

Pressure gradient wave propagation in the left atrium and left ventricle during early diastole

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Introduction: Diastolic dysfunction (impaired relaxation and filling of the left ventricle) is the cause of 50% of heart failure cases¹ and likely a contributing factor in all cases. Existing indices of diastolic function, such as blood and tissue velocities, are generally indirect and have unknown relationships to the physical mechanisms governing filling. Intracardiac pressure gradients are an appealing measure of diastolic function because they provide a direct assessment of the forces responsible for driving blood flow. Pressure gradients have recently been reported in the form of the peak pressure difference (ΔP = the integrated pressure gradient) measured following mitral valve opening over the full length of the left ventricle (LV) in several clinical studies²⁻⁴. This single value collapses the spatially and temporally varying pressure gradient field into a single value (ΔP_{peak}), and neglects the left atrium (LA) which is an important contributor to filling, particularly if the ventricular contribution to filling is impaired.

Purpose: To characterize pressure gradients throughout the LA and LV during early filling. It will be shown that pressure gradients present as waves that originate at the mitral annulus and propagate in opposite directions into both the LA and LV. Pressure gradient waves have not previously been observed or measured in the filling heart.

Methods: Pressure gradients (dP/dx) can be calculated from blood velocity data using the Euler equation: $dP/dx = -\rho(\partial v/\partial t + v \cdot \partial v/\partial x)$, x = distance, ρ = density, v = velocity, t = time, which consists of inertial ($\partial v/\partial t$) and convective ($v \cdot \partial v/\partial x$) terms. Evaluation of this equation along a line that spans the left atrium and ventricle (Fig. 1) yields a spatiotemporal representation of dP/dx (Fig. 2) that allows the space-time analysis required to characterize wave properties. Here, we measure pressure gradient wave speeds, amplitudes, and directions in the LA and LV in addition to the conventional ΔP_{peak} in the LA, LV, and the entire left heart.

In 7 healthy volunteers blood velocity data was acquired using phase contrast MRI. In-plane velocities were acquired during separate breath-holds in the 4-chamber slice orientation (Siemens Sonata 1.5T scanner, Erlangen, Germany). Pulse sequence parameters are: matrix = $128 \times (60-90)$, slice thickness = 6 mm, TE/TR = 3.0/5.0 ms, flip angle = 12° , GRAPPA R = 2, V_{enc} = 100 cm/s, with retrospective gating. Temporal resolution is approximately 30 ms, interpolated to 10 ms for all analyses.

Results: A negative pressure gradient wave is observed first near the mitral annulus following mitral valve opening and later in time at points into the LA and LV (Fig. 1). Similar spatial and temporal pressure gradient fields are observed in all subjects. In the LA, both the inertial and convective terms are negative and in the ventricle, the inertial term is negative and the convective term is positive yielding a larger amplitude wave in the atrium than in the ventricle. Measured parameters:

- Wave speed: 46.0 ± 6.8 cm/s (LA), 61.1 ± 9.4 cm/s (LV)
- Wave amplitude: -85.8 ± 17.2 mmHg/m (LA), -27.9 ± 6.0 mmHg/m (LV)
- ΔP_{peak} : -2.91 ± 0.56 mmHg (LA), -1.55 ± 0.51 mmHg (LV), -4.13 ± 0.89 mmHg (LA+LV)

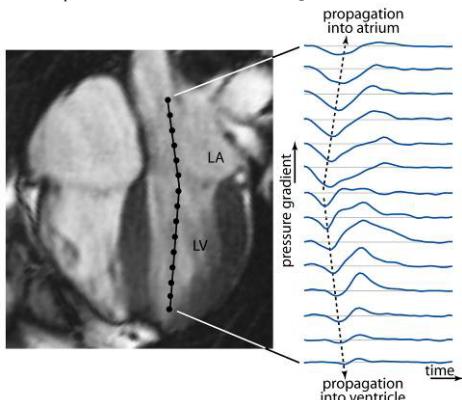


Fig. 1: The time course of pressure gradients (following mitral valve opening) is shown at evenly spaced points in the left atrium and ventricle, showing wave propagation.

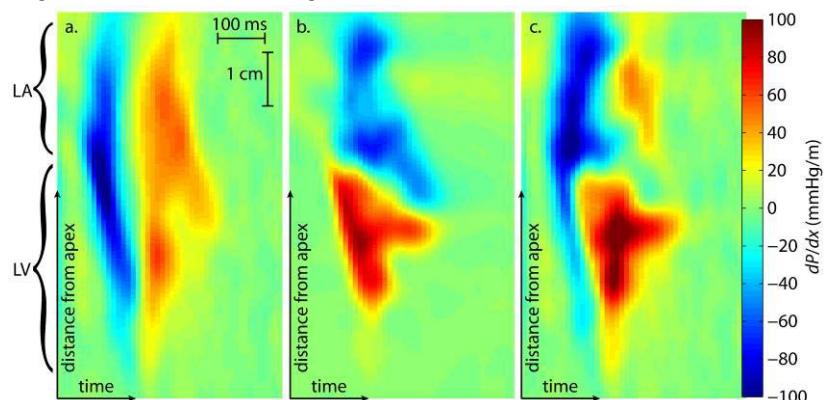


Fig. 2: The inertial (a), convective (b) and total pressure gradient (c) calculated along the line indicated in Fig. 1 is displayed.

Conclusions: We have shown, for the first time, that pressure gradients present as waves in the left heart during early filling, with readily measurable amplitudes and speeds. The forward ventricular wave is likely the source of the commonly observed flow propagation, which is a sensitive and load-independent marker of ventricular relaxation and stiffness⁵. We expect that pressure gradients, because of their more direct link to forces that drive blood flow, will ultimately provide new insight into the mechanisms of normal and abnormal diastolic function, with the potential to differentiate the distinct contributions from the ventricle and atrium.

References: 1. Paulus WJ, et al. *Eur Heart J*, 2007. 28(20):2539-50. 2. Greenberg NL, et al. *Am J Physiol Heart Circ Physiol*, 2001. 280(6):H2507-15. 3. Fristenberg MS, et al. *Circ*, 2001. 104(12 Suppl 1):I330-5. 4. Popovic ZB, et al. *Am J Physiol Heart Circ Physiol*, 2006. 290(4):H14154-9. 5. Brun P, et al. *J Am Coll Cardiol*, 1992. 20(2):420-32.