Increased Diastolic Pressure Gradients are Measured During Dobutamine Stress Tests

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Introduction: Recently, there has been considerable interest in intraventricular pressure gradients (IVPGs) as a measure of diastolic function[1-7]. Early diastolic filling is driven by a positive pressure gradient between the left atrium and left ventricle, generated largely by the rapid relaxation of the left ventricle. These gradients are thought to be a measure of the ability of the ventricle to facilitate its filling using diastolic suction, which is a consequence of the elastic recoil of the left ventricle during the isovolumic relaxation period[1,2]. Preload, from the left atrium, is also a determinant of the filling IVPGs[3]. Diastolic IVPGs, estimated using color M-mode Doppler ultrasound, have been shown to be associated with the capacity for enhanced performance during exercise[4] and increased values are predictive of exercise capacity in heart failure patients[5]. As an alternative to exercise, dobutamine is commonly used in stress-MRI and stress-echo studies of systolic function, but diastolic function is rarely considered. We examine the change in early diastolic IVPGs with dobutamine stress in order assess changes in ventricular suction and preload from resting levels using this standard pharmacologic stress protocol. The feasibility of measuring diastolic IVPGs during dobutamine stress with phase-contrast MRI is illustrated, and significantly increased values are reported.

Methods: IVPGs are related to blood velocities by Euler's equation. The pressure gradient ($^{dP}/_{dx}$) is equal to the sum of inertial ($\rho\cdot{}^{dv}/_{dt}$) and convective ($\rho\cdot v\cdot{}^{dv}/_{dt}$) components (ρ=density, v=velocity, t=time). Pressure gradients are usually integrated over space to yield pressure differences (ΔP) between key points. In this study, ΔP values are measured at rest and peak dobutamine stress between two sets of points. ΔP between the top of the left atrium and the apex of the left ventricle (LA-LV) represents the entire left heart, and ΔP between the tips of the mitral leaflets and the apex of the ventricle (LV) represents the left ventricle only (Figure 1). Previous studies have considered only the LV gradients[1-7]. Sample integration paths and pressure difference time curves are shown in Figure 1a and 1b. We limited our analysis to the peak positive ΔP of the E-wave, similar to these previous studies.

MRI experiments were performed using a Siemens Sonata 1.5T MRI scanner. Phase contrast images were acquired in the four-chamber view (Figure 1), similar to the long axis view used in previous Doppler studies. Pulse sequence parameters: 128 x (60-96) matrix, TE/TR = 3.0/5.0 ms, 12° flip angle, 6 mm slice, 2 in-plane velocity directions, V_{enc} = 100 cm/s, GRAPPA (R = 2), with retrospective gating. Breath-hold durations were ~15 seconds for a temporal resolution of 30 to 40 ms at resting heart rates and 15 to 20 ms at peak heart rates. A total of 8 subjects sets were studied, all with normal resting ejection fractions (>50%). The peak dose of dobutamine was 40mcg/kg/min.

Results: Resting heart rates of volunteers range from 58 to 77 bpm, with similar filling pressure gradients. Heart rates at peak stress range from 103 to 160 bpm. Peak LV ΔP values and LA-LV ΔP values are shown in Figure 2 as a function of heart rate. As expected, ΔP values increase with the administration of dobutamine. ΔP values are significantly larger when the atrium in included in the measurement ($p < 0.001$). For both measurement approaches, increased heart rates are associated with larger filling gradients, with moderate linear correlations.

Conclusion: Changes in filling pressure gradients can be measured at peak dobutamine stress levels in a single breath-hold. Larger pressure gradients are associated with higher heart rates, with a moderate linear correlation. It is still unclear where in space the gradients should be evaluated to best represent diastolic function, for this or any application, but including the atrium significantly increases the total pressure gradient. Dobutamine stress is distinct from exercise stress in that pre-load does not significantly increase in the former. It was observed that end-diastolic and end-systolic volumes were reduced at peak stress compared to rest in all subjects (EDV reduced 35±16 ml from rest to stress), indicating that increased ΔP is most likely due to increased ventricular suction as opposed to increased pre-load.

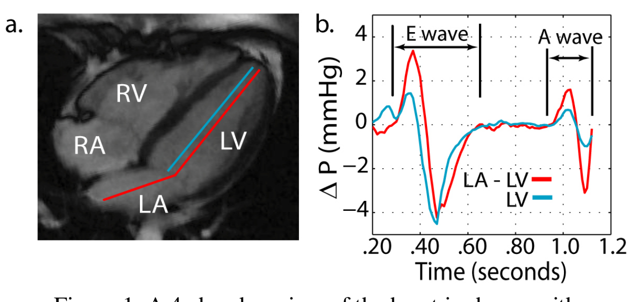

Figure 1. A 4 chamber view of the heart is shown with the locations of LA-LV and LV paths (a). Resulting ΔP plots are also shown (b).

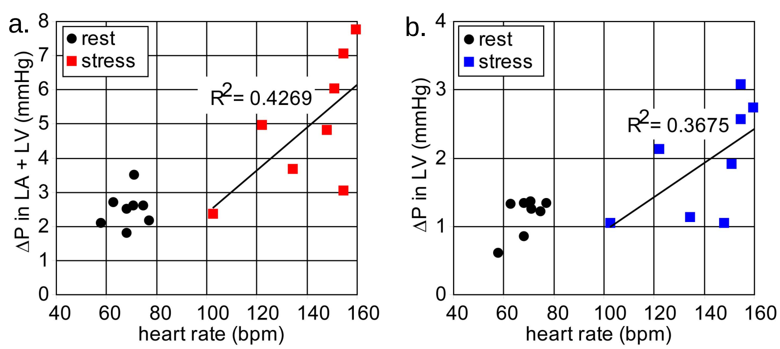

Figure 2. Maximum LA-LV (a) and LV (b) ΔP values are plotted at rest and stress as a function of heart rate.

References:
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