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EFFECT OF POSITIVE AND NEGATIVE STEP CHANGES IN INTRATHORACIC PRESSURE ON LEFT VENTRICULAR FUNCTION IN CONSCIOUS MAN

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SUMMARY

1. Breathing affects left ventricular stroke volume (LVSV) in normal subjects. The observed relationship may result from interaction between the effects of changing lung volume and intrathoracic pressure (IP).

2. To investigate the effect of IP on LVSV with minimal changes in lung volume, beat-by-beat LVSV (pulsed Doppler ultrasound) and systemic blood pressure (Finapres) were measured during obstructed inspiratory and expiratory efforts causing step changes in IP of $\pm$ 15 cmH_2O for 10 s, in seven subjects. Changes in mouth pressure (MP) during airway occlusion were used to indicate changes in IP. Group-averaged data for each second were compared to that in the second before the change in MP using Dunnet's multiple range test.

3. Step reductions in MP resulted in immediate and significant falls in LVSV ($P < 0{\cdot}05$) and systolic blood pressure ($P < 0{\cdot}01$) and increased heart rate, although this was not significant. These responses were transient, lasting only 3 s despite 10 s of reduced MP.

4. Step increases in MP caused biphasic cardiovascular responses. LVSV increased immediately, then fell significantly below control after 8 s ($P < 0{\cdot}01$). Heart rate increased significantly between 5 and 9 s after the onset of the increase in MP ($P < 0{\cdot}05$), suggesting activation of the baroreflexes by the accompanying progressive fall in systolic blood pressure.

5. The asymmetry in time course and magnitude between the responses to positive and negative pressure may reflect asymmetrical effects of MP on systemic venous return, right ventricular output, pulmonary venous return and left ventricular (LV) after-load, with the baroreceptors limiting changes in arterial pressure.

6. With negative pressure, systolic blood pressure fell by more than IP; this argues against an important role for LV after-load in depressing LVSV during negative pressure. These results therefore provide indirect support for the concept of ventricular interdependence, in which enhanced right ventricular filling impairs left ventricular filling.

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INTRODUCTION

Beat-by-beat measurements of left ventricular ejection during breathing and positive-pressure ventilation in man (Innes, De Cort, Kox & Guz, 1993) reveal a complex relationship between left ventricular stroke volume (LVSV) and the respiratory cycle, with marked differences in phase and magnitude between subjects. Part of this complexity may result from the interaction between the effects of changing lung volume and the simultaneous effects of changing intrathoracic pressure on the left ventricle.

Forced expiratory effort against a closed airway (the Valsalva manoeuvre) and the corresponding obstructed inspiratory effort (Müller manoeuvre), can be used to study the effects of respiratory excursions in intrathoracic pressure on left ventricular function in the absence of significant changes in lung volume. In the absence of airflow and with the glottis open, changes in the pressure measured at the mouth (during obstructed efforts) will correspond to changes in pressure of similar magnitude in the alveoli and pleura.

The purpose of the present study was to investigate the effects of controlled changes in intrathoracic pressure on left ventricular ejection at constant lung volume using non-invasive, beat-by-beat recordings of blood pressure, heart rate and left ventricular stroke volume in normal subjects.

Results of this study have already been presented in preliminary form (Innes, De Cort & Guz, 1992).

METHODS

Subjects

Seven normal subjects (3 female, 4 male, age range 24–40 years) were studied. All had normal hearts and lungs, as judged by clinical examination and chest X-ray and none were taking any medication at the time of the study. Subjects were selected in whom high quality Doppler signals from the ascending aorta could easily be obtained (i.e. minimal spectral broadening; Innes, 1987). The subjects gave informed consent for the study.

Protocols

Subjects sat in a chair and breathed through a mouthpiece connected to a 3-way tap, which could be used to obstruct the airway. A small fixed leak in the mouthpiece (30 ml s^{-1} at +15 cmH_2O) was used to ensure that the glottis remained open throughout. The integrated airflow signal from a pneumotachograph (Fleisch, Switzerland) attached to the tap was used to time interventions to the appropriate phase of respiration. Pressure in the mouthpiece was monitored using a pressure transducer (Validyne, CA, USA) and displayed to the subject on an oscilloscope. When instructed to do so, the subject relaxed at the end of a normal expiration (functional residual capacity, FRC) and the tap was turned to occlude the airway. After 5 s of relaxed breath holding (to achieve a stable cardiovascular baseline), the subject attempted to inspire against the occlusion, using visual feedback of the mouth pressure to achieve and maintain a pressure of −15 cmH_2O for 10 s. This procedure was repeated six times, with approximately 2 min of recovery time between each intervention. The procedure was then repeated, but this time the subjects were instructed to hold their breath for 5 s (with the glottis open) at the end of a normal inspiration and then to attempt to blow out against the occluded airway for 10 s. Visual feedback of the mouth pressure signal was used to achieve and maintain a positive pressure of 15 cmH_2O. This was repeated six times, with approximately 2 min of rest between each attempt. Different starting volumes were chosen for inspiratory and expiratory efforts to make the straining manoeuvre easy for the subjects.

Cardiovascular measurements

Left ventricular stroke volume was calculated from pulsed Doppler ultrasound measurements (Pedof, Vingmed, Norway and Doptek, Chichester) of blood velocity in the ascending aorta, multiplied by echocardiographic measurements of aortic cross-sectional area (Irex, 2-D echocardiograph, NJ, USA). This method has previously been validated for beat-by-beat measurements by Innes, Mills, Noble, Murphy, Pugh, Shore and Guz (1987). Heart rate was derived from an ECG, and left ventricular output from the product of heart rate and LVSV. There is a theoretical risk that altered IP could change aortic cross-sectional area and influence the LVSV measurements. From the aortic compliance data of Greenfield & Patel (1962), the predicted change in the stroke volume calculation assuming that all the +15 cmH_2O was added to the aortic transmural pressure would be around 3·6 %. In two of the subjects, we compared aortic diameter at MP of 0 and +15 cmH_2O and found a non-significant fall of 2·2 % ($P = 0·47$, unpaired t test). It is, therefore, unlikely that this effect is a significant source of error in these measurements.

Blood pressure was measured non-invasively beat-by-beat with a finger cuff (Finapres, Ohmeida, Englewood, CO, USA). This technique has been validated at rest (Molhoek *et al.* 1984; Wesseling, Settels & De Wit, 1986; Kurki, Smith, Head, Dec-Silver & Quinn, 1987; Imholz, Van-Montfrans, Settels, Van Der Hoeven, Karemaker & Weiling, 1988). In our hands, beat-to-beat comparison of Finapres with simultaneous contralateral radial artery pressure in one subject during a Valsalva manoeuvre yielded a mean difference (radial-Finapres) for systolic pressure of −0·8 mmHg (95 % confidence interval (CI) of −6·0 to 4·4 mmHg). Corresponding figures for diastolic pressure were +4·8 mmHg (95 % CI 0·1 to 9·6 mmHg).

Data analysis

The time of each heart beat after the onset of the change in MP was calculated and the data for the six runs were pooled and averaged in 1 s time bins for each subject from 5 s before to 10 s after the change in MP. A mean for each second for all seven subjects was then calculated, except in the case of blood pressure where due to technical problems satisfactory recordings were only obtained in five subjects. The value for each of the first 9 s of the intervention was then compared to the value for the second immediately before the change in MP using Dunnet's multiple range test. This comparison was done separately for positive and negative changes in MP. To compare the responses between individual subjects of different body size, LVSV in each subject was also calculated as a percentage of the value in the second immediately preceding the pressure change in that subject.

RESULTS

Negative intrathoracic pressure

With the aid of visual feedback, the subjects achieved a rapid and accurate reduction in MP which they maintained for 10 s. Mean results for the group are shown in Fig. 1. There was an immediate and significant fall in LVSV which was maintained for 3 s ($P < 0·01$ in the first 2 s, $P < 0·05$ in the third). LVSV then increased back towards the baseline value. There was also an immediate increase in heart rate, although this did not achieve statistical significance. Cardiac output fell in the first 6 s after the fall in MP; this fall was significant ($P < 0·05$) in the second, fifth and seventh second. There was an abrupt fall in systolic blood pressure ($P < 0·01$ within the first 2 s), accompanied by a rise in diastolic blood pressure ($P < 0·05$) followed by an equally abrupt return to the baseline value.

The immediate decrease in LVSV relative to the control value was very similar in magnitude and time course for the seven subjects in the first 4 s after the pressure change (Fig. 2). As the negative pressure was sustained, relative LVSV became more variable between subjects.

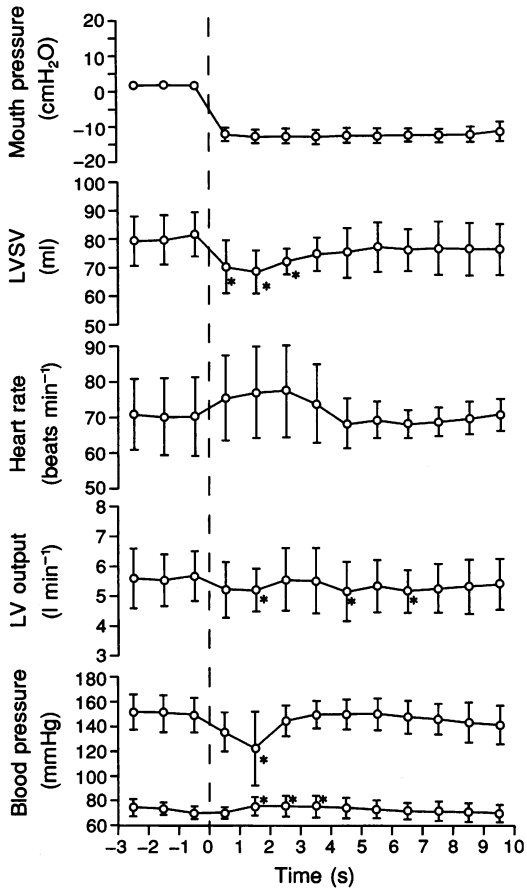

Fig. 1. Mean ± S.D. ($n = 7$) values each second for mouth pressure, left ventricular stroke volume (LVSV), heart rate, left ventricular output and systolic and diastolic blood pressure ($n = 5$) during a step change in MP of -15 cmH_2O. Time 0 represents the time of onset of the step change in MP. *shows values which are significantly different from the data point immediately before the change in MP (* $P < 0{\cdot}05$).

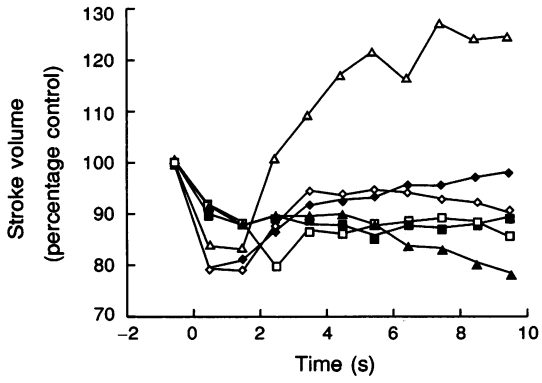

Fig. 2. LVSV expressed as a percentage of the value in the second immediately before a step change in MP of -15 cmH_2O; data are 1 s means for individual subjects.

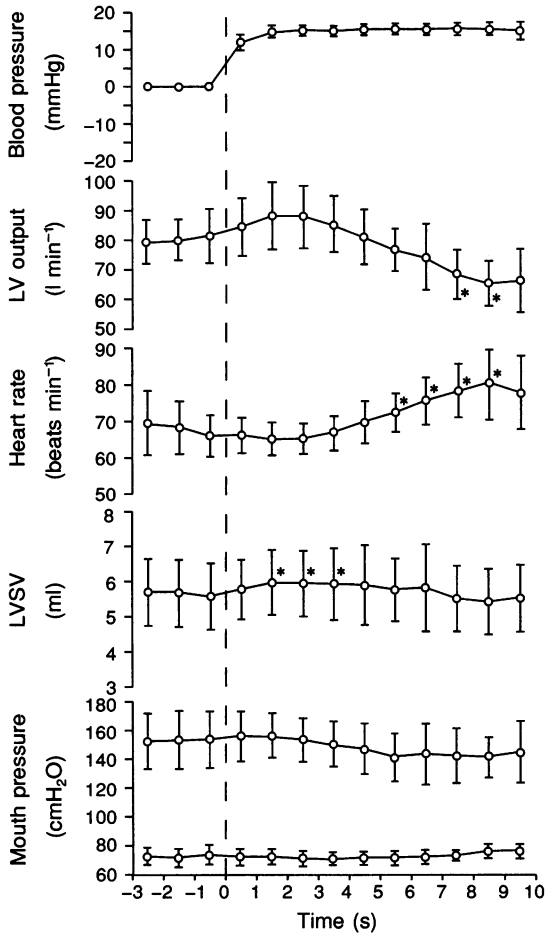

Fig. 3. Mean ± S.D. ($n = 7$) values each second for mouth pressure, left ventricular stroke volume, heart rate, left ventricular output and systolic and diastolic blood pressure ($n = 5$) during a step change in MP of +15 cmH_2O. Time 0 represents the time of onset of the step change in MP. *shows values which are significantly different from the data point immediately before the change in MP (* $P < 0{\cdot}05$).

Positive intrathoracic pressure

Following an abrupt increase in MP, there was a biphasic response in LVSV consisting of an immediate (but not statistically significant) increase in the first 2 s and a decrease thereafter, which became significant ($P < 0{\cdot}001$) in the seventh and eighth second. Mean results for the group are shown in Fig. 3. Heart rate did not change significantly until the sixth second, when it increased above the baseline value ($P < 0{\cdot}05$), and continued to increase in the next 3 s ($P < 0{\cdot}01$). Cardiac output increased immediately following the increase in MP, the increase becoming significant in the second, third and fourth seconds ($P < 0{\cdot}05$), and decreased back toward the baseline value thereafter. There was no significant change in systolic or diastolic blood pressure throughout the period of increased MP.

Again, the immediate relative change in LVSV following the pressure change was similar between subjects until around 4 s after the intervention, when the response became more variable (Fig. 4).

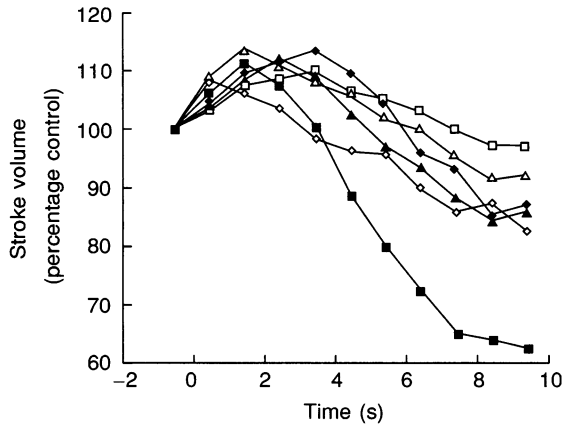

Fig. 4. LVSV expressed as a percentage of the value in the second immediately before a step change in MP of +15 cmH_2O; data are 1 s means for individual subjects.

DISCUSSION

Sudden inspiratory or expiratory efforts against a closed airway have immediate and opposite effects on left ventricular function. The observed immediate changes can be ascribed mainly to the effects of pressure, since lung volume changes during these manoeuvres will be small; the small leak used to ensure glottic patency allowed only 30 ml s^{-1} volume change during straining, and gas compression by 15 cmH_2O is of the order of 1–2 % at sea level. With sustained effort, the immediate cardiovascular changes are progressively compensated for by autoregulatory mechanisms. The magnitude of both immediate and secondary changes vary between subjects, although the time course is remarkably consistent.

Mechanism of action of intrathoracic pressure on the left ventricle

Negative pressure (Müller manoeuvre)

With obstructed inspiratory efforts there is an immediate and significant fall in LVSV and a simultaneous significant fall in systolic blood pressure. Both effects are transient, lasting only 3 s despite a sustained fall in intrathoracic pressure.

The immediate effects could be due to the reduced intrathoracic pressure impairing left ventricular ejection since it increases the pressure gradient up which blood must be ejected into the extrathoracic systemic circulation (LV after-load; Buda, Pinsky, Ingels, Daughters, Stinson & Alderman, 1979). This is not supported by the current data, however, which show that systolic blood pressure actually falls by more than intrathoracic pressure; thus LV after-load decreased rather than increased in the current study. This implies that left ventricular stroke volume falls because LV filling is impaired. Opdyke & Brecher (1950) and Scharf, Brown, Saunders & Green (1979) showed in dogs that during obstructed inspiratory efforts

the left atrial pressure fell significantly less than the pleural pressure, hence transmural left atrial pressure rose suggesting that there was indeed impairment of left ventricular filling, presumably due to reduced left ventricular compliance. The mechanism of this fall in compliance is disputed, but it may represent the effect of augmented right ventricular filling (due to enhanced systemic venous return) with displacement of the interventricular septum. Septal displacement has been observed using echocardiography in man by Brinker *et al.* (1980), and may be one mechanism contributing to ventricular interdependence (Santamore, Lynch, Meier, Heckman & Bove, 1976; Robotham, Lixfield, Holland, MacGregor, Bryan & Rabson, 1978). The resulting augmented right ventricular output may then contribute to the subsequent recovery of left ventricular output seen during sustained negative intrathoracic pressure.

These results, obtained during obstructed inspiratory effort, suggest that impaired LV filling may be one mechanism connecting the fall in IP seen with inspiration against narrowed airways to the accompanying fall in blood pressure; the clinical phenomenon of pulsus paradoxus.

Positive pressure (*Valsalva manoeuvre*)

A sudden increase in intrathoracic pressure resulted in an immediate, although statistically insignificant increase in LVSV, followed by secondary decreases in LVSV and systolic blood pressure and an increase in heart rate. The data of Opdyke & Brecher (1950) in dogs indicate that left atrial pressure rises slightly less than pleural pressure during obstructed expiratory efforts. This is compatible with the idea that LV compliance, and therefore filling, is transiently increased early during the Valsalva manoeuvre. Such a rise in LV compliance may result (through the mechanism of ventricular interdependence) from the reduced RV filling which occurs during expiratory straining.

In addition to the early effects of the Valsalva manoeuvre on LV filling, ejection from the left ventricle will be immediately assisted by the augmented pressure gradient between the chest and the extrathoracic space (Robotham *et al.* 1978; Jardin, Farcot, Gueret, Prost, Ozier & Bourdarias, 1983), causing a transient increase in LVSV.

The progressive fall in LVSV seen later during sustained expiratory straining probably results from the raised intrathoracic pressure impeding venous return to the right atrium and ventricle, reducing right heart output and progressively depleting the pulmonary circulation and therefore left atrial filling. As LVSV and blood pressure fall, heart rate rises, presumably triggered by the baroreflexes.

The time course and relative magnitude of the immediate changes in LVSV following changes in intrathoracic pressure showed a remarkable consistency between subjects, contrasting with the variability in LVSV changes during positive pressure ventilation and normal breathing observed in our previous studies (Innes *et al.* 1993). The combination of lung inflation and intrathoracic pressure changes may have a more complex effect on LVSV than pressure changes alone. Variability in LVSV responses during the latter part of the Valsalva and Müller manoeuvres points to variability in the compensatory baroreceptor mechanisms rather than in the direct effect of pressure changes on the heart.

In conclusion, these observations illustrate that the response of the left ventricle to changes in intrathoracic pressure are the result of a complex interaction between systemic venous return, right ventricular output and after-load, with the arterial baroreceptors acting to limit sudden changes in blood pressure.

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