The Effect of Deep Inspiration and Forced Expiration on Doppler Transmitral Flow, Cardiac Output

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Abstract
This study was carried out on 20 normal apparently healthy male volunteers, aged 18-36 years in order to study the effect of deep inspiration and forced expiration on mitral valve inflow, cardiac output, by using non-invasive techniques. Mercury sphygmomanometer for measuring the blood pressure (BP), Doppler echocardiography for estimating of stroke volume (SV), cardiac output (CO), velocity time integral (VTI), Mitral valve area (MVA), pressure half time (PHT), acceleration, deceleration time of passive atrial filling (E wave, acceleration time (T1), deceleration time (T2) and acceleration time (T3), deceleration time (T4) of atrial contraction, A wave.

The results: SV, CO, VTI were significantly higher and PHT significantly lower in baseline expiratory than inspiration. There were no significant changes in MBP, HR, T1, T2, T3 and T4.

Comparison between deep inspiration and forced expiration shows that the MBP, SV, CO, VTI, PHT and T1 were significantly higher during forced expiration than that of deep inspiration, where as there are no significant differences in HR, T2, T3 and T4.

Comparison between baseline quite breathing (inspiratory phase) and deep inspiration:
The results indicate that there were no significant changes in SV, CO, MBP, HR, VTI, PHT, T1, T2, T3 and T4 between baseline and deep inspiration. Comparison between control and forced expiration, shows no significant changes in SV, CO, HR, MBP, VTI, PHT, T1, T2, T3, and T4. The aim of the present research is first: to investigate the changes of mitral valve inflow and its effect on cardiac output during deep inspiration and forced expiration.

**Introduction:**

**DOPPLER ECHOCARDIOGRAPHIC ASSESSMENT OF TRANSMITRAL FLOW**

Many of the problems in the assessment of diastolic function in cardiac disease have been caused by its multifactorial nature and the lack of accurate methods for its assessment. Hi-fi pressure recording, angiography, radionuclide techniques and combined pressure–volume relationships have been used but these methods are invasive and cannot be used for repeated examinations (Stevenson, 1989).

Physical examination, electrocardiogram, and chest radiographs are unreliable in making the diagnosis of LV diastolic dysfunction in most individuals, and invasive measurement of cardiac pressure, rates of LV relaxation, and LV compliance are costly, clinically impracticable as they carry increased risk and require special catheter and software analysis programs (Appleton et. al., 2000).

Recent studies have validated Doppler flow and tissue velocity measurements for reliable and non invasive evaluation of LV filling dynamic and rational therapeutic strategies in patient presenting with disturbed transmitral flow manifested as signs and symptoms of heart failure (Bonow and Udelson 1992; Nishimura and Tajik 1997).

**DOPPLER ASSESSMENT OF TRANSMITRAL FLOW**

Normal transmitral Doppler flow velocity pattern

Doppler echocardiography provides a non invasive means to study LV diastolic function, by recording transmitral blood flow velocities versus time. These velocity waveforms are determined by the complex interplay of hemodynamics (instantaneous pressure differences) and several other factors including:

- Rate of relaxation
- Diastolic suction
- Ventricular interaction (RV overload)
- Viscoelasticity
- Elastic properties (Hypertrophy, fibrosis, scar and amyloid)
- Extent of relaxation
- Pericardium (Effusion, constriction)
- Coronary engorgement (reperfusion)

Transmitral PWD flow velocities are recorded within the apical four chamber or apical long axis views and several measurement can be used to define left ventricular filling hemodynamics. As the mitral valve is funnel-shaped, the velocities increase progressively across the mitral valve apparatus towards the outlet of the mitral funnel. For reasons of reproducibility, all transmitral PWD flow measurement should be made with the sample volume in the same position at the outlet of the mitral valve funnel.

Normal transmitral flow is laminar and relatively low in velocity (usually< 100 cm/sec). There is an early diastolic velocity caused by the continued myocardial relaxation resulting in a LV pressure below LA pressure that causes the mitral valve to open and rapid LV filling to occur (E wave).
E wave acceleration is directly determined by LA pressure and inversely related to myocardial relaxation (Roelandt and Pozzoli 2001). Viscoelastic properties and compliance of the myocardium then come into play, raising LV pressure and resulting in a decreased transmitral flow velocity. The rate of fall in velocity is represented by the deceleration time (DT) and is measure of how rapidly early diastolic filling stops. DT becomes shorter when LV compliance decreases (Ohno et. al., 1994). There is an inverse relationship between the mean LA pressure and DT. Inertia effects may cause continued forward low velocity flow during mid – diastole. The higher LA pressure during its contraction causes an increase in velocity (A wave) and is an important parameter of diastolic function. Commonly, the E/A ratio is used to assess LV diastolic function and its normal value is > 1 (Roelandt and Pozzoli 2001).

Material and Method:
Subjects:
This study was carried out on 20 apparently normal healthy male volunteers, with no symptoms of any diseases, in the private clinic of Dr. Akeel Zwain starting at November 2007 till October 2008.

Materials:
A. Echocardiography
The study is performed by using Siemens versa plus sonoline equipment with 2-4 MHz transducer, made in Germany. Transthoracic 2-D guided M-mode and Doppler echocardiography techniques are used.

B. Mercury sphygmomanometer and stethoscope
The sphygmomanometer is the standard and the most widely used non-invasive method used for recording arterial BP in the clinical practice (Tein et. al., 1982). The auscultatory method is the most popular method for BP measurement today (Simpson and Wicks, 1988) by using phase one of Korotkoff sound to point out the SBP and phase five for DBP reading (Hoffler and Robert, 2001).

Method:
A full clinical history and anthropometric data are taken prior to the test.
A. Study protocol
It consist of three phases:
Phase -1 (supine control state): The subject first placed in supine position for 5 minutes then measurements of blood pressure and heart rate are made after a control steady state (steady state: means that the heart rate is consecutive minute changing by less than 3 beat per minute) (AL –Shamma and Al-Zubaidy, 1999). Then echocardiographic examination is done during control phase to measure the MVA during mid-diastole, VTI, HR, SV, CO (CO=HR X SV), PHT, T1, T2, T3, and T4.
Phase -2 (supine – deep inspiration): during this phase measurements of blood pressure, heart rate during deep inspiration echocardiographic examination done to calculate the same variables.
Phase -3 (supine – deep expiration): during this phase also blood pressure and heart rate measure. echocardiographic technique used to evaluate same variables.
In all these three phases the blood pressure (SBP and DBP) is measured by standard cuff sphygmomanometer.
The mean arterial BP (MBP) is calculated as DBP plus one third of pulse pressure (difference between SBP and DBP) (Rushmer, 1976; Nixon et. al., 1982). The Doppler echocardiography is used to calculate, stroke volume (SV), velocity time integral (VTI), mitral valve area (MVA), flow velocity across mitral valve, and pressure half time (PHT).

B. Measurement of cardiac output:

The cross sectional area of the mitral valve is calculated at rest steady state with the subject in left lateral lying position by measuring the circular area using the cursor of the echo with 2-D echocardiography.

VTI is determined by integrating the peak velocity curve (from the flow through mitral valve) over time. Peak velocity curves is integrated by computerized software built in the echo equipment (Patrick et. al., 1985; Zwain, and Ismaeel,A. 2008).

So we use the following equations:

\[ SV = 0.785 \times D^2 \times VTI \]  (Fiegenbaum, 1972)
\[ CO = SV \times HR \]  (Ganong, 2005)

2.4. Statistical Analysis

The data were expressed as mean ±SD, paired t-test was used to determine:

(a) If there are differences in mitral valve flow during steady state, deep inspiration and forced expiration.

(b) If there are differences in the mitral valve inflow during deep inspiration and quite breathing.

(c) If there are differences in the mitral valve inflow during forced expiration and quite breathing.

The differences are considered significant if P< 0.05, all calculation, tables and graphs performed by Microsoft SPSS and Excel computerized programs (Lwanga et. al., 1999).

The Results:

1- Cardiovascular reflex responses to control inspiration and expiration and to deep inspiration and forced expiration in supine position

In comparison between baseline control of quite breathing inspiration and expiration, the result indicates that SV,CO,VTI are significantly higher and PHT significantly lower in control expiration than inspiration and there are no significant changes in MBP,HR,T1,T2,T3 and T4.

Comparison between deep inspiration and forced expiration shows that the MBP,SV,CO,VTI,PHT and T1 are significantly higher during forced expiration than that of deep inspiration, where as there are no significant differences in HR,T2,T3 and T4 as shown in Table 2Figures(1-10).
Table (1): Cardiovascular reflex responses to change from control quite breathing and responses to deep breathing: stroke volume (SV), cardiac output (CO) blood pressure (MBP), heart rate (HR), velocity time integral (VTI), pressure half time (PHT), T1: Acceleration time, T2: Deceleration time (passive atrial filling: E wave). T3: Acceleration time, T4: Deceleration time (Atrial contraction: A wave).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ±SD</th>
<th>Control inspiratory wave</th>
<th>Control expiratory wave</th>
<th>difference</th>
<th>P-value</th>
<th>Deep inspiration</th>
<th>Forced expiration</th>
<th>difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV (ml)</td>
<td>86.6±13.9</td>
<td>*103.1±16.0</td>
<td>16.4±10.6</td>
<td>&lt;0.05</td>
<td>78.3±15.1</td>
<td>*98.7±13.2</td>
<td>20.3±15.6</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>CO (L/m)</td>
<td>6.4±1.4</td>
<td>*7.6±1.6</td>
<td>0.7±1.2</td>
<td>&lt;0.05</td>
<td>5.6±1.1</td>
<td>*7.1±1.2</td>
<td>1.5±1.1</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>MBP (mm.Hg)</td>
<td>90.8±4.9</td>
<td>90.8±4.9</td>
<td>0</td>
<td>&gt;0.05</td>
<td>89±4.4</td>
<td>*93.9±4.1</td>
<td>-4.4±5.5</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>HR (Bpm)</td>
<td>74.1±9.6</td>
<td>74.1±9.6</td>
<td>0</td>
<td>&gt;0.05</td>
<td>71.6±7.0</td>
<td>72.1±8.2</td>
<td>0.6±5.6</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>VTI (cm)</td>
<td>11.3±1.7</td>
<td>*13.4±1.8</td>
<td>2.0±1.2</td>
<td>&lt;0.05</td>
<td>10.2±2.0</td>
<td>*12.8±1.6</td>
<td>2.5±2.0</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>PHT (cm)</td>
<td>4.1±0.8</td>
<td>*3.4±0.7</td>
<td>-0.5±0.6</td>
<td>&lt;0.05</td>
<td>3.4±0.7</td>
<td>*4.3±1.2</td>
<td>0.8±1.4</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>T1 (m/s)</td>
<td>85.8±16.4</td>
<td>85.5±11.7</td>
<td>2.1±6.6</td>
<td>&gt;0.05</td>
<td>81.5±12.9</td>
<td>*91.5±16.2</td>
<td>-9.9±17.6</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>T2 (m/s)</td>
<td>134.5±35.6</td>
<td>132.5±28.4</td>
<td>2.8±25.7</td>
<td>&gt;0.05</td>
<td>134.7±52.1</td>
<td>117.2±19.1</td>
<td>17.5±45.1</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>T3 (m/s)</td>
<td>52.5±12.1</td>
<td>54.3±12.1</td>
<td>-3.6±15.2</td>
<td>&gt;0.05</td>
<td>51.4±9.9</td>
<td>53.4±10.6</td>
<td>-2±14.6</td>
<td>&gt;0.05</td>
<td></td>
</tr>
<tr>
<td>T4 (m/s)</td>
<td>52.5±12.1</td>
<td>54.3±12.1</td>
<td>-3.6±15.2</td>
<td>&gt;0.05</td>
<td>51.4±9.9</td>
<td>53.4±10.6</td>
<td>-2±14.6</td>
<td>&gt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

*= significant
Figure (1): Stroke volume (SV) in control and deep inspiration and forced expiration.

Figure (2): Cardiac output (CO) in control and deep inspiration and forced expiration.
Figure (3): Mean blood pressure (MBP) in control and deep inspiration and forced expiration

Figure (4): Heart rate (HR) in control and deep inspiration and forced expiration
Figure (5): Velocity time integral (VTI) in control and deep inspiration and forced expiration.

Figure (6): Pressure half time (PHT) in control and deep inspiration and forced expiration.
Figure (7): Acceleration time of E wave (T1) in control and deep inspiration and forced expiration.

Figure (8): Deceleration time of E wave (T2) in control and deep inspiration and forced expiration.
Acceleration time (T3) of A wave

Figure (9): Acceleration time of A wave (T3) in control and deep inspiration and forced expiration.

Deceleration time (T4) of A wave

Figure (10): Deceleration time of A wave (T4) in control and deep inspiration and forced expiration.
Differences in cardiovascular reflex responses between control and deep inspiration and the difference between control and forced expiration at supine position.

Comparison between control and deep inspiration:
The results indicate that there are no significant changes in SV, MBP, HR, VTI, PHT, T1, T2, T3 and T4 between control and deep inspiration, only CO is lower in deep inspiration than that of base line control inspiration but not reach to significant level, comparison between control and forced expiration, shows no significant changes in all variables as shown in Table(3), figures(11-20).

Table(3): cardiovascular reflex responses as comparing control and deep inspiration and forced expiration

<table>
<thead>
<tr>
<th>Parameters</th>
<th>During inspiration</th>
<th>During expiration</th>
<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV(ml)</td>
<td>86.6±13.9</td>
<td>78.3±15.1</td>
<td>7.11±16.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>CO(L/m)</td>
<td>6.4±1.4</td>
<td>5.6±1.1</td>
<td>0.8±1.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MBP(mm.Hg)</td>
<td>90.8±4.9</td>
<td>89.7±4.4</td>
<td>1.3±4.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HR(Bpm)</td>
<td>74.1±9.4</td>
<td>71.6±7.0</td>
<td>2.5±5.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VTI(cm)</td>
<td>11.3±1.7</td>
<td>10.2±2.0</td>
<td>1.0±1.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PHT(cm)</td>
<td>3.6±0.6</td>
<td>3.4±0.7</td>
<td>0.2±0.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T1(m/s)</td>
<td>85.8±16.4</td>
<td>81.5±4.2</td>
<td>4.2±22.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T2(m/s)</td>
<td>134.5±35.6</td>
<td>134.7±52.1</td>
<td>-0.2±56.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T3(m/s)</td>
<td>54.3±12.1</td>
<td>51.4±10.1</td>
<td>1.1±13.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>T4(m/s)</td>
<td>54.3±12.1</td>
<td>51.4±10.1</td>
<td>1.1±13.3</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

SV = stroke volume, CO = cardiac output, MBP = mean blood pressure, HR = heart rate, VTI = velocity time integral, PHT = pressure half time, T1 = acceleration time of E wave, T2 = deceleration time of E wave, T3 = acceleration time of A wave, T4 = deceleration time of A wave.

SV = stroke volume, CO = cardiac output, MBP = mean blood pressure, HR = heart rate, VTI = velocity time integral, PHT = pressure half time, T1 = acceleration time of E wave, T2 = deceleration time of E wave, T3 = acceleration time of A wave, T4 = deceleration time of A wave.
Figure (11): Stroke volume (SV) in control (C) and deep (D) inspiration with control and forced expiration.

Figure (12): Cardiac output (CO) in control (C) and deep (D) inspiration with control and forced expiration.
Figure (13): Mean blood pressure (MBP) in control (C) and deep (D) inspiration with control and forced expiration.

Figure (14): Heart rate in control (C) and deep (D) inspiration with control and forced expiration.
Figure (15): Velocity time integral (VTI) in control (C) and deep (D) inspiration with control and forced expiration.

Figure (16): Pressure half time (PHT) in baseline control breathing (C) and deep (D) inspiration with baseline control breathing and forced expiration.
Figure (17): Acceleration time (T1) of the E wave in control (C) and deep (D) inspiration with control and forced expiration.

Figure (18): Deceleration time (T2) of the E wave in control (C) and deep (D) inspiration with control and forced expiration.
Figure (19): Acceleration time (T3) of the A wave in control (C) and deep (D) inspiration with control and forced expiration.

Figure (20): Deceleration time (T4) of the A wave in control (C) and deep (D) inspiration with control and forced expiration.
Discussion
I-1-Comparison between base line quite breathing (inspiratory and expiratory phase):

The results of this study shows that SV significantly higher in base line expiratory phase than base line inspiratory phase which is mostly because during inspiration more negative intrapulmonary pressure causing draining of blood into the right side of the heart and therefore the right cardiac output increases and the left decreases at early and mid inspiration. During late inspiration venous return continue to flow from the lung to the heart and there is increase in venous capacitance of pulmonary veins. (Guyton, 2006).

During deep inspiration there is increase blood passing to the right side of the heart through superior and inferior vena cava and due to increase intrathoracic negative pressure, so more blood passing to the lungs, Cardiac output restore to normal during late inspiration and then in forced expiration, venous return from the lung through pulmonary veins to the left side of the heart increase leading to increase blood flow through the mitral valve to the left ventricle. (Al Shamma and Ismael, 2008).

For the same reason cardiac output is also increased during expiration although HR shows no any significant changes in both control inspiratory phase and control expiratory phase, according to the equation:

\[ CO = SV \times HR \] (Guyton, 2006).

Mean blood pressure shows no significant changes in both base line inspiration and expiration since it is measured during the period of normal breathing.

VTI significantly higher in base line expiratory phase than base line inspiratory phase which is due to increased SV as show in the equation:

\[ SV = 0.785 \times D^2 \times VTI \] (Fiegunbaum’s, 1972).

There is a significant decrease in the pressure half time in control inspiration comparing with the control expiratory phase. (Peter Wild, 1990).

There are no significant difference in acceleration, deceleration time (passive ventricular filling, T1, T2), and acceleration, deceleration time (atrial contraction T3, T4) (John Chambers, 1995), but no studies to what happened to these variables in normal individuals responses to these maneuvers.

2-Comparison between forced inspiration and deep expiration:

Mean blood pressure is significantly increase during forced expiration than that of deep inspiration which is probably due to increase blood flow and pressure gradient through the mitral valve and the left ventricle (Otto, 2007).

Stroke volume and CO significantly increase during forced expiration than that of deep inspiration which is most likely due to the fact that during inspiration more negative intrathoracic pressure causes draining of blood into the right side of the heart as mentioned before, and therefore the right cardiac output increases and the left decreases at early and mid inspiration. During late inspiration venous return continue to flow from the lung to the heart. (Guyton, 2006). For the same reason, cardiac output also increases during expiration as more blood pass to the left side of the heart which is measured after 20 second because after that time more blood reach through the pulmonary veins to the left side of the heart may be more than its normal value (John Chambers, 1995).

Also there is significant increase in VTI during forced expiration than that of deep inspiration, probably due to increase stroke volume which is proportionate to the velocity time integral (Otto, 2007).
There is also a significant increase in acceleration time of passive filling (T1) during forced expiration than deep inspiration, whereas no significant changes in deceleration time (passive filling, T2) and acceleration, deceleration of atrial contraction (T3, T4), probably due increased amount of blood passing to the left atrium from the lungs during forced expiration (John Chambers, 1995).

3- Comparison between cardiovascular changes in control and deep inspiration:

There are changes in SV, HR but they are of no significance and since both are not change greatly, so CO also not change according to equation:

\[ CO = SV \times HR \]  

(Guyton, 2006).

Also there are no significant changes in MBP, PHT, VTI, acceleration, deceleration time of passive atrial filling (T1, T2) and acceleration, deceleration time of atrial contraction (T3, T4), (Peter Wilde, 1990; John Chambers, 1995).

All these variables change but not significantly probably due to that minor changes in variables between control and deep inspiration of nearly all volunteers during practical work of this study (Zwain, 2007).

4- Comparison between cardiovascular changes in base line breathing and forced expiration:

There are no significant changes in SV, CO, HR, MBP, VTI, PHT, T1, T2, T3, and T4. (Peter Wilde, 1990; John Chambers, 1995; Ganong, 2005).

References:

15- Roelandt JRTC, Pozzoli M(2001). Noninvasive assessment of left ventricular diastolic dysfunction and filling pressure. Home SVCC :Thorax centre,Erasmus university Medical centre, Rotterdam, The Netherlands ; Department of cardiology, A Mazoni Hospital , Lecco, Italy. article :12 pages.