

Mitral Annuloplasty as a Ventricular Restoration Method for the Failing Left Ventricle: A Pilot Study

Tadaaki Koyama¹, Yoshiharu Soga¹, Oriyanhan Unimonh¹, Kazunobu Nishimura², Masashi Komeda¹

¹Department of Cardiovascular Surgery, Kyoto University, Graduate School of Medicine, Kyoto, ²Department of Cardiovascular Surgery, Tenri Hospital, Nara, Japan

Background and aim of the study: Undersized mitral annuloplasty (MAP) is effective in patients with dilated cardiomyopathy and functional mitral regurgitation (MR) since, as well as addressing the MR, the MAP may also reshape the dilated left ventricular (LV) base. However, the direct benefits of this possible reshaping on LV function in the absence of underlying MR remain incompletely understood. The study aim was to identify these benefits in a canine model of acute heart failure.

Methods: Six dogs underwent MAP with a prosthetic band on the posterior mitral annulus, using four mattress sutures. The sutures were passed individually through four tourniquets and exteriorized untied via the left atriotomy. Sonomicrometry crystals were implanted around the mitral annulus and left ventricle to measure geometry and regional function. Acute heart failure was induced by propranolol and volume loading after weaning from cardiopulmonary bypass; an absence of MR was confirmed by echocardiography. MAP was accomplished by cinching the tourniquets. Data were acquired at baseline, after

induction of acute heart failure, and after MAP.

Results: MAP decreased mitral annular dimensions in both commissure-commissure and septal-lateral directions. Concomitantly, the diastolic diameter of the LV base and LV sphericity decreased (i.e., improved) from 37.4 ± 9.3 to 35.9 ± 10 mm ($p = 0.063$), and from $67.9 \pm 18.6\%$ to $65.3 \pm 18.9\%$ ($p = 0.016$), respectively. Decreases were evident in both LV end-diastolic pressure (from 17 ± 7 to 15 ± 6 mmHg, $p = 0.0480$ and Tau (from 48 ± 8 to 45 ± 8 ms, $p < 0.01$), while fractional shortening at the LV base increased from $7.7 \pm 4.5\%$ to $9.4 \pm 4.5\%$ ($p = 0.045$). After MAP, increases were identified in both cardiac output (from 1.54 ± 0.57 to 1.65 ± 0.57 l/min) and E_{\max} (from 1.86 ± 0.9 to 2.41 ± 1.31 mmHg/ml).

Conclusion: The data acquired suggest that isolated MAP may have certain benefits on LV dimension/function in acute heart failure, even in the absence of MR. However, further investigations are warranted in a model of chronic heart failure.

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Although heart transplantation represents the ideal surgical therapy for dilated cardiomyopathy (DCM), the procedure may be problematic due to a shortage of donor hearts. Recently, some good results were achieved for an alternative surgical therapy for DCM, when Bolling and colleagues reported excellent early and mid-term results of mitral annuloplasty (MAP) for DCM with mitral regurgitation (MR) (1-3). These authors suggested that one reason for these excellent

results might be an acute remodeling of the left ventricular (LV) base by undersizing the mitral annular ring. Subsequently, further positive results were reported with MAP for DCM with MR (4,5). Although, in 1997, Batista et al. performed a successful partial left ventriculectomy for DCM (6), the mortality rate for this procedure was generally high (7-11). In addition, a considerable number of cases were complicated by recurrent heart failure.

The geometry of the left ventricle is important for LV plasty in DCM. Suma and colleagues and Koyama et al. reported excellent results for a partial left ventriculectomy (12,13), and highlighted the importance of basal reconstruction. Likewise, in a previous study partial left ventriculectomy for the LV area from the middle to the base was shown to be superior to that from the middle to the apex (14). However, the direct benefits on LV function of acute LV reshaping follow-

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Address for correspondence:
Masashi Komeda MD, PhD, Department of Cardiovascular Surgery,
Kyoto University Graduate School of Medicine, 54 Kawahara-cho
Shogoin Sakyo-ku Kyoto, Japan
e-mail: komelab@kuhp.kyoto-u.ac.jp

ing undersized MAP in the absence of underlying MR remain incompletely understood. Thus, the study aim was to investigate the direct effect of mitral annular reduction on LV function in a canine model of acute heart failure, without concomitant MR.

Materials and methods

Animals

Six mongrel dogs of bodyweight 20-25 kg were used in these studies. All animals received humane care in compliance with the *Principles of Laboratory Animal Care* formulated by the National Society for Medical Research and the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (revised 1996).

Surgical procedure

All dogs were premedicated with an intramuscular injection of ketamine hydrochloride (20 mg/kg). General anesthesia was induced with an intravenous injection of sodium pentobarbital (10-15 mg/kg), after which an endotracheal tube was inserted. During surgery, general anesthesia was maintained with oxygen and isoflurane (0.5-1.5%). A 7-Fr CritiCath™ thermodilution catheter (Ohmeda, Singapore) was inserted into the pulmonary artery via the right external femoral vein. Cardiac output (CO) was monitored using the thermodilution technique. Each animal was placed in the right lateral decubitus position, and a left thoracotomy made through the fifth intercostal space. The pericardium was opened and the heart suspended in a pericardial cradle.

After general heparinization (300 IU/kg), the animal was placed on cardiopulmonary bypass (CPB), with cannulation of the descending aorta, the right atrium

and the pulmonary artery. The ascending aorta was cross-clamped, and the heart arrested with cold cardioplegia solution delivered into the aortic root. The mitral valve was exposed through a left atrial appendage. The annular size of the mitral valve was determined according to the distance between the right and left trigone by an obturator of the Duran ring. A polytetrafluoroethylene (PTFE) strip was used as a prosthetic ring. Four stitches of 2-0 Ethibond (Ethicon, Somerville, NJ, USA) were placed along the posterior annulus, between the right and left trigones. Those stitches were placed individually through the tourniquets, without tying (Fig. 1), after which four sonomicrometer crystals (SonoMetrics Corp., London, Ontario, Canada) were placed on the mitral annulus (Fig. 2). Crystals #1 and #2 were placed in the septal-lateral axis, while crystals #3 and #4 were placed at both ends of the annulus, in the commissure-commissure axis. The PTFE ring was secured down to the mitral annulus. All sutures in the mitral annulus and crystal leads were led out through the left atriotomy. Three sonomicrometer crystals were placed in the subepicardium, in the left ventricle (Fig. 2). The dimension of the short axis was calculated as the distance between crystals #5 and #6, and of the long axis between crystals #6 and #7. A disposable manometer-tipped catheter (Millar Instruments, Inc., Houston, Texas, USA) and $\Sigma 5$ conductance catheter (2S-RH 6DA-116; Alpha Medical Ins., Mission Viejo, CA, USA) were placed in the left ventricle via the apex.

Induction of acute heart failure

After weaning from CPB, acute heart failure was induced by an intravenous infusion of propranolol (mean dose 39.6 ± 16.2 mg; range: 20 to 69 mg; Wako, Osaka, Japan) and transfusion of blood from the CPB reservoir. The end-point of induced heart failure was considered to be when the pulmonary capillary wedge

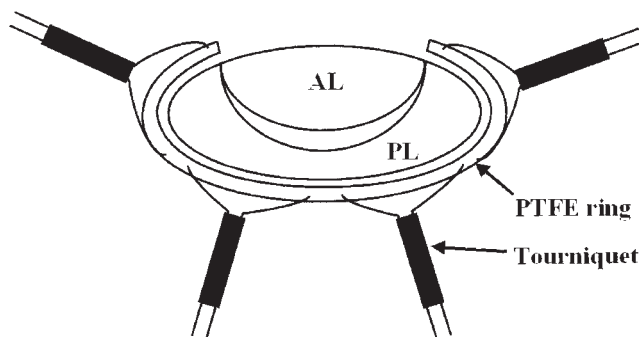


Figure 1: The scheme of mitral annuloplasty. AL: Anterior leaflet; PL: Posterior leaflet; PTFE: Polytetrafluoroethylene.

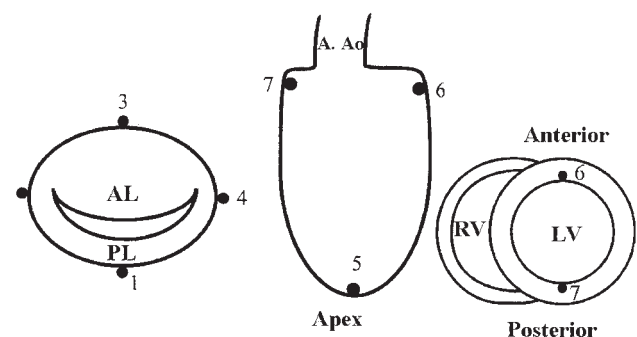


Figure 2: The crystal array. Left: The mitral annulus. Right: The left ventricle. The solid circles show the positions of the sonomicrometer crystals. A. Ao: Ascending aorta; AL: Anterior leaflet; LV: Left ventricle; PL: Posterior leaflet; RV: Right ventricle.

Table I: Dimensions of the mitral annulus before and after annuloplasty.

Inter-crystal dimensions (mm)	Baseline	Heart failure	Annuloplasty
#2 to #4 (intercommissural)	20.7 ± 4.9	21.7 ± 6.0 [†]	18.6 ± 6.6 [‡]
#1 to #3 (septolateral)	17.1 ± 4.7	17.7 ± 4.9	16.0 ± 3.8

[†]p <0.05 versus baseline; [‡]p <0.05 versus heart failure.

pressure increased more than 5 mmHg in comparison to pulmonary capillary wedge pressure just before induction of heart failure. Left atrial pacing was commenced following the propranolol infusion, at a heart rate of 120 bpm, and maintained until completion of the experiment. Epicardial and Doppler echocardiography failed to detect MR in any of the animals.

Mitral annuloplasty

After induction of acute heart failure, MAP was accomplished by cinching up all of the sutures through tourniquets. Mitral stenosis did not cause complications in any of the animals, as verified by epicardial echocardiography.

Data acquisition

Experimental data were collected from all six dogs at three time points: (i) immediately before induction of acute heart failure (baseline); (ii) after induction of acute heart failure (failure); and (iii) immediately after MAP (MAP). Maximum elastance (E_{\max}) and Tau (a preload-independent measure of isovolumetric relaxation) of the left ventricle were monitored using a manometer-tipped catheter and a conductance catheter, respectively. The dimension between two crystals at any position was measured using SonoSOFT™ software (SonoMetrics Corp.) to evaluate regional fractional shortening in the short and long

axes. Left ventricular regional fractional shortening (LVFS) was calculated from the end-diastolic and end-systolic dimensions as follows:

$$\text{LVFS} = [(\text{end-diastolic dimension} - \text{end-systolic dimension}) / (\text{end-diastolic dimension})] \times 100.$$

Global LV shape was assessed by calculating the sphericity using the formula:

$$[(\text{end-diastolic dimension of short axis}) / (\text{end-diastolic dimension of long axis})] \times 100.$$

Statistical analysis

All data were reported as mean ± SD. The statistical analysis was performed using a paired *t*-test. A p-value <0.05 was considered to be statistically significant.

Results

Hemodynamics

The hemodynamic data are listed in Table I. The heart rate was unchanged after pacing, and there were no changes in LV systolic pressure, CO and E_{\max} after MAP. In contrast, the LV end-diastolic pressure decreased from 17 ± 7 to 15 ± 6 mmHg, and Tau from 46.3 ± 8.4 to 43.7 ± 8.4 ms.

Mitral annulus dimension, LV dimension and contractility with sonomicrometry

The mitral annulus was decreased in both commis-

Table II: Hemodynamics before and after mitral annuloplasty.

Parameter	Baseline	Heart failure	Annuloplasty
HR (beats/min)	158 ± 15	120 [†]	120
LVSP (mmHg)	126 ± 24	91 ± 25 [†]	94 ± 33
LVEDP (mmHg)	10 ± 4	17 ± 7 [†]	15 ± 6 [‡]
CO (l/min)	3.6 ± 1.8	1.5 ± 0.6 [†]	1.7 ± 0.5
E_{\max} (mmHg/ml)	4.2 ± 2.3	2.0 ± 0.9	2.8 ± 1.6
Tau (ms)	28.0 ± 3.1	46.3 ± 8.4 [†]	43.7 ± 8.4 [‡]

Values are mean ± SD.

[†]p <0.05 versus baseline; [‡]p <0.05 versus heart failure.

CO: Cardiac output; E_{\max} : LV maximal elastance; HR: Heart rate; LVEDP: Left ventricular end-diastolic pressure; LVSP: Left ventricular systolic pressure; MAP: Mitral annuloplasty.

Table III: Left ventricular dimensions and contractility as monitored with sonomicrometry.

Parameter	Baseline	Heart failure	Annuloplasty
LVDd (mm)			
Short axis	35.2 ± 8.9	37.4 ± 9.4 [†]	35.9 ± 10.4
Long axis	55.2 ± 4.3	55.7 ± 3.2	55.0 ± 10.4
LVFS (%)			
Short axis	12.5 ± 5.6	7.7 ± 4.5 [†]	9.4 ± 4.5 [†]
Long axis	8.1 ± 1.3	3.9 ± 1.7 [†]	5.0 ± 2.0
Sphericity (%)	64.4 ± 18.5	67.9 ± 18.6 [†]	65.3 ± 18.9 [†]

Values are mean ± SD.

[†]p <0.05 versus baseline; †p <0.05 versus heart failure.

LVDd: Left ventricular diastolic dimension; LVFS: Left ventricular fractional shortening; MAP: Mitral annuloplasty

sure-commissure and septolateral dimensions after MAP (Table II). Data relating to LV dimensions and regional wall motion are listed in Table III. The LV diameter in the short axis (crystals #6 and #7) decreased from 37.4 ± 9.4 mm to 35.9 ± 10.4 mm (p = 0.063), whereas that in the long axis (crystals #3 and #5) was unchanged. After MAP, the LV sphericity was decreased from 67.9 ± 18.6% to 65.3 ± 18.9% (p = 0.016), whereas LV fractional shortening in the short axis was increased after MAP. Fractional shortening in the long axis also increased after MAP, although not significantly so.

Discussion

In the present study, the direct effects were investigated of MAP on LV with acute heart failure, but in the absence of MR. Previously, Bolling and colleagues discussed the possibility of acute remodeling of the LV base by undersizing the mitral annular ring (1-3), the aim being to re-establish an ellipsoid shape to the base of the LV cavity. However, it is difficult to compare the level of benefit which stemmed from the elimination of MR or from the direct effect of LV reshaping at the base. Thus, in order to evaluate the *net* effect of MAP on the left ventricle, an animal model of acute heart failure, without MR, was utilized.

The present data, acquired using sonomicrometry, showed that both the distance between the two commissures and the septolateral dimension were decreased to similar degrees, and this equated with a reduction of the mitral annulus by two sizes. This was considered relevant to clinical practice and confirmed the validity of the MAP method used (i.e., cinching the sutures through tourniquets from outside the heart). Because of the flexibility of the PTFE band, the annuloplasty in the present study was essentially similar to the widely accepted method of using a flexible and partial MAP ring in the clinical setting. For example, Tibayan et al. (15) performed another MAP by using a

modified Paneth Burr suture annuloplasty. Although this annuloplasty was simple and secure, difficulties were encountered when adjusting the annular size to reduce the mitral annulus by two sizes. In the DCM heart, the basal diameter of the left ventricle is the largest, and therefore it is important (and effective) to reduce the LV base. Reduction of the LV base diameter by partial left ventriculectomy is difficult because the LV wall at the base is thick and close to the main circumflex coronary artery. In other words, a surgical incision near the LV base has a high risk of critical bleeding or major coronary stenosis. In the present study, the LV dimension at its base was decreased from 37.7 to 35.9 mm after MAP, although the LV dimension in the long axis was unaffected; consequently, the LV was restored to more of an ellipsoid shape. Thus, MAP may not only eliminate the MR but also lead to a reshaping of the left ventricle. Moreover, MAP may also boost the effect of LV restoration by partial left ventriculectomy or other LV restoration surgery in DCM patients, even in the absence of MR.

Left ventricular and mitral annular dilation decreases the coaptation zone of the mitral valve, and is one of the major causes of functional MR (16,17). It is well known that when MR develops there is an increase in LV preload as well as further LV dilatation, which in turn further increases the MR, leading to a vicious cycle. Once established, MR engenders a poor prognosis in patients (18,19); thus, it is important to prevent the development of MR if the prognosis of DCM patients is to be improved. The results of the present study suggest that adding MAP to a partial left ventriculectomy or other LV restoration surgery that cannot repair the LV base may help not only to prevent MR but also to improve LV geometry/shape and function, even if the heart is not complicated by MR before surgery. As a consequence, the prognosis of the patients would also be improved.

Today, there is on-going debate as to whether it is beneficial to perform MAP in patients with heart fail-

ure (e.g., cardiomyopathy) and mild MR. As not only DCM but also ischemic cardiomyopathy is characterized by global LV dilatation and dysfunction, often accompanied by mitral annular dilatation, a more aggressive use of MAP might be justified in patients when basal LV dilatation is detected, even when the MR is minimal. However, this hypothesis must be tested with further investigations using an animal model of chronic heart failure.

Study limitations

The main limitation was that, by using a model of acute heart failure, only a 'snap' effect would have been recorded. It is also possible that the animals' condition may have changed during the experiment, although the surgery was performed quickly and the effects on the mitral annulus were confirmed by sonomicrometry. Nonetheless, the late results after MAP should be confirmed in a model of chronic heart failure, without MR. A second limitation was that cinching of the sutures rather than tying individually allowed only four sutures to be placed. Although the effects of MAP were confirmed by sonomicrometry, some minor differences from MAP in the clinical setting may have occurred. A third limitation was that, by using a beta-blocker to induce global heart failure, the degree of benefit of MAP might differ from that in the left ventricle with regional dysfunction.

In conclusion, LV basal dimension/function was improved after MAP in a model of acute heart failure with no MR, which suggested that there were direct and beneficial effects of MAP on the LV base. However, in order to create a more effective use of MAP, further investigation is warranted in a model of chronic heart failure, without MR.

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