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The Influence of Mitral Annuloplasty on Left Ventricular Flow Dynamics

Walter RT Witschey, PhD^{#1}, Donald Zhang^{#2}, Francisco Contijoch, MS², Jeremy R McGarvey, MD², Madonna Lee, MD², Satoshi Takebayashi, MD², Chikashi Aoki, MD², Yuchi Han, MD, MMSc³, Joyce Han, BA³, Alex J. Barker, PhD⁴, James J Pilla, PhD¹, Robert C Gorman, MD², and Joseph H Gorman III, MD²

¹Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA

²Gorman Cardiovascular Research Group, University of Pennsylvania, Philadelphia, PA, USA

³Cardiovascular Division, University of Pennsylvania, Philadelphia, PA, USA

⁴Northwestern University, Chicago, IL, USA

[#] These authors contributed equally to this work.

Abstract

Background—Mitral valve (MV) repair using annuloplasty rings is the preferred method of treatment for MV regurgitation, but the impact of annuloplasty ring placement on LV intraventricular flow has not been studied.

Methods—Annuloplasty rings of varying sizes were placed in 5 healthy sheep (intercommissural ring size = 24, 26, 28, 30, and 32 mm) and 3D phase-contrast MRI (“4D flow MRI”) was performed prior to and one week after ring placement. Normal diastolic flow consisted of diastolic intraventricular vortices that naturally unwound during systole.

Results—Post-surgical intraventricular flow was highly disturbed in all sheep and the disturbance was greatest for undersized rings. Ring size was highly correlated with the diastolic inflow angle (Pearson’s $r = -0.62$, $P < 0.1$, CI (95%) = $[-0.92 \ 0.14]$). There was a mean angle increase of mean diastolic inflow angle increase = 12.3° (< 30 mm, $P < 0.01$, CI (95%) = $[4.8^\circ, 19.6^\circ]$) for rings < 30 mm. There was an inverse relationship between peak velocity and annuloplasty ring area (Pearson’s $r = -0.80$, $P < 0.05$, CI (95%) = $[-0.96 \ -0.2]$). Transmitral pressure gradients increased significantly from baseline 0.73 ± 0.18 mmHg to post-annuloplasty 2.31 ± 1.04 mmHg ($P < 0.05$).

Conclusions—MV annuloplasty ring placement disturbs normal LV intraventricular flow patterns and the degree of disturbance is closely associated with annuloplasty ring size.

Address for Correspondence: Walter RT Witschey, PhD Department of Radiology Perelman School of Medicine University of Pennsylvania 1 Silverstein 3400 Spruce Street Philadelphia, PA, USA 19104 Tel: +1 215-662-2310 Fax +1 215-746-2375 witschey@mail.med.upenn.edu.

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Keywords

mitral valve disease; valvular disease; 4d flow; phase contrast MRI; mitral valve repair; annuloplasty; left ventricular flow; hemodynamics

Introduction

Mitral valve (MV) repair is currently the preferred method of treatment for most cases of MV regurgitation, independent of etiology¹. This preference is based on the enhanced event-free survival and improved left ventricular (LV) function associated with valve repair relative to valve replacement. In addition to various leaflet and subvalvular techniques, current MV repair procedures almost uniformly employ the placement of annuloplasty rings to restore normal annular geometry. The goal of all repair procedures is to normalize valve geometry and function.

Although the effect of annuloplasty ring placement on MV function has received extensive study by our group and others, little data exists on the effect of ring annuloplasty on LV blood flow dynamics. *In vitro* and *in vivo* studies demonstrate that intraventricular flow patterns are complex², particularly during diastole when vortices develop. These vortices may be important energetically^{3–5} and may influence both LV and MV function. Therefore assessment of LV flow patterns may be helpful in assessing the efficacy of MV repair techniques and annuloplasty ring designs.

This study was designed to determine the effect of annuloplasty ring placement on normal ventricular flow in healthy sheep using time-resolved 3D phase contrast magnetic resonance imaging (4D Flow MRI)⁶. We hypothesized that mitral annuloplasty surgery alters intraventricular flow dynamics. This study could provide insight into the effectiveness of MV annuloplasty and reveal informative details regarding the impact of ring size on the resulting flow patterns after surgery.

Material and Methods

Mitral Valve Annuloplasty Ring Placement

Animals were treated under an experimental protocol in compliance with National Institutes of Health's "Guide for the Care and Use of Laboratory Animals" (NIH publication 85-23, revised 1996) and approved by the University of Pennsylvania Institutional Animal Care and Use Committee. Healthy Dorset sheep (N = 5, mean weight = 62.6 ± 21.6 kg) were sedated, intubated and anesthesia was maintained with a mixture of isoflurane throughout the procedure. Central arterial access was obtained surgically via the left carotid artery for LV blood pressure monitoring.

After a baseline MRI scan, each sheep underwent placement of a MV annuloplasty ring. Each animal received a different sized ring: Carpentier-Edwards Physio (Edwards Lifesciences; Irvine, CA) 24, 26, 28, 30, and 32 mm. Normal intercommissural distance for sheep of the size used in this study is 32 mm. Devices less than 32 mm were considered undersized in this model.

Magnetic Resonance Imaging

Each animal underwent a baseline and, after MV annuloplasty ring placement, a follow-up MRI one week later. Images were acquired using a 3 T whole-body MRI system (Tim Trio; Siemens Healthcare; Erlangen, Germany). Cardiac gating was performed using a pressure transducer (5F, Mikrotip; Millar Instruments, Houston, TX) positioned in the LV under fluoroscopy (Siemens).

Cine MRI was obtained in the short axis, 2, 3 and 4 chamber views, using a 2D retrospectively-gated balanced steady-state free-precession acquisition with the following imaging parameters, TE = 1.2 ms, TR = 2.4 ms, matrix = 192 × 156, FOV = 260-340 × 260-340 mm², BW = 1184 Hz/pixel, segments = 7, temporal resolution = 20 ms, cardiac phases = 30, slice thickness = 4 mm and no gap between slices.

4D flow MRI was performed with a dual cardiac and respiratory prospectively-gated cine phase-contrast MRI sequence with the following parameters: temporal resolution = 20.8 ms, spatial resolution = 2 × 2 × 2 mm³, flip angle = 8°, field of view = 320 mm × 320 mm, pixel bandwidth 460 Hz/pixel. The velocity encoding (V_{enc}) sensitivity was adjusted for each animal to minimize velocity aliasing during diastole ($V_{enc} = 75\text{--}185$ cm/s).

Image Analysis

LV function measurements were computed from 2D multislice short axis cine MRI (QMass, Medis; Netherlands). End-systolic and diastolic volume (ESV, EDV) contouring was performed by detailed manual tracing of the endocardial border in cine images. ESV and EDV were selected as the cardiac phase with the smallest and largest volume. Ejection fraction (EF) was calculated as the stroke volume 100% × (SV = EDV-ESV) divided by the EDV.

The 4D flow MRI data was spatially filtered with a 2D 3×3 median filter kernel to reduce image noise and the background phase from induced eddy-currents and regions of phase aliasing were restored (MatLab, The MathWorks, Natick, MA)⁷.

Analysis of the 4D flow data was performed in a fluid dynamics software package (Ensign, CEI, Apex, NC). Pathlines were computed inside a square volume containing both the LV and left atrium (LA) at all cardiac phases. The location of the vena contracta was identified as the narrowest region of the diastolic inflow jet, as determined from the pathline data. A circular plane S was manually placed at the vena contracta perpendicular to the diastolic flow at peak diastole (Figure 1a). The average velocity of the inflow jet was calculated at each time point,

$$\bar{v} = \frac{\int_S (\mathbf{v} \cdot \mathbf{n}) dA}{A},$$

where the integral is over the surface S with infinitesimal area dA , $\mathbf{v}$ is the velocity vector, $\mathbf{n}$ is the unit normal vector to the surface, and A is the area of the surface S . Peak mean velocity was defined as the maximum value of $\bar{v}_{avg}$ during the cardiac cycle. Transmittal

pressure gradients were calculated using the simplified Bernoulli equation ($P = 4v^2$) at the vena contracta. The inflow jet angle α was measured and defined as the angle between two lines: one line intersecting the MV coaptation point and the vena contracta, and the other line intersecting the coaptation point and the LV apex (Figure 1b).

Statistical Analysis

Measured statistics are reported as mean $\pm$ standard deviation. Differences between baseline and post-surgical diastolic inflow angle were assessed using a paired Student's t-test. $P < 0.05$ were considered statistically significant. The relationship between peak velocity and annuloplasty ring area was determined using a linear regression analysis and correlation reported as Pearson's coefficient with 95% confidence intervals (CI).

Results

LV Function

LV function parameters were computed from cine MRI for all animals. There were no significant differences between baseline and 1 week post-surgical ESV, EDV or EF or other measurements of LV function (paired t-test, $P > 0.05$). All LV function parameters at baseline and post-surgical MRI are shown in Table 1.

Qualitative Description of Baseline and Post-Surgical LV Flow Dynamics

As seen from a 3-chamber long-axis view, transmitral blood flow in naïve sheep is characterized by the formation of two vortices distal to and behind the anterior and posterior MV leaflets in early diastole (Fig. 2a). These vortices are counter-rotating and roughly equal in size. Between the vortices, a central column of fluid is directed towards the LV apex. At late diastole (Fig. 2b), the blood velocity decreased and vortex intensity decreased. At systole (Fig. 2c), the blood was transported across the LV outflow tract (LVOT), exhibiting a natural unwinding of the LV vortex. This flow pattern was highly conserved among all the baseline studies and consistent with previous reports.

Post-surgical LV flow dynamics were highly abnormal (Fig. 2, **bottom row**) and dependent on annuloplasty size. LV flow dynamics of the smallest ring used in the study (24 mm Physio) were characterized by the formation of a single, large posterior vortex early in diastole (Fig. 2d). The anterior vortex was absent. The lone posterior vortex continues to circulate through late diastole until the beginning of systole, when the blood flows from the vortex into the LVOT. The inflow jet was also redirected towards the septum.

Moderately sized rings had varied, but generally less dramatic, alterations on LV flow dynamics. The flow dynamics of a 26 mm Physio ring is shown in Fig. 3. For the 26 mm Physio ring (Fig. 3d-f), diastolic inflow was redirected towards the septum and resulted in a large vortex that rotated counterclockwise, with respect to a 3-chamber view. The vortex was sustained through late diastole and was redirected towards the LVOT at early-systole. However, this vortex did not occupy the entire ventricle as it did for the 24 mm Physio (**cf.** Fig. 2e **and** 3e, notice differences at the apex). Other vortices were observed, including

several at early-diastole that resembled the early anterior and posterior vortices in normal animals.

30 and 32 mm rings resulted in flow dynamics that were abnormal but were closer to baseline than the smaller rings. For the 32 mm Physio, the largest ring used in the study, the physiological vortices form during early diastole (Fig. 4d) but two additional, non-physiological vortices form during late diastole (Fig. 4e). Both pairs of vortices were counter-rotating, but with the opposite orientation as expected.

For the 28 and 30 mm Physio rings, LV flow dynamics were moderately abnormal, containing features observed in both the smaller 26 and larger 32 mm rings.

Effects of Mitral Valve Annuloplasty Ring Placement on Diastolic Inflow Angle

Redirection of normal diastolic LV inflow was quantified by measuring the difference in inflow angle between baseline and post-annuloplasty MRI at peak diastolic flow rate. Flow angle and peak velocity data are shown for all animals in Table 2. Overall, the inflow jet was reoriented clockwise towards the anterior leaflet and septum with an inverse correlation between ring area and the change in inflow angle post-repair (Pearson's $r = -0.62$, $P < 0.1$, CI (95%) = $[-0.92, 0.14]$, Fig. 5a). While the flow redirection was considerable for undersized rings (< 30 mm, $P < 0.01$, mean angle increase = 12.3° , CI (95%) = $[4.8^\circ, 19.6^\circ]$), it was varied for larger annuloplasty rings (≥ 30 mm). The smallest undersized ring had the most adverse effect on inflow angle, resulting in a 14.2° increases for the 24 mm Physio ring.

Effects of Mitral Valve Annuloplasty on Inflow Velocity and Transmitral Pressure

We investigated the relationship between the inflow jet peak velocity and annuloplasty ring size. Overall, there was a significant increase in velocity from baseline $v = 42.5 \pm 5.4$ cm/s compared to post-annuloplasty $v = 74.6 \pm 15.6$ cm/s (paired t-test, $P < 0.001$, mean difference = -32.1 cm/s). This increase was observed for every animal, including for the large 32 mm Physio ring. There was an inverse relationship between peak velocity and annuloplasty ring area (Pearson's $r = -0.80$, $P < 0.05$, CI (95%) = $[-0.96, -0.2]$, Fig. 5b). Again, small undersized rings tended to result in higher peak transmitral velocity. Transmitral pressure gradients also increased significantly from baseline 0.73 ± 0.18 mmHg to post-annuloplasty 2.31 ± 1.04 mmHg ($P < 0.05$).

Comment

These studies suggest that MV annuloplasty ring placement alters normal LV flow, resulting in redirection of the atrioventricular diastolic inflow jet towards the septum. The redirected blood flow has consequences on normal LV flow dynamics, altering or eliminating the dual counter-rotating vortices observed distal to the MV annular plane. Increasingly smaller (undersized) annuloplasty rings have a proportional effect on the LV flow disturbance, with the smallest 24 mm rings having the greatest effect. Despite the expectation that MV annuloplasty ring placement conserves normal valve and hemodynamic function, we found that placement of an undersized annuloplasty ring greatly altered normal blood flow dynamics of the LV.

In general, surgeries for MV disease have been observed to alter normal LV flow^{8–10} and it might be expected from these results that almost any alteration of LV or MV geometry would disturb normal flow. Machler, et al. found that the orientation of mechanical bileaflet valves significantly disturbed physiologic flow in sheep, but that valve orientation was not as significant a perturbation as the replacement itself⁸. In another study, among 10 patients receiving 3 different types of prosthetic valves, there was significantly higher LV energy dissipation compared to normal subjects⁹ and that this partly depended on the type, orientation and position of the prosthetic valve and LV geometry. These studies focused on patients who had MV replacement, but not MV repair with ring annuloplasty. We expected that annuloplasty would have minimal effects on flow compared to replacement because the valve apparatus remains intact after surgery, yet rings were found to reorient the direction of diastolic inflow and, in undersized rings, reverse the direction of circulating flow in the ventricle. Pedrezetti, et al. recently showed that there was a deviation from the longitudinal direction of flow in a patient with MV repair, but without alterations in vortex rotation¹¹. Our results indicate that the relative size of the annuloplasty ring to the annulus appears to be a determinant for this effect.

There were no significant differences in observed LV function after surgery (Table 1). If annuloplasty did significantly affect LV energy efficiency, it is unclear if this had a short-term effect on cardiac output or LV performance. Differences in heart rate or contractility may contribute additional variability that would mask early changes in LV function. While we did not directly measure the contractile function of the LV, the heart rate of all animals before and after surgery was maintained within a narrow range, minimizing the effect on intraventricular pressure gradients and normal flow.

The use of animals allowed us to control for the annular and ring sizes, before and after surgery, minimizing variations in flow based on LV size or mass. LV flow fields in healthy sheep resemble those in normal humans, suggesting that sheep can serve as a useful animal model of human LV hemodynamics. In sheep, as in normal humans, the overall shape of the diastolic vortex field was a toroid and formed distal to the mitral valve, peaking in early diastole. We have observed that sheep have greater LV asymmetry than humans, with increased long-to-short axis geometric ratio. We observed that in normal sheep, as in healthy humans⁹, the anterior vortex was dominant. In general, it is not clear how subtle variations in LV geometry among mammals may affect LV flow patterns or whether this information may provide insight about evolutionarily conserved LV efficiency.

The implications of disturbed transmitral flow on normal ventricular function are uncertain. *In vitro* studies have suggested that vortex formation is important for efficient flow of blood between the heart chambers and aorta, and that abnormal vortex formation is correlated with poor heart function^{3,4}. Intraventricular vortices may be important from the perspective of LV efficiency, optimally designed to avoid energy dissipation¹². The looped structure of the heart demands that blood be redirected 120 degrees from the transmitral annulus in diastole towards the LV outflow tract in systole. Potential energy is stored in the LV and work is performed to overcome the LV-aortic pressure gradient; however, less energy is required if the blood has momentum. Preservation of fluid kinetic energy in a vortex structure may mitigate some of the work required to eject blood from the ventricle.

The increase in transmitral pressure and inflow velocity that we observed are indicative of functional mitral valve stenosis. As described previously, there are several possible mechanisms that can lead to this result¹³. Small undersized rings as well as the presence of redundant tissue can lower the effective orifice area of the valve. The procedure can also decrease the mobility of the posterior leaflet. Finally, rigidity of the annuloplasty ring can limit the natural expansion of the annulus during diastole. All these factors could contribute towards inducing functional mitral valve stenosis, leading to increased pressure gradients, and by Bernoulli's principle, increased inflow jet velocity. Abnormal hemodynamic measurements and impaired exercise stress test results have been reported for restrictive annuloplasty patients compared to controls, potentially leading to worse clinical outcomes^{13,14}.

A similar study in humans with MV disease would be of great importance. To achieve this goal the 4D flow acquisition used in this animal study would require a considerably reduced scan time, compromising both spatial and temporal resolution. To address this concern, there is ongoing development to optimize MRI pulse sequences and protocols and introduce novel methodology using multiple radiofrequency detectors and reconstruction algorithms. Nevertheless, the sheep model remains important because many aspects of surgically-induced MV disease and repair in sheep emulate the human condition and are therefore an essential methodology to understand human valvular disease and surgical repair under highly controlled and reproducible conditions. These results may ultimately guide the development of surgical approaches that correctly restore intraventricular hemodynamics. In surgeries for ischemic MV regurgitation, it would be expected that alterations in LV geometry or size would affect intraventricular flow patterns. Using similar methods, Carlhäll, et al. reported that the fraction of the total diastolic inflow that is immediately ejected during the next systolic event is reduced in patients with heart failure¹⁷. Surgical correction for LV remodeling, in addition to MVR, may therefore be a critical criterion for treatment of ischemic MV disease. Finally, these findings in normal animals revealed several potential drawbacks of methods for MVR. MVR greatly disturbed normal intraventricular flow and this finding was unexpected, given that MVR was assumed to normalize ventricular hemodynamics. It was reasonable to assume that undersized annuloplasty rings would result in MV stenosis, however, the implications of stenosis on intraventricular flow has not been previously characterized. In addition to increased peak diastolic MV pressure gradients, we observed using 4D flow MRI that the hemodynamic flow trajectory was highly disturbed and such an observation has not been observed under conventional echocardiography because of its poor characterization of complex flow.

Conclusions

In summary, we found that annuloplasty rings, regardless of size, disturb physiological intraventricular flow. While the rings attempt to maintain physiological valve function, they result in abnormal LV blood flow dynamics and the degree of abnormality is strongly dependent on the size of the ring. These factors may cause impaired heart function and this may be concerning since MV annuloplasty is a common procedure for MV repairs. Especially for cases of ischemic mitral regurgitation (IMR), there is a large propensity to undersize the ring in order to promote leaflet coaptation. The poor outcomes and high

recurrence rate of regurgitation associated with the use of restrictive annuloplasty to treat IMR may be a related consequence of the worsened hemodynamics we have observed. Attempts to preserve physiological flow patterns may lead to improved designs for annuloplasty rings in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

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Figure 1.

Methods for analysis of diastolic blood flow and assessment of inflow angle. (a), streamlines showing the orientation of the flow field during mid-diastole. *S* indicates the surface positioned at the vena contracta for assessment of peak inflow velocity. (b), a cine MR image of the position of the LV and LA in a 4 chamber perspective, indicating the relative orientation of the left heart chambers in (a). (c), calculation of the diastolic inflow angle α between the line intersecting the mitral coaptation point and apex and the line parallel to flow at the vena contracta. (d), a cine MR image of the position of the LV and LV in a 3 chamber perspective, indicating the relative orientation of the left heart chambers in c. LA = left atrium, LV = left ventricle, VC = vena contracta, Ao = aorta.

Figure 2.

LV flow dynamics before (a-c) and 1 week after MV annuloplasty ring placement (d-f) with an undersized 24 mm Physio annuloplasty ring. Cardiac phases are indicated (a and d) mid-diastole, (b and e) late-diastole, (c and f) early-systole. (a) Counter-rotating vortices are positioned distal to the anterior and posterior MV leaflets, as seen from a 3-chamber perspective. (b,c) The vortices reduce intensity and unwind, as blood is redirected towards the LV outflow tract. In (d), there is a single prominent posterior vortex after annuloplasty replacement. In (e), The posterior vortex continues to circulate deep into the apex throughout diastole, sustained by MV stenosis and is unwound in early systole (f). Animations of LV hemodynamics at baseline and post-surgery are provided in videos 1 and 2.

Figure 3.

LV hemodynamics before (a-c) and 1 week after MV annuloplasty ring placement (d-f) with a 26 mm Physio annuloplasty ring. Cardiac phases are indicated (a and d) mid-diastole, (b and e) late-diastole, (c and f) early-systole. (a) Counter-rotating vortices are positioned distal to the anterior and posterior MV leaflets, as seen from a 3-chamber perspective. (b,c) The vortices reduce intensity and unwind, as blood is redirected towards the LV outflow tract. (d) After MV annuloplasty ring placement, diastolic flow is oriented towards the septum (cf. Fig. 3a), although the overall peak velocity is reduced and reorientation of flow is somewhat reduced compared to the 24 mm undersized ring (cf. Fig. 2d). (e-f) A single vortex distal to the MV, rotating counter-clockwise, is sustained during late diastole and is unwound towards the LV outflow tract in systole. Animations of LV hemodynamics at baseline and post-surgery are provided in videos 3 and 4.

Figure 4.

LV hemodynamics before (a-c) and 1 week after MV annuloplasty ring placement (d-f) with a 32 mm Physio annuloplasty ring. Cardiac phases are indicated (a and d) mid-diastole, (b and e) late diastole, (c and f) early-systole. (a-c) Normal hemodynamics resemble those of other animals (cf. Fig. 2 and 3). (d) As compared to 24 and 26 mm undersized Physio rings (cf. Fig 2d and 3d, respectively), the 32 mm ring preserves normal mid-diastolic hemodynamics at higher peak velocity. Anterior and posterior counter-rotating vortices resemble hemodynamics of a normal animal. (e) In late-diastole, the counter-rotating vortices propagate towards the apex and reverse rotation. (f) vortices reduce intensity and unwind flow directed towards the outflow tract in early-systole. Animations of LV hemodynamics at baseline and post-surgery are provided in videos 5 and 6.

Figure 5.

(a) Influence of ring size on inflow angle (b) peak diastolic velocity, as measured at the vena contracta, before (blue circles) and after (red circles) annuloplasty ring placement for all 5 ring sizes. The x-axis refers to post-surgery ring area. A correlation between peak velocity and ring area was observed for all rings.

Table 1

Hemodynamic variables of the sheep at baseline and post-MV annuloplasty ring placement.

Hemodynamic Variables	Baseline (n=5)	Post-Surgery (n=5)
Heart rate, bpm	99.2 ± 7.6	103.8 ± 15.8
EDV _{LV} , mL	74.5 ± 16.4	68.2 ± 16.2
ESV _{LV} , mL	32.6 ± 8.7	27.6 ± 6.4
SV _{LV} , mL	43.8 ± 8.6	40.6 ± 10.3
EF _{LV} , %	57.8 ± 4.0	59.3 ± 2.7
CO _{LV} , L/min	4.3 ± 0.8	4.2 ± 0.6
Transmitral Pressure (mmHg)	0.73 ± 0.18	2.31 ± 1.04

Table 2

Mitral annuloplasty ring characteristics.

Ring	Area (mm ²)	Baseline Angle (°)	Post-surgery Angle (°)	Baseline Peak Velocity (cm/s)	Post-surgery Peak Velocity (cm/s)
24mm Physio	264	11.5	25.7	40.3	107.2
26mm Physio	322	11.3	19.7	47.4	77.6
28mm Physio	360	11.5	17.6	48.9	66.0
30mm Physio	432	10.0	21.7	31.0	65.8
32mm Physio	510	13.1	12.2	38.7	59.5