Saddle-Shaped Annuloplasty Improves Leaflet Coaptation in Repair for Ischemic Mitral Regurgitation

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Background. **Current repair results for ischemic mitral regurgitation (IMR) with undersized annuloplasty rings are characterized by high IMR recurrence rates. Current annuloplasty rings treat annular dilatation, but they do little to improve (and may actually exacerbate) leaflet tethering. New saddle-shaped annuloplasty rings have been shown to maintain or restore a more physiologic annular and leaflet geometry and function. Using a porcine IMR model, we sought to demonstrate the influence of annuloplasty ring shape on leaflet coaptation.**

Methods. **Eight weeks after posterolateral infarct, eight pigs with grade 2+ or higher IMR were randomized to undergo either a 28-mm flat ring annuloplasty (n = 4) or a 28-mm saddle-shaped ring annuloplasty (n = 4). Real-time three-dimensional echocardiography and a customized image analysis protocol allowed three-dimensional assessment of leaflet coaptation before and after annuloplasty.**

Results. **Total leaflet coaptation area was significantly higher after saddle-shaped ring annuloplasty (109.6 ± 26.9 mm^2) compared with flat ring annuloplasty (46.2 ± 7.7 mm^2, p <0.01). After annuloplasty, total coaptation area decreased by 87.5 mm^2 (or 65%) in the flat annuloplasty group (p = 0.01), whereas total coaptation area increased by 22.2 mm^2 (or 25%) in the saddle-shaped annuloplasty group (p = 0.28).**

Conclusions. **This study shows that the use of undersized saddle-shaped annuloplasty rings in mitral valve repair for IMR improves leaflet coaptation, whereas the use of undersized flat annuloplasty rings worsens leaflet coaptation. Because one of Carpentier's fundamental principles of mitral valve repair (durability) is to create a large surface of coaptation, saddle-shaped annuloplasty may increase repair durability.**

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Ischemic mitral regurgitation (IMR) is common, and its presence strongly affects prognosis [1, 2]. Even a mild degree of IMR adversely affects survival, with a strongly graded relationship between severity and reduced survival [1, 2]. In IMR the main pathophysiologic mechanism is ischemia-induced left ventricular (LV) remodeling with papillary muscle displacement and apical tethering or tenting of the mitral valve leaflets combined with annular dilatation and attenuation of the physiologic annular saddle shape [3]. Both annular dilatation (and flattening) (Carpentier type I dysfunction) and leaflet tethering (and flattening) (Carpentier type IIIb dysfunction) reduce leaflet coaptation and render the mitral valve insufficient [3]. Undersized ring annuloplasty does not address the main pathophysiologic mechanism of IMR, but it can provide reliable repair results by treating annular dilatation in patients with less advanced forms of LV dilatation and mitral valve tethering [4].

Although mitral valve repair with undersized ring annuloplasty, typically performed in conjunction with coronary artery bypass grafting, has become the preferred treatment [5, 6], the overall rate of IMR persistence and recurrence (moderate or severe IMR) remains high (up to 30% after 6 months and up to 60% after 3 to 5 years) [7, 8]. Undersized ring annuloplasty may potentiate leaflet tethering by displacing the posterior annulus anteriorly, which leads to increased posterior leaflet tethering [9]. Essentially, the mitral valve becomes functionally unileaflet. Leaflet tethering decreases leaflet curvature and results in increased leaflet and chordal stress [10]. The limited repair durability may explain the difficulty in demonstrating a survival benefit of annuloplasty for IMR [11].

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Abbreviations and Acronyms

2D	=	two-dimensional
3D	=	three-dimensional
CPB	=	cardiopulmonary bypass
IMR	=	ischemic mitral regurgitation
IV	=	intravenous
LV	=	left ventricular

The development of quantitative three-dimensional (3D) echocardiographic imaging has improved our understanding of mitral annular geometry [12, 13]. These new insights have led to the introduction of saddle-shaped annuloplasty rings to restore normal mitral annular 3D geometry. We have previously shown that saddle-shaped annuloplasty restores or maintains a more physiologic annular and leaflet geometry and function compared with flat annuloplasty [10, 14, 15] and that it reduces leaflet strain by increasing leaflet curvature [10, 14].

Based on this work we hypothesized that, despite the negative influence of undersized annuloplasty on leaflet coaptation, undersized saddle-shaped annuloplasty for IMR would promote a larger area of leaflet coaptation compared with undersized flat annuloplasty. To test this hypothesis we applied real-time 3D echocardiography and mitral valve tracing after mitral valve repair in a porcine IMR model.

Material and Methods

Surgical Protocol

The study protocol was reviewed and approved by the University of Pennsylvania School of Medicine Institutional Animal Care and Use Committee (IACUC) in Philadelphia and was in compliance with the *Guide for the Care and Use of Laboratory Animals* (US National Institutes of Health publication No. 85-23, revised 1996).

Eight adult male pigs were pretreated with buprenorphine (2 mg/kg); anesthesia was then induced with intravenous (IV) sodium thiopental (10 to 15 mg/kg), and the animals were intubated and anesthetized with isoflurane (1.5% to 2.0%) and oxygen. All animals received IV glycopyrrolate (0.02 mg/kg) and IV cefazolin (1.0 g). All animals underwent a right thoracotomy to allow ligation of the left circumflex coronary artery and mid-posterior descending artery to create a 20% to 25% area of infarction [16]. Permanent occlusion of these arteries results in a transmural posterobasal myocardial infarction that involves approximately 20% to 25% of the LV mass and typically includes the entire posterior papillary muscle [16–18]. Animals received IV magnesium sulfate (1 g), IV amiodarone (90 mg by infusion over an hour), and IV lidocaine (3 mg/kg bolus, then 2 mg/min infusion) before infarction as antiarrhythmic prophylaxis. After hemodynamic and electrophysiologic stabilization, the thoracotomy was closed, and the animal was permitted to recover.

Eight weeks after infarction, animals were returned to the operating room. Anesthesia was once more induced, as described earlier, and all animals underwent epicardial echocardiography to assess the degree of IMR. All animals had grade 2+ or higher IMR. The mitral annulus was sized at 32 mm in all animals, and a 28-mm undersized annuloplasty ring (two sizes under) was used in each animal. Animals were randomized to undergo placement of a 28-mm flat mitral annuloplasty ring (Carpentier-Edwards Physio annuloplasty ring, Edwards Lifesciences, Irvine, CA) (Figs 1A, 1B) or to undergo placement of a 28-mm saddle-shaped mitral annuloplasty ring (Medtronic Profile 3D annuloplasty ring, Medtronic, Minneapolis, MN) (Figs 1C, 1D). Valve repair was performed through a left thoracotomy using cardiopulmonary bypass (CPB) and standard cardiac surgical techniques. The heart was arrested with antegrade cold crystalloid cardioplegia (PlegisolW, Hospira Inc, Lake Forest, IL), and the mitral valve was approached through a left atriotomy. After annuloplasty ring implantation the valve was tested in standard fashion and the atriotomy was closed, after which air was removed from the heart, and the animal was weaned from CPB. After separation from bypass and acquisition of epicardial echocardiographic data, animals were euthanized by an overdose of potassium administered into a clamped aortic root. After euthanasia, the heart was excised and the LV was opened through the interventricular septum. After repair inspection a digital photograph of the opened LV was taken and the infarct location was verified. All photographs were imported into an image analysis program (Image Pro Plus, MediaCybernetics; Silver Spring, MD), and computer-assisted planimetry was performed on the photographic image to quantify the infarct size as a percentage of the LV.

Echocardiographic Protocol

Full-volume data sets of the mitral valve were acquired using real-time 3D echocardiography with a Philips X7-2t handheld probe (Philips, Bothell, WA). Epicardial echocardiography was performed at the time of valve repair before instituting CPB and again after valve repair, approximately 1 hour after separation from bypass. All real-time 3D echocardiography studies were performed at an arterial systolic pressure of 150 mm Hg. Severity of IMR was determined semiquantitatively by assessing the area of the regurgitant jet as a percentage of left atrial area in the apical four-chamber view. The following grading scale was used: grade 0, no IMR; grade 1+, less than 20%; grade 2+, 20% to 40%; grade 3+, 40% to 60%; and grade 4+, more than 60% [19].

Image Segmentation

Each full-volume 3D data set was exported to an Echo-View 5.4 (TomTec Imaging Systems, Munich, Germany) software workstation. All analyses were performed at midsystole. The anterior and posterior commissures were defined as annular points at the junction between the anterior and posterior leaflets (middle of commissural region) and were interactively identified.