# Ischemic Mitral Regurgitation Contributes to Alterations in Left Ventricular Three-Dimensional Intracardiac Flow Patterns

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## Introduction

Intracardiac blood flow is a complex process as blood transitions from filling during diastole to ejection during systole within a matter of milliseconds. In the healthy heart, observation of left ventricular (LV) vortex ring formation during diastolic filling has been thought to contribute to the energy-preserving efficiency of blood volume ejection, however, this process is believed to be compromised in certain pathologies. (1,2) Vortex rings have previously been described in a number of in vitro and in vivo fluid dynamic studies, but quantification of complex three-dimensional (3D) intraccardiac flow patterns and application of these measurements to pathologic clinical conditions have been limited. (2, 3) In this study, we assessed vortex ring formation in post-infarction animals with the development of ischemic mitral regurgitation (IMR), and quantified 3D blood flow patterns of the LV.

## Methods

*Animal Model.* 10 Yorkshire swine weighing approximately 50 kg were used in this study approved by the Institutional Animal Care and Use Committee at the University of Pennsylvania. Using a well established model of IMR, five animals were subjected to a posterolateral myocardial infarction (MI) using direct coronary ligation, involving 20% of the LV including the posterior papillary muscle. Eight weeks following surgically-induced MI, a pressure transducer (Millar Instruments, Houston TX) was guided into the left ventricle for cardiac gating and the animal was transported to an MRI scanner where cardiac imaging was performed. Five additional naïve animals underwent identical imaging protocols to serve as controls.

*In Vivo MRI.* 4D time-resolved, flow sensitive MRI imaging, 3D MRI cine imaging and 2D phase contrast, high temporal resolution imaging of the mitral valve, left ventricle and aortic outflow tract were acquired on all 10 animals. The 4D flow pulse sequence parameters used for acquisition were as follows: Venc = 75 cm/s, spatial resolution = 2 x 2 x 2 mm and temporal resolution = 20.8 ms. Cardiac pressure tracings were collected at the time of imaging.

*Flow Analysis.* Net aortic and mitral transvalvular flows, including regurgitant volume fraction, were determined using the Argus method. End diastolic and end systolic 3D volumes were calculated from cine reconstructions. Sphericity index (SI) was calculated using the following equation: $LVESV/[(4/3 \times \pi \times ((D/2)^3)]$, where LVESV is the end systolic 3D volume and D is the long axis diameter of the left ventricle from the apex to annular plane. Left ventricular vortex ring formation was quantified using a 4D flow peak curl assessment.

## Results

Average net flow through the aortic valve was equal to average net flow through the mitral valve in both cohorts. Regurgitant fraction was 10.2 ± 5.2% in the ischemic group. End diastolic volumes for the ischemic group (compared to controls) were 133.9 ± 22.0 ml (65.8 ± 26 ml, P=0.001) Similarly, end systolic volumes increased for the ischemic group 94.4 ± 16.8 ml (33.1 ± 13.9 ml, P<0.001). Ejection fraction decreased from 51.3 ± 8.9% at baseline to 29.6 ± 5.4% (P=0.003) with the development of IMR. SI for control animals was 0.11 ± 0.01 whereas the SI increased for the ischemic animals to 0.24 ± 0.02 (P<0.001). Vortex flow formation was symmetric under the anterior and posterior leaflets in the control group with an average peak curl of 0.061 ± 0.007 1/sec. In contrast, diastolic ventricular vortex formation in the ischemic cohort demonstrated a marked asymmetry with larger vortices under the anterior leaflet relative to the posterior leaflet and average peak curl of 0.048 ± 0.004 1/sec (P<0.05).

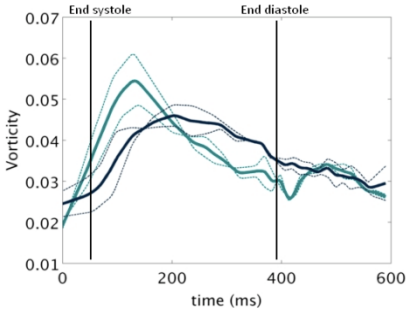


Figure 1. Average vortex curl (solid lines) vs time curve for baseline (green) and ischemic (dark blue) animals. SD= dotted lines.

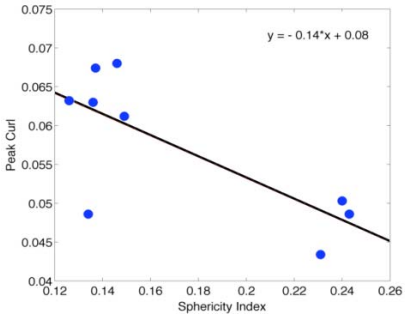


Figure 2. Correlation between sphericity index and peak curl depicting that as the LV dilates and becomes more spherical in shape, the peak curl of the vortex rings decreases.

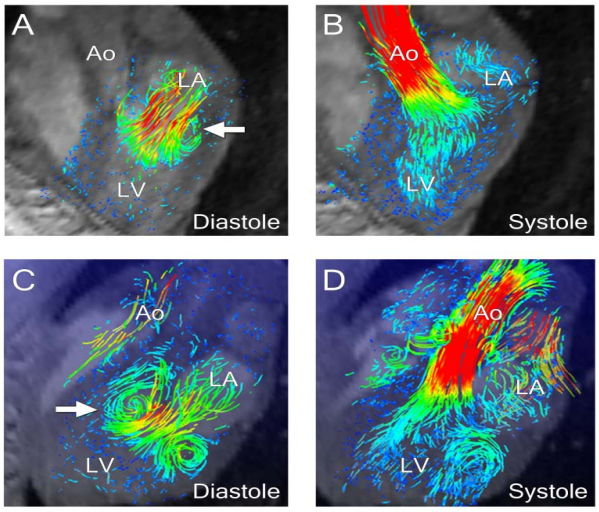


Figure 3. Normal diastolic LV vortex formation showing symmetric and tight vortex rings. (Panel A, white arrow) Normal systolic ejection in a healthy heart. (Panel B) Diastolic filling in IMR showing the formation of a large anterior vortex ring (white arrow) which is symmetrically different from the posterior vortex. (Panel C) Systolic ejection in IMR. (Panel D)

## Discussion

Animals with IMR demonstrate asymmetric vortex ring formation with the anterior vortex being less tightly curled, and thus of slower velocity, relative to its posterior counterpart. In contrast, normal ventricles create symmetric and tightly curled vortices in the basal chamber just underneath the mitral leaflets which conserve kinetic energy and aid in effective ejection. Asymmetric vortex ring formation correlated with an increase in SI, which suggests that as the left ventricle dilates and remodels in IMR, the resultant alterations in 4D blood flow patterns lead to abnormal vortex ring formation. These findings are important in understanding how blood is transferred through the heart in dilated ischemic cardiomyopathy, and may help explain the decrease in forward flow in this pathology. Moreover, quantification of such parameters is essential for determining the impact with which fluid dynamics has on left ventricular residual volumes and mitral annular and leaflet dynamics. Finally, this is the first step in determining whether optimization and/or restoration of normal flow patterns via therapeutic intervention with assist devices, mechanical valves or undersized annuloplasty rings aids in improving cardiac physiology in this condition.

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**References:** (1) Gharib, et al. PNAS (2006); 103: 6305-08. (2) Carlhäll, et al. Circ Heart Fail. (2010); 3:326-31. (3) Barker, et al. Magn Reson Med. (2011); May Epub ahead of print.