Acute Feasibility Study of a Novel Device for the Treatment of Mitral Regurgitation in a Normal Canine Model

Tohru Takaseya, MD, PhD, Hideyuki Fumoto, MD,* Roberto M. Saraiva, MD, PhD,† Akira Shiose, MD, PhD,* Yoko Arakawa, MD,* Margaret Park, BS,† Santosh Rao, MD,* Raymond Dessoffy, AA,* Larry D. Kramer, Jr.,* Mark Juravic, AA,‡ Pierluca Lombardi, MD, PhD,‡ and Kiyotaka Fukamachi, MD, PhD**

Objective: The purpose of this study was to evaluate the implantability of a novel epicardial mitral annuloplasty device and its ability to reduce the septal-lateral (S-L) dimension of the mitral annulus.

Methods: The devices were implanted on the beating heart in 2 healthy dogs (the 24-mm long device in dog A and the 27-mm and 24-mm standard devices in dog B) by sliding the anterior arm onto the floor of the transverse sinus and positioning the posterior arm just apical to the atrioventricular groove on the left ventricular posterolateral wall. The devices were secured with titanium helical tacks driven through the device into the ventricular wall. Two-dimensional epicardial echocardiograms were performed before and after device implantation to evaluate the degree of mitral regurgitation (MR) and the S-L dimension.

Results: Device implantation was uneventful, taking only ~30 seconds to deploy. MR (1+) in both dogs at baseline was reduced to zero after implant. The reductions in S-L dimension in systole for the 24-mm device were 7.5% in dog A and 30.5% in dog B. For the 27-mm device in dog B, S-L reduction in systole was 29.9%. The leaflet coaptation length was increased in both cases.

Conclusions: The new device was effective in reducing S-L dimension and 1+ MR without requiring the use of cardiopulmonary bypass. We are currently evaluating this device for the treatment of MR in a rapid-pacing canine heart failure model.

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From the *Department of Biomedical Engineering, Lerner Research Institute, and †Department of Cardiovascular Medicine, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH USA; and ‡MAQUET Cardiovascular LLC, San Jose, CA USA.

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Address correspondence and reprint requests to: Kiyotaka Fukamachi, MD, PhD, Department of Biomedical Engineering/ND20, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195 USA. E-mail: fukamak@ccf.org.

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Chronic ischemic mitral regurgitation (MR), also called functional or secondary MR, is an independent predictor of higher mortality and higher risk of developing heart failure in the postmyocardial infarction population.[1,2] Functional MR occurs with a structurally normal valve as a complication of left ventricular (LV) dysfunction arising from ischemia or dilated cardiomyopathy. Almost half the patients with LV dysfunction have at least moderate MR.[3,4] Because of its vicious downward cycle, the prognosis is poor in patients with functional MR.[2,3] Mild and moderate functional MR has also been associated with significantly decreased survival, independent of ventricular function, in patients undergoing coronary artery bypass grafting (CABG).[5] Surgical annuloplasty is widely used as a means of mitral valve repair, but it requires the patient to be placed on cardiopulmonary bypass (CPB).

The Mitral Touch (MAQUET Cardiovascular LLC, San Jose, CA) is an epicardial mitral annuloplasty device intended to correct valve dysfunction without requiring the use of CPB. Initial target patients for this device would be those undergoing other cardiac procedures, such as CABG, who might also benefit from the restoration of mitral valve competence. The main purpose of this acute feasibility study was to evaluate the implantability of the device and the feasibility of reducing the septal-lateral (S-L) dimension in normal dogs.

METHODS

Study Design

Two mongrel dogs (dog A, 29.8 kg; dog B, 26.0 kg) were used for acute evaluation of the device. The study was approved by the Institutional Animal Care and Use Committee, and both animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Labora-

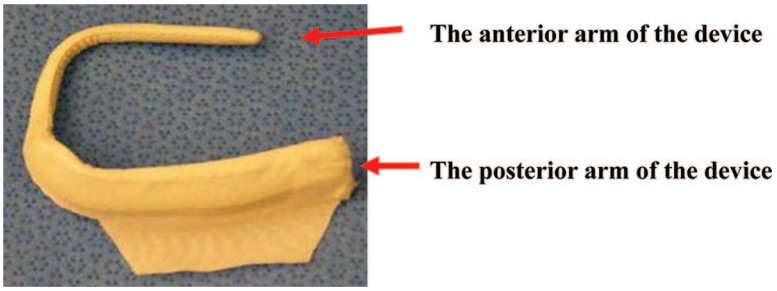

FIGURE 1. A picture of the Mitral Touch device. Both the anterior arm and the posterior arm of the device compress toward the anterior and posterior mitral annulus, respectively.

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Mitral Touch Device Description

The Mitral Touch is an epicardial mitral annuloplasty device. It consists of a titanium wire backbone, silicone bulking, and polyester fabric cover with a flap of ~1 cm for securing it to the heart (Fig. 1). The device is available in 21-, 24-, 27-, and 30-mm S-L dimensions, with a choice of standard- or long-arm lengths for each design. The long-arm device has longer arms than the standard-arm device. The Mitral Touch is not a complete ring, but it has the arms that can reduce S-L dimension of the mitral annulus (Fig. 2). The Mitral Touch is implanted by sliding the anterior arm into the transverse sinus and positioning the posterior arm just apical to the atrioventricular groove on the LV posterolateral wall (Fig. 3). The Mitral Touch device is secured in place with two or more titanium helical tacks driven through the device's fabric flap and into the ventricular wall.

Surgical Procedure

The animal was anesthetized with intravenous thiopental (500 mg). After endotracheal intubation, anesthesia was maintained with isoflurane. The animal was placed on the surgical table in the supine position, and electrocardiographic leads were attached to the extremities.

An arterial pressure monitoring line was inserted from the left carotid artery. Lidocaine was started at 2 mg/kg/H to prevent ventricular arrhythmia. A median sternotomy was performed. A two-dimensional epicardial echocardiogram was performed to evaluate the mitral annular geometry.

We implanted the 24-mm long-arm device in dog A. We first tried the 27-mm standard-arm and secondarily implanted a 24-mm standard-arm device in dog B. After implantation, MR grade and S-L dimension were rechecked.

After echocardiography, the dogs were killed by rapid intravenous injection of sodium pentobarbital (100 mg/kg) and potassium chloride (40 mEq). We explanted each heart with the device in place. The external and internal surfaces of the heart were investigated and photographed.

Echocardiographic Analysis

Echocardiographic data were collected using a Vivid 7 echocardiography machine (GE Medical, Milwaukee, WI). The LV end-diastolic and end-systolic volumes, LV ejection fraction, S-L dimension of the mitral annulus, and degree of MR were collected. MR grade was categorized according to the extent and width of the regurgitation jet. The S-L dimension of the mitral annulus was measured using a three-chamber apical view, and the LV diameters at midpapillary muscle level were measured using the short-axis view. LV volumes and ejection fraction were determined by the modified Simpson's rule with images obtained from apical four- and two-chamber views.

The whole length of the anterior leaflet during diastole (Ad) and the length of uncoapted-free portion of anterior leaflet at end systole (Ac) were measured. Coaptation length

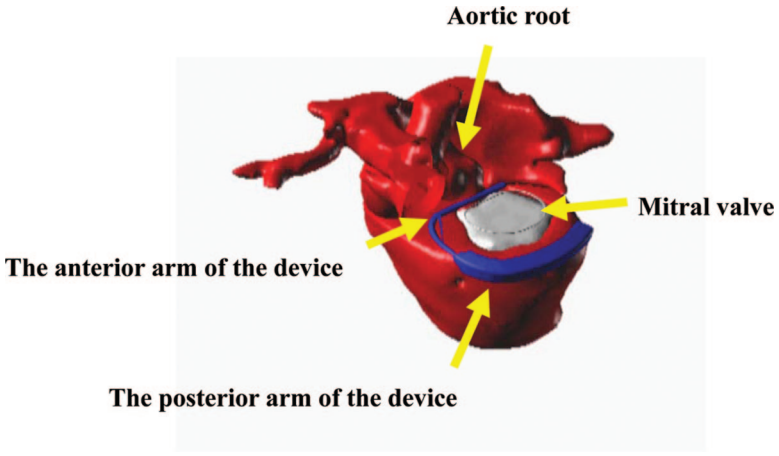

FIGURE 2. An illustration that shows the Mitral Touch and its relationship to the level of the mitral annulus and aortic root (the left atrium is removed). The anterior arm of the device is placed at the transverse sinus, between the anterior mitral annulus and aortic root, and the posterior arm is placed at the atrioventricular groove on the LV posterolateral wall.

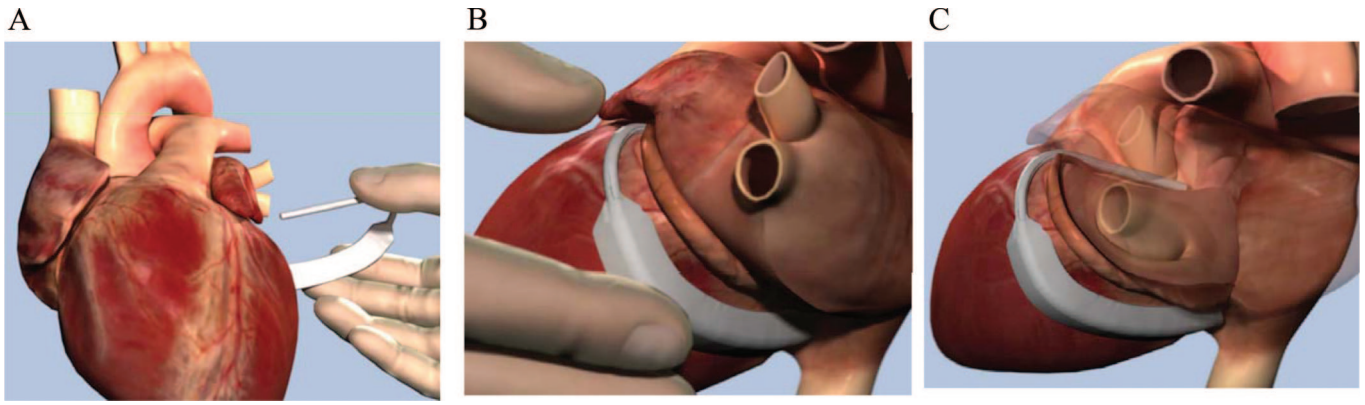

FIGURE 3. Illustration of placement of the Mitral Touch. A, The tip of the anterior arm of the Mitral Touch is toward the transverse sinus, and the posterior arm is just apical to the atrioventricular groove. B, The Mitral Touch slides onto the heart. C, The Mitral Touch as properly positioned on the heart.

was defined as and could be calculated from the following equation:

$$\text{Coaptation length} = \text{Ad} - \text{Ac}^{6}$$

RESULTS

We were able to place the devices without complications in both dogs. It took only between 10 and 30 seconds to slide and fit the device around the heart.

MR 1+ in both dogs at baseline was reduced to zero after implant (Fig. 4). The reductions in S-L dimensions (systole and diastole) for the 24-mm device were 7.5% and 10.1% in dog A and 30.5% and 26.6% in dog B, respectively. For the 27-mm device in dog B, S-L reductions were 29.9% and 23.7% (Table 1). Mitral valve coaptation length for the 24-mm long-arm device was increased from 3.9 to 4.6 mm in dog A, and that for the 27- and 24-mm standard-arm devices was increased from 4.3 to 4.5 mm in dog B. There was no change in LV diameter at midlevel between baseline and postimplantation. There was also no change in LV volume or ejection fraction between baseline and after the device implantation.

The anterior arm was located at the floor of the transverse sinus, and the tip of the anterior arm was closed to the right atrium. The middle of the posterior fabric pad was placed just at the atrioventricular groove on the posterior LV lateral wall (Fig. 5). When we opened the left atrium, we were able to see the bulge of the anterior arm ~10 mm above the anterior mitral annulus and the bulge of the posterior arm just above the posterior annulus.

DISCUSSION

Ischemic MR occurs in 10% to 20% of the patients with coronary artery disease,[7] translating to an incidence of ~50,000 to 100,000 patients. There is general agreement that patients with severe ischemic MR should undergo mitral valve surgery at the time of CABG.[5,8] However, the indication of mitral valve surgery for mild or moderate ischemic

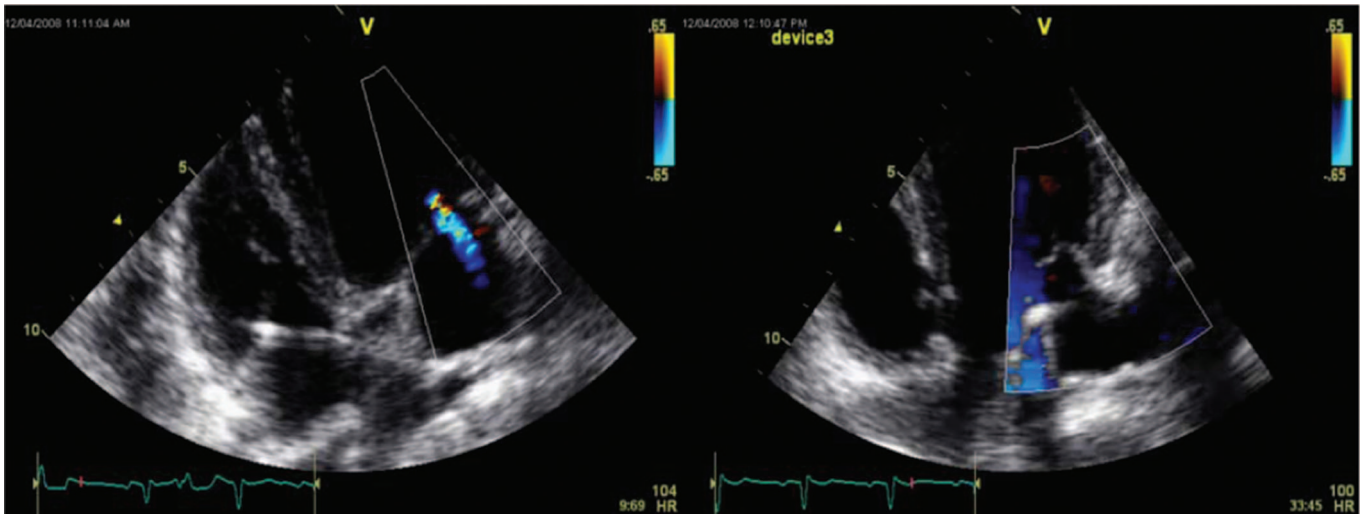

FIGURE 4. MR of 1+ in dog A at baseline was reduced to zero after device implant. Left panel, at baseline; right panel, with 24-mm long-arm device.

TABLE 1. Echocardiographic Data

Dog	Conditions	MR Grade	S-L Dimension (mm)	Percentage of Reduction	CL (mm)	LV Diameter (mm)	LV Volume (mL)	LV EF (%)
A	Baseline							
	Systole	1+	20.1	NA	3.9	31.8	52.2	42.9
	Diastole		18.9	NA		38.0	91.5	
	24-mm Long arm							
	Systole	0	18.6	7.5	4.6	31.4	47.7	43.7
	Diastole		17.0	10.1		37.0	84.9	
B	Baseline							
	Systole	1+	24.3	NA	4.3	31.8	51.1	39.2
	Diastole		20.7	NA		35.9	84.1	
	27-mm Standard arm							
	Systole	0	17.2	29.9	4.5	36.7	46.8	40.1
	Diastole		15.8	23.7		33.0	78.3	
	24-mm Standard arm							
	Systole	0	16.9	30.5	4.5	36.4	47.7	40.8
	Diastole		15.2	26.6		32.5	80.5	

CL indicates mitral valve coaptation length; LV, left ventricular; EF, ejection fraction; NA, not applicable.

MR is still controversial,[9,10] because mitral valve surgery, such as annuloplasty, requires access to and manipulation of the valve annulus via a left atriotomy. Furthermore, the procedure currently requires the patient to be placed on CPB to facilitate the treatment. Finally, the outcome of the annuloplasty ring placement cannot be adequately assessed until the patient is weaned from bypass. These complications result in added procedural and anesthetic times and are typical reasons for increased morbidity/mortality rates in treated patients. The increased morbidity/mortality profile leads directly to nontreatment of MR in the patient with early stage heart failure.

Liddicoat et al[11] reported development of percutaneous catheter-based approaches to mitral annuloplasty that exploit the anatomic proximity of the coronary sinus. Some of them are under clinical trials for diagnostic evaluation,[12] and permanent implants are ongoing.[13] There are, however, potential disadvantages to the use of the above annuloplasty devices that pass through the coronary sinus: The anatomic proximity of the coronary sinus and mitral annulus is of great concern. The pass through the coronary sinus is only applied along the posterior annulus, leaving the anterior annulus untreated. The delivery of a device, precise placement, deployment, and redeployment are technically challenging. There are risks of coronary sinus erosion, dissection or perforation, and thrombosis due to the device. Finally, a device in the coronary sinus may conflict with other therapies, such as ablations, cardiac resynchronization, and retrograde cardioplegia.

We are developing an epicardial mitral annuloplasty device that can be implanted concomitant with off-pump CABG to help treat the underserved chronic ischemic MR patient. The Mitral Touch, which was designed to restore the S-L dimension, has the advantage of being placed without CPB and open-heart access. The Mitral Touch does not have any of the disadvantages such as percutaneous catheter-based approaches to mitral annuloplasty that exploit the anatomic proximity of the coronary sinus. The Mitral Touch implantation was uneventful, taking only ~30 seconds to slide and fit the device around the heart in this experiment. MR in both

FIGURE 5. The explanted heart with the Mitral Touch (24-mm standard-arm device) tacked in place. The anterior arm (left) is located at the floor of the transverse sinus, and the posterior arm (right) at the atrioventricular groove on the LV posterolateral wall.

dogs at baseline was reduced after implant. The S-L dimension (systole, diastole) were decreased after implant. We were also able to see an increase in leaflet coaptation in both cases. Epicardial placement will allow for implantation without the need for heparinization and the immediate assessment of the device without the need for weaning from bypass. The Mitral Touch can correct valve dysfunction without requiring the use of CPB.

The epicardial mitral annuloplasty ring might have some potential disadvantages. First, this device treats only the annulus and not the ventricle. We previously reported that the Coapsys device reduced functional MR and improved parameters regarding MR acutely and chronically.[14] The Coapsys can create both annular reduction and papillary muscle repositioning. Some studies have demonstrated that annuloplasty alone does not ensure successful and durable elimination of MR.[15] Both annular reduction and papillary muscle repositioning may create the most ideal, chronically effective treatment for functional MR. Second, the device may obstruct the left coronary artery, because the rigid device compresses the heart from the epicardial side. We did not perform coronary angiography in these cases; however, we did not see any ischemic changes in electrocardiogram after device implantation. We will evaluate coronary angiograms in our future studies using the canine heart failure model. In addition, the anterior arm of the device may create a bulge in the left atrium. The compression may cause not only stenosis of the mitral orifice but also erosion of the left atrial wall. Chronic studies will need to evaluate these potential issues.

This was an acute preliminary study of the feasibility and efficacy of the epicardial mitral annuloplasty device in normal dogs. One limitation of this study is the small number of studied animals (n = 2). Second, we have yet to evaluate the device for reduction of MR grade and S-L dimension in animals with moderate/severe MR. Finally, long-term safety and efficacy of the device were not evaluated in an animal model of chronic MR. Chronic studies will need to be performed to evaluate the safety and efficacy of this device in the long term.

CONCLUSION

The new epicardial mitral annuloplasty device was effective in reducing S-L dimension and 1+ MR without requiring the use of CPB. We are currently evaluating this device for the treatment of MR in a rapid-pacing canine heart failure model.

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CLINICAL PERSPECTIVE

This is a preliminary report describing a novel epicardial mitral annuloplasty device and its ability to reduce the septal-lateral dimension (SLD) of the mitral annulus. This technology is aimed at treating functional mitral regurgitation. The device was examined in the beating heart in two healthy dogs. It was implanted epicardially by sliding the anterior arm into the transverse sinus and positioning the posterior arm just apical to the atrioventricular groove on the left ventricular posterior lateral wall. The device has the advantage of extremely easy placement. It was able to reduce the SLD in systole between 7.5% and 30.5%. Leaflet coaptation length was also increased. However, the device was implanted in healthy dogs so there was no real ability to access reduction in mitral regurgitation. These early studies suggest the need for further chronic studies. Readers are to be reminded that this device has a number of potential disadvantages which are discussed by the authors. It treats only the annulus and not the ventricle. It also causes unusual compression of the left atrium which may lead to erosion, coronary compromise or less likely mitral stenosis. We look forward to further data on this technology in order to determine whether this device may have a role in the treatment of functional mitral regurgitation.

