On-line Supplement: Effect of Large Volume Infusion on Left Ventricular Volumes, Performance and Contractility Parameters in Normal Volunteers

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Running Title: Volume Infusion in Normal Volunteers

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Methods

Subjects. This study received Institutional Review Board (IRB) approval at Rush-Presbyterian-St. Luke’s Medical Center and at Northwestern University Medical Center. Thirty-two healthy males age 18-38 within 15% of ideal body weight (Metropolitan Life tables) volunteered and gave informed consent for this study. Complete history, physical exam, and electrocardiogram (ECG) performed within two weeks of the research study were unremarkable. Screening laboratory parameters were determined to be normal in all subjects before enrollment.

Protocol. On the day of the study, the subjects were admitted to the procedure room of the medical intensive care unit (MICU) after an overnight fast. Non-invasive assessment of hemodynamics was accomplished using echocardiography prior to saline infusion. Following baseline vitals and echocardiography, normal saline infusion was begun intravenously at a rate of one liter an hour for three hours, then decreased to 500 mL per hour for two hours. Repeat echocardiograms were performed three hours (after 3L saline infusion) and five hours (after 4 L saline infusion) after infusion initiation for comparison to baseline.

Recordings. Data acquisition was performed using a Hewlett Packard 5500 ultrasound imaging device. A 2.25 or 3.5 MHz transducer was used for echocardiographic, external carotid pulse and phonocardiographic recordings. Phonocardiograms were recorded from the right upper sternal border. All subjects were continuously monitored with ECG, automatic sphyngomanometry (Dynmap®), and pulse oximetry. The Dynmap® instrument has been previously documented to yield systolic, diastolic and mean blood pressures with a high degree of accuracy and reproducibility [1].

Measurements and Calculations. Standard echocardiographic views were obtained including parasternal long and short axis, apical four chamber views and Doppler outflow across the aortic
valve at each study time point. For each study, simultaneous recordings of left ventricular echocardiogram, phonocardiogram, carotid pulse tracings, electrocardiogram and systolic/diastolic blood pressure were made.

Stroke volume (SV) was determined using the measured left ventricular outflow (aortic valve) diameter from the parasternal long axis view and the Doppler-determined outflow tract velocity [2]. Cardiac output (CO) was calculated with this obtained SV multiplied by the simultaneous heart rate. The total peripheral resistance (TPR) was determined using this calculated CO and the measured mean arterial pressure (MAP) from the Dynamap® using the formula TPR (dyne/sec/cm⁻⁵) = (MAP)(79.9)/CO. The right atrial pressure (RAP) was omitted in this calculation because of the negligible effect that the RAP exerts on this calculation in these normal volunteers.

Left ventricular internal dimension (chamber diameter) and left ventricular posterior wall thickness were measured at end-diastole (defined as the Q wave of the electrocardiogram) and end-systole (defined as the first high frequency component of the aortic second heart sound) in five cardiac cycles. Left ventricular volumes were obtained by Simpson’s Rule (method of disks) utilizing the average of volumes from apical four and two chamber views at the same points [3]. From these, mean values were derived. Ejection fraction (EF) was obtained by subtracting end-systolic volume (ESV) from EDV and dividing by EDV. The left ventricular percent fractional shortening was calculated as end-diastolic dimension minus end-systolic dimension, divided by end-diastolic dimension. Left ventricular ejection time was measured from the simultaneous carotid pulse tracing and taken as the average of five beats. The ejection time was rate-corrected to a heart rate of 60 beats/min by dividing by the square root of the RR interval. The mean velocity of circumferential fiber shortening of the left ventricle was calculated and normalized to
the end-diastolic dimension by dividing fractional shortening by the ejection time. The rate-corrected velocity of shortening was calculated by dividing the fractional shortening by the rate-corrected ejection time.

The left ventricular end-systolic meridional wall stress (\(\Phi_{es}\)) was calculated as described by Grossman et al [4].

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\Phi_{es} = \frac{(1.35)(Pes)(Des)}{(4)(hes)[1 + (hes/Des)]}
\]

where \(\Phi_{es}\) is left ventricular wall stress (g/cm²), \(Pes\) is left ventricular pressure (mm Hg), \(Des\) is the left ventricular internal dimension (cm) and \(hes\) is the posterior wall thickness (cm), each at end-systole. In addition, 1.35 is a conversion factor (mm Hg to g/cm²) and 4 is a geometric factor that derives from conversion of radius to internal dimension.

The methodology of calibration of the carotid pulse tracings has been previously described [5]. Systolic and diastolic blood pressures were respectively assigned to the peak and trough of the trace of the carotid trace. Linear interpolation to the level of the incisura was performed to estimate the end-systolic pressure. Previous studies have demonstrated that the correlation co-efficient of this value to simultaneous central aortic values is approximately 97% with differences in values of only 3±4 mm Hg (mean ± standard deviation) [6].

Echocardiograms, phonocardiograms, and carotid pulse tracings were read by a single, highly experienced echocardiographer blinded to the subject and study sequence. Previous studies have demonstrated that mean changes of greater than 2% in EDV, 5% in ESV and 2% in EF in groups of subjects of comparable size to this study represent clinically significant alterations [7]. Accuracy of ventricular volumes was internally validated by comparing stroke
volumes derived from integration of the flow velocity across the aortic valve and subtraction of the end-systolic volume from the end-diastolic volume.

**Blood Viscosity.** In a separate group of 10 healthy subjects, blood samples were drawn into heparinized tubes and assessed for viscosity at baseline and 10%, 20% and 30% dilution with normal saline. All subjects fasted for a minimum of 12 hours. Blood was drawn from healthy non-smoking subjects who were seated for a minimum of five minutes. A tourniquet was applied lightly and for less than one minute. Blood viscosity samples were made within 60 minutes following venipuncture. Blood viscosity measurements were performed at 37°C with the Contraves LS-40 microviscometer and a DIN 412 measuring cup (Mettler-Toledo AG; Greifensee, Switzerland) [8]. Measurements were acquired during 3.45 minutes. The viscosity measurements are reported at shear rates of 100, 10, 1 and 0.1 s⁻¹. The batch coefficients of variation for blood viscosity measurements acquired at 100 s⁻¹ and 0.05 s⁻¹ are 2.3% and 7.9%, respectively. Viscosity measured under different shear conditions at various dilutions was compared as a percentage change to that at baseline (predilution) conditions.
<table>
<thead>
<tr>
<th>Blood dilution</th>
<th>Shear rate 100 s⁻¹</th>
<th>Shear rate 10 s⁻¹</th>
<th>Shear rate 1 s⁻¹</th>
<th>Shear rate 0.1 s⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>-20.7 ± 1.2 %</td>
<td>-28.6 ± 1.7 %</td>
<td>-40.5 ± 1.8 %</td>
<td>-50.6 ± 2.6 %</td>
</tr>
<tr>
<td>20%</td>
<td>-31.7 ± 1.0 %</td>
<td>-42.4 ± 1.5 %</td>
<td>-58.7 ± 1.4 %</td>
<td>-67.7 ± 1.6 %</td>
</tr>
<tr>
<td>30%</td>
<td>-42.8 ± 1.0 %</td>
<td>-56.8 ± 1.0 %</td>
<td>-76.2 ± 0.9 %</td>
<td>-84.2 ± 1.1 %</td>
</tr>
</tbody>
</table>

Mean decrease (± standard error of the mean) of blood viscosity at indicated degree of hemodilution and shear rate (in-vitro)
Reference List


