 121.9 ± 4.07 to 123.1 ± 5.9 mm Hg (p = NS). Diastolic blood pressure (from 63.7 ± 3.7
Lower Body Negative Pressure (mm Hg)

**Figure 2.** The effect of lower body negative pressure on diastolic velocity integral (A) and left ventricular (LV) diastolic dimension (B). Lower body negative pressure, by decreasing venous return, produced a reduction in diastolic velocity integral and left ventricular diastolic dimension (preload).

Effect on Doppler filling velocities and E/A ratio. Lower body negative pressure decreased the peak early velocity (E) from $59.2 \pm 3.8$ to $39.1 \pm 1.7$ cm/s ($p < 0.0001$). This progressive decrease was not only significant overall, but also between rest and $-20$ mm Hg and between $-20$ and $-50$ mm Hg (Fig. 4A). Although the E velocity decreased progressively, there were no changes in the height of the Doppler filling velocities produced by atrial systole: from $35.58 \pm 1.5$ to $33.52 \pm 1.4$ cm/s ($p = 0.517$) (Fig. 4A). Thus, the decrease in the early filling velocities with maintenance of the late atrial filling velocities (A) led to a progressive decrease in the E/A ratio from $1.7 \pm 0.13$ to $1.19 \pm 0.08$ ($p = 0.0087$) (Fig. 4B).

Effect on acceleration, deceleration and pressure half-time. With increasing grades of lower body negative pressure, there was a significant reduction in the mean acceleration (from $482 \pm 37$ to $390 \pm 27$ cm/s², $p = 0.03$) and deceleration (from $327 \pm 31$ to $169 \pm 21$ cm/s², $p < 0.001$) of the early filling wave (Fig. 5A). Although peak acceleration (from $907 \pm 42$ to $829 \pm 29$ cm/s²) and deceleration (from $771 \pm 94$ to $547 \pm 76$ cm/s²) also decreased, these changes were not significant. This reduction in the deceleration of the early filling wave induced a prolongation of the pressure half-time from $64.3 \pm 3.0$ to $86.9 \pm 4.9$ ms ($p = 0.0017$) (Fig. 5B).

Discussion

Role of reduced left ventricular preload. This study confirms the ability of lower body negative pressure to decrease left ventricular preload. Venous return, as represented by transmitral flow velocity integral, decreased by 30%, producing a 13% decrease in left ventricular diastolic dimensions measured by M-mode echocardiography. In abnormal and normal subjects without evidence of wall motion abnormalities, such alterations have been shown to represent an...
The influence of preload reduction on left ventricular filling was studied. Lower body negative pressure (mm Hg) was applied to reduce preload, and the effect on transmitral flow velocities (Vet) and E/A ratio (ratio of early filling (E) and atrial filling (A) velocities) was observed.

**Figure 4.** The effect of lower body negative pressure on transmitral velocities (Vet) (A) and E/A ratio (ratio of early filling (E) and atrial filling (A) velocities) (B). Lower body negative pressure decreased the maximal early velocity without changing the atrial velocity. Thus, the E/A ratio decreased.

An absolute decrease in left ventricular volume and pressure (27-29) reduces in preload significantly alters the Doppler transmitral flow velocity profile in normal humans (Fig. 5). Similar changes in diastolic transmitral patterns occur in a stepwise fashion and mimic those associated with impairment of left ventricular diastolic relaxation (30).

**Effect of preload reduction on transmitral filling patterns.** The decrease in early diastolic velocities (E), maintenance of velocities due to atrial systole (A), reduction in mean acceleration and deceleration of the early filling velocities and consequent prolongation of the pressure half-time are changes similar to those observed by other investigators in dogs (31,32) and in patients with cardiac disease (26,29,33) when preload was reduced. Choong et al. (32,33) and Stoddard et al. (26) with nitroglycerin and Courtois et al. (31) with inferior vena cava occlusion, all demonstrated a decrease in peak velocity as well as a reduction in the acceleration and deceleration of the velocities recorded in early diastole. Courtois et al. (31), however, also showed a reduction in the late diastolic velocities recorded during atrial systole, whereas Stoddard et al. (26) and Choong et al. (32,33), like vs, did not.

There are two possible explanations for these differences: First, nitroglycerin, like lower body negative pressure, produces a more gradual reduction in preload than inferior vena cava occlusion, which is more abrupt. A second possible reason is that the study of Courtois et al. (31), inferior vena cava occlusion did not change heart rate, whereas heart rate increased in our study as well as in those of Choong et al. (32,33) and Stoddard et al. (26). An increase in heart rate, even in the physiologic range, increases atrial velocities (34). Thus, the increase in atrial velocities associated with a more rapid heart rate could have maintained late atrial velocities despite a reduction in preload.
Figure 6. A representative example of a transmitral flow velocity profile recorded at the level of the mitral valve anulus at rest and at -20 and -50 mm Hg lower body negative pressure. There is a significant reduction in the early filling velocity (first deflection) as well as slowing of acceleration and deceleration of the early filling wave. The atrial velocity is unchanged (second deflection).

Hemodynamic and Doppler echocardiographic correlates. The Doppler velocity changes induced by altering ventricular load are consistent with the concept that transmitral flow reflects the left atrial-left ventricular pressure gradient (31-33,35). Thus, when preload is decreased, the gradient between the left atrium and left ventricle in early diastole will be reduced, diminishing early filling velocities and prolonging deceleration. Theoretic and experimental data (36,37) suggest that the initial peak pressure gradient between the left atrium and left ventricle and the chamber compliance of the left ventricle have significant influences on the pressure half-time and, thus, could potentially lead to errors in the use of this measure (for example, before and after balloon valvotomy). These errors are thought to occur because of abrupt changes in hemodynamic conditions, that is, chamber compliance and peak pressure gradients after valvotomy. This would be consistent with the predicted shortening of pressure half-time that has been seen with volume loading before and after mitral valvotomy (38) as well as the prolongation in pressure half-time produced by diminishing preload in normal subjects with use of lower body negative pressure.

Thus, marked volume overload or an increase in preload (such as might occur in mitral regurgitation) would result in a higher left atrial pressure with greater early filling velocities, more rapid deceleration and shorter pressure half-time, which may reverse the findings associated with a reduction in preload (or impaired relaxation). It is therefore also possible that by altering existing loading conditions, an abnormal transmitral filling pattern consistent with impaired relaxation may be converted to a more "normal" or a restrictive pattern (39). Thus, the ability to pseudonormalize and change transmitral filling patterns by virtue of alterations in preload significantly compromises the assessment of diastolic performance by Doppler echocardiography.

Sample volume location. We elected to place the pulsed Doppler sample at the level of the annulus because it is a location where changes in diastolic cross-sectional area arc minimal, therefore allowing velocity to be related to volumetric changes. Although the transmitral filling patterns obtained at the annulus and the tips of the mitral valve leaflets are similar, atrial velocities obtained at the level of the annulus are generally higher than at the tips of the leaflets (40). In our first eight patients, however, we did measure beats from both the tips and the annulus and found no difference in the statistical results of the data obtained.

Method of altering preload. Lower body negative pressure is a useful technique for altering preload with predictable reductions in left ventricular diastolic dimension and other hemodynamic variables. However, it does result in complex reflex changes, including increases in heart rate and systemic vascular resistance as well as a reduction in cardiac output. In our subjects, systolic and diastolic pressures were unchanged. In contrast, nitroglycerin produces a decrease in preload and systolic blood pressure; in addition, viscous effects may be reduced, diastolic suction may be increased secondary to the decrease in left ventricular volume and myocardial stiffness may increase as a result of coronary turgor effects (41). Thus, lower body negative pressure in contrast to nitroglycerin or abrupt inferior vena cava occlusion reduces preload gradually in a controlled fashion, with little change in afterload (that is, decrease in left ventricular dimensions and unchanged systolic blood pressure).

References
Influence of preload reduction on left ventricular filling

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