Update on Mitral Repair in Dilated Cardiomyopathy

Matthew A. Romano, M.D., and Steven F. Bolling, M.D.

University of Michigan, Section of Cardiac Surgery, Ann Arbor, Michigan

ABSTRACT Heart failure is one of the leading causes of hospitalization worldwide. Mitral regurgitation (MR) is a known complication of end-stage cardiomyopathy and is associated with a poor prognosis due to progressive mitral annular dilation. A vicious cycle of continuing volume overload, ventricular dilation, progression of annular dilation, increased LV wall tension, and worsening of MR and CHF occur. Commonly, these patients were managed medically with diuretics and afterload reduction, and frequently with mitral valve replacement, both of which have poor long term survival in patients with CHF and MR. Over a 10-year period we prospectively studied over 200 patients with cardiomyopathy and severe MR who underwent mitral valve repair utilizing an undersizing overcorrecting annuloplasty ring. The mortality was low with one intraoperative death and eight 30-day mortalities. There were 26 late deaths; 2 of these patients had progression of heart failure and underwent transplantation. The 1-, 2-, and 5-year actuarial survivals have been 82%, 71%, and 52%, respectively. The NYHA class has improved for all patients from a preoperative mean of 3.2 $\pm$ 0.2 to 1.8 $\pm$ 0.4 postoperatively. All patients demonstrated improvement in ejection fraction, cardiac output, and end diastolic volumes with a reduction in sphericity index and regurgitant volume at 2 years post operation. All of the observed changes contribute to reverse remodeling and restoration of the normal left ventricular geometry. Mitral valve repair is a safe and effective operative intervention that corrects MR and offers a new strategy for patients with MR and end-stage cardiomyopathy.
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The management of patients with congestive heart failure (CHF) is a worldwide heath care problem, and a leading cause of hospitalization and mortality. Despite improvements in medical management, approximately 50% of patients with severe CHF die within 3 years of presentation.[1] In the United States alone, nearly 4.9 million people are suffering from heart failure; however, less than 3000 of the 500,000 patients diagnosed annually are offered transplantation due to limitations of donor availability, comorbid medical conditions, and often the advanced age of this patient population.[2] Functional MR is a significant complication of end-stage cardiomyopathy and may effect almost all heart failure patients as a preterminal or terminal event. Those with CHF and MR have a life expectancy of less than 12 months.[3] In an effort to resolve this problem and deficiency, mitral valve reconstruction has evolved as a surgical alternative to treat heart failure.

To address the issue of CHF and MR and its management, one needs to understand the anatomy of the mitral valve. Mitral competence depends on the coordinated function of the components of the mitral apparatus: the leaflets, annulus, papillary muscles, chordae tendinae, and the entire left ventricle (LV). Maintenance of the chordal, annular, subvalvar continuity, and mitral geometric relationships are important in the preservation of overall ventricular function; it may be even more important in patients with compromised function. As the ventricle fails, the progressive dilatation of the LV gives rise to MR. This action leads to a cycle of volume overload within an already dilated ventricle, progression of annular dilation, increased LV wall tension, increased degrees of MR, and worsened CHF. Mitral regurgitation is a significant complication of dilated cardiomyopathy and end-stage heart disease, and the incidence of MR complicating dilated cardiomyopathy has been reported in as high as 60% of patients.[4] Patients with CHF and MR refractory to medical therapy have a poor long-term survival, with only 46% 1-year survival without transplantation.[3] Furthermore, as little as 30 ml of regurgitant volume in the setting of ischemic MR is associated with only 47% 5-year survival.[5]

The functional MR that develops in CHF can be seen in patients with either idiopathic or ischemic cardiomyopathy. In patients with nonischemic dilated cardiomyopathy, in the absence of intrinsic mitral valve disease (i.e., myxomatous degeneration, calcific, or rheumatic disease), MR is due to a progressive dilation of the annular-ventricular apparatus with altered ventricular geometry and a subsequent loss of leaflet coaptation (Fig. 1).[6,7] In patients with ischemic cardiomyopathy, more complex mechanisms contribute to MR. The failure of leaflet coaptation may be related to a combination of dilation of the annular-ventricular apparatus and LV wall/papillary muscle dysfunction. A large leaflet area is required for coaptation because mitral leaflet area is $2^1/_2$ times greater than the area of the mitral orifice.[8] There is a critical reduction in the tissue available for coaptation as more leaflet tissue is utilized

Address for correspondence: Steven F. Bolling, M.D., Department of Surgery, 2120 Taubman Center, Box 0348, 1500 E. Medical Center Dr., Ann Arbor, Michigan 48109-0348. Fax: 734-764-2255; e-mail: sbolling@umich.edu

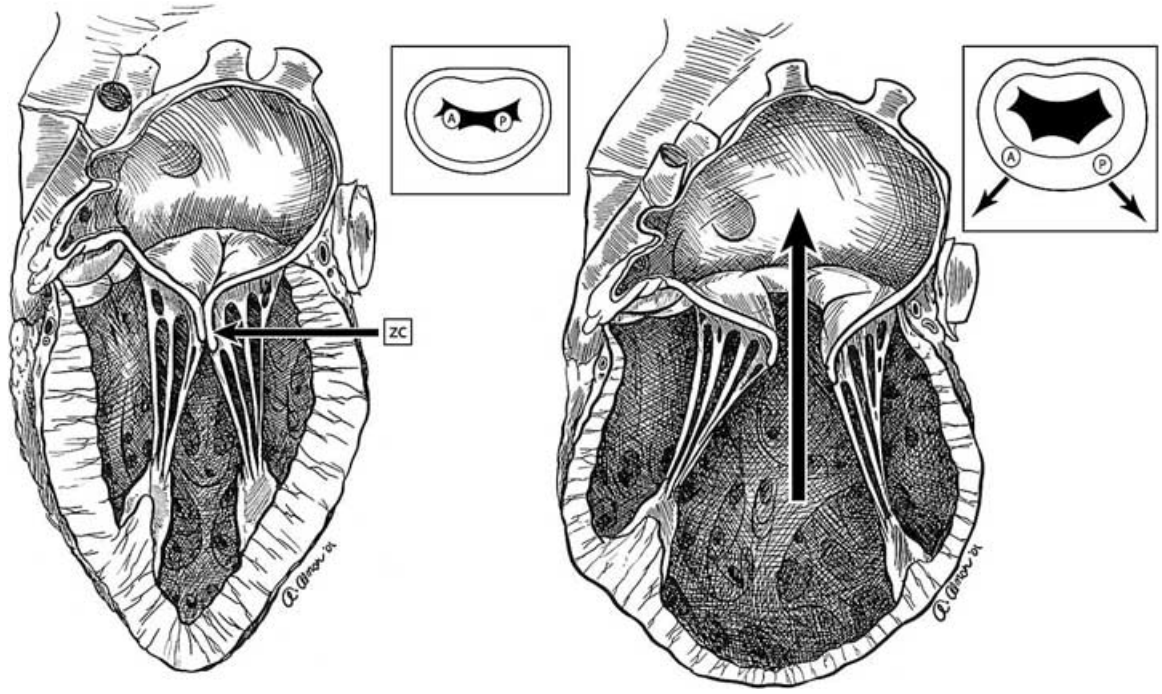

Figure 1. *The morphologic changes seen in heart failure. Shown on the left is the normal mitral apparatus and its effective zone of coaptation (ZC), while changes that occur in heart failure are shown on the right. Theses alterations include myocardial thinning and dilatation, blunting of the aorto-mitral angle, widening of the interpapillary distance, increased leaflet tethering, and decreased leaflet-closing forces. This leads to altered force vectors on the papillary muscles (see insets). These morphologic changes combine to result in loss of the zone of coaptation and central mitral regurgitation.*

for the enlarging orifice. Eventually, the leaflet coaptation becomes ineffective and a central regurgitant jet of functional insufficiency develops.[9] Therefore, the most significant determinant of mitral valve coaptation, leaflet orifice area, and MR are the dimensions of the mitral valve annulus. The LV dimension is less important in functional MR because chordal and papillary muscle length are not significantly altered in people with idiopathic cardiomyopathy with or without MR.[6]

In a recent study of patients with severe heart failure managed with pharmacologic agents (diuretics, nitrates, and afterload reduction agents), the observed decrease in filling pressure and systemic vascular resistance led to a reduction in the dynamic MR associated with their heart failure. This was attributed to a reduction in the regurgitant orifice area related to the decrease in LV volume and annular distension.[10] This complex relationship between mitral annular area and leaflet coaptation may explain why, paradoxically, an undersized "valvular" repair can help a myopathic "muscular" problem.

Increases in LV preload, wall tension, diastolic volume, and stroke volume are all documented ventricular adaptations to severe MR. There is a significant decrease in the efficiency of the LV contraction and the work expended by the LV, which produces flow that ultimately does not contribute to effective forward cardiac output. In these patients, maintenance of forward flow becomes more difficult because up to 50% of the stroke volume is ejected into the left atrium before the aortic valve even opens.[11] Eliminating the reversal of flow or regurgitant volume alleviates the excessive work place on the LV. In cases of severe myocardial dysfunction, the positive effects of the elimination of the regurgitant flow may be even more pronounced. By utilizing mitral valve repair to restore the alterations in the annular-ventricular unit, serves to not only restore valvular competency but also to improve ventricular function.[12–16]

MANAGEMENT

For patients with cardiomyopathy and functional MR, treatment of the underlying CHF with the use of diuretics, ACE-inhibitors, and beta blockers remains the mainstay of medical management. Mitral valve replacement has historically been the surgical approach to patients with MR. However, little was understood of the adverse consequences that interruption of the annulus-papillary muscle continuity had on LV systolic function.[17] Ultimately, this method of mitral valve replacement in patients with heart failure was associated with high mortality rates.[18,19] In fact, it has been shown that the mortality ascribed to these patients from mitral valve replacement was due to the disruption of the subvalvar apparatus and loss of LV function.[20–23] Several studies have demonstrated that preservation of the annulus-papillary muscle continuity is of paramount importance for the preservation of LV function.[24,25] Preserving the mitral valve apparatus and LV with mitral valve repair has been demonstrated to enhance and maintain LV function and geometry and decrease wall stress.[26,27] Therefore, maintaining the chordal, annular, and subvalvar continuity positively impacts mitral geometric relationships and improves overall ventricular function. It may prove most crucial in patients

with compromised LV function. Mitral valve repair has been shown to be safe with a significant decrease in operative morbidity and mortality and good long-term outcomes.

While surgically treating heart failure, it is important to recall that the diameter of the mitral valve annulus is the most significant determining factor of leaflet coaptation and MR.[10] Utilizing the technique of undersizing and overcorrecting to repair the mitral valve serves to restore the zone of coaptation (ZC) and permits its effective application to patients with diminished heart failure (Fig. 2). This would seem intuitive given the fact that the left ventricular dimensions are of less importance in functional MR wherein the length of the chordae and papillary muscles are similar in myopathic hearts regardless of the presence of MR. The degree of LV dilation does not determine the degree of dilation of the mitral ring because they are independent processes. Furthermore, there is increased understanding and knowledge of what happens to the left ventricular unit of the mitral valve. We now know that the intertrigone distance is not fixed and does indeed dilate.[28,29] These new findings assist us in the advancing surgical approaches to heart failure. As the distance between the fibrous trigones is not stable and dilation occurs along both the insertion of the posterior leaflet and in the anterior portion, the role and applicability of undersizing and overcorrecting with a complete annuloplasty ring is further classified.

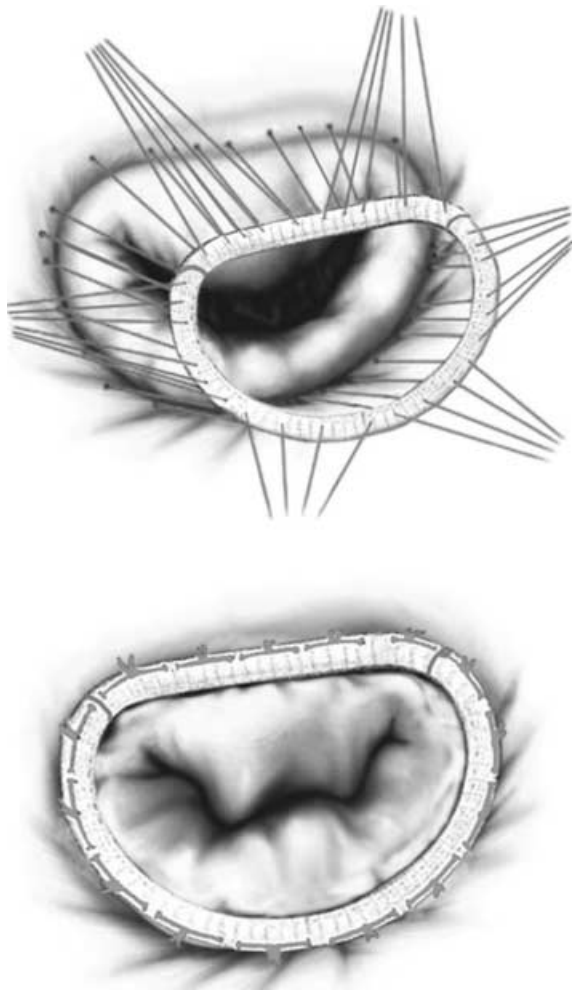

Figure 2. *Geometric mitral reconstruction. Successful augmentation of the zone of coaptation and prevention of recurrent MR can be achieved by the placement of multiple annular sutures followed by an undersized circumferential flexible annuloplasty ring.*

Several technical points are worthy of mention. We advocate the use of a circumferential ring, which results in a better distribution of forces. Additionally, numerous sutures should be used to secure the ring. Doing so will decrease the stress placed on each individual suture. Because the beta receptors are down-regulated in these patients due to beta overstimulation, we routinely use other means for inotropic support during surgery. This includes the phosphodiesterase inhibitor Milrinone used concomitantly with norepinephrine. Additionally, Aprotinin is used for hemostasis.

The relative contraindications to this operation are right ventricular failure, severely enlarged left ventricular diameter and volumes, elevated pulmonary artery pressures, extremely high norepinephrine levels, TNF, and BNP. All of these are markers of long-term CHF. Unfortunately, modalities of medical treatment that included the use of recombinant agents directed at TNF-α receptors and antiendothelin have failed to improve treatment and outcome. There is a condition when the technique of undersizing and overcorrecting for MR in myopathic hearts may not have optimal results. This is when there is asymmetrical left ventricular geometry. Conceivably, the development of new shaped rings could reverse these 3D geometrical changes.

To date, at the University of Michigan (1994–2003), over 200 patients with end-stage cardiomyopathy and refractory MR have undergone mitral valve repair with an undersized flexible annuloplasty ring. All patients had NYHA Class III or IV heart failure despite receiving maximal medical therapy including diuretics, nitrates, afterload reduction agents, particularly ACE inhibitors, and beta blockade. Patients had severe LV systolic dysfunction with a mean ejection fraction of 16 ± 5. Overall operative mortality was 5%. There have been eight 30-day mortalities: one intraoperative death due to right ventricular failure, two from CHF, two from a cerebrovascular bleed, and three succumbed to multisystem organ failure. Five patients required IABP support, and there were no patients who required the use of a LV assist device. The mean duration of follow-up in these patients was 49 months (range 1–74 months), with 1-, 2-, and 5-year actuarial survival of 82%, 71%, and 52%, respectively. There have been 26 late deaths: 12 from sudden ventricular arrhythmias, 8 from progression of CHF without MR, 3 secondary to complications for other operative procedures, 2 that progressed to transplantation, and 1 from suicide.

The immediate postoperative echocardiograms showed a mean transmitral gradient of 3 ± 1 mmHg (range 2–6mmHg). At 7 years of follow-up, patients are in NYHA Class I or II, with a mean ejection fraction of 26 ± 8. The NYHA Class improved for each patient and all patients reported subjective improvement in functional status. There was a demonstrated improvement in LV ejection fraction (LVEF), cardiac output, and end-diastolic volumes for all patients, with a reduction in

sphericity index and regurgitant fraction. Although significant undersizing of the mitral annulus was employed to overcorrect for the ZC, no mitral stenosis was induced and there was no evidence of systolic anterior motion (SAM). This was most likely due to widening of the aorto-mitral angle and increased LV size seen in myopathic patients. In addition, acute remodeling of the base of the heart from the undersizing of the mitral annular ring may also contribute to the improvement seen in these myopathic hearts. This may re-establish the ellipsoid shape and somewhat normal geometry to the base of the LV.[12–15] These encouraging results have been confirmed in several recent studies. Bitran et al.[30] noted a decrease in heart failure symptoms and a decrease in New York Heart Association (NYHA) functional class in 115 patients. In another report of 81 patients undergoing mitral valve surgery for mitral valve regurgitation in dilated cardiomyopathy, LVEF improved from 24% to 32% and there was an improvement in NYHA class from 3.3 to 1.6. Survival in this study was 73%, 58%, and 38% at 1, 3, and 5 years, respectively.[16] Finally, in a series of 44 patients who underwent isolated mitral valve surgery, LVEF improved from 28% to 36% and NYHA functional class decreased from 2.9 to 1.2. Survival was 89%, 86%, and 67% at 1, 2, and 5 years, respectively. Furthermore, this study noted a decrease in the left ventricular chamber sphericity.[31] Interestingly, following the repair patients were able to tolerate even higher does of medical therapy.

Further evidence of underlying mechanisms of why mitral valve repair for patients with cardiomyopathy may be successful is taken from a study of the coronary flow characteristics in patients with MR, in the absence of coronary artery disease. This study assessed coronary flow characteristics in patients before and after mitral valve reconstruction. Coronary flow reserve was limited in patients with MR due to an increase in baseline coronary flow and flow velocity, which was related to LV volume overload, hypertrophy, and preload (LV wall stress). The restriction in coronary flow reserve improved following mitral valve reconstruction because of a reduction in the baseline coronary flow and flow velocity, once the LV preload, work, and mass were reduced.[32] Based on this study in patients with MR and cardiomyopathy, a restriction in the coronary flow reserve would seem probable and an improvement in flow reserve and velocity would be expected following mitral valve repair. Ultimately mitral valve repair within this setting leads to an improved LV geometry.

SUMMARY

The MR associated with end-stage heart failure is thought to occur due to a progressive dilation of the annular-ventricular apparatus, altered ventricular geometry, loss of leaflet coaptation, and LV wall-papillary muscle dysfunction. In this setting, medical management alone may not be sufficient and the perceived high morbidity and mortality of surgical interventions associated with end-stage heart failure patients no longer apply. Mitral valve repair with an annuloplasty ring effectively corrects MR in cardiomyopathy patients. It is safe in this high-risk patient population, and has acceptable operative mortality. The effects of this procedure with severe myocardial dysfunction may be attributed to a decrease in the regurgitant orifice area, better effective forward flow, and an increase in coronary flow reserve, all of which contribute to restoration of the LV geometry. Combined with optimal medical management, the treatment of end-stage heart failure can be expanded with results that approach that of transplantation without the need for immunosuppression while decreasing the need for anticoagulation. Thus, by restoring mitral competency and ventricular geometry, mitral reconstruction offers expanded treatment strategy for end-stage heart failure.

REFERENCES

1. Tavazzi L: Epidemiology of dilated cardiomyopathy: A still undetermined entity. Eur Heart J 1997;18(1):4-6.
2. Hunt SA: Current status of cardiac transplantation. JAMA 1998;280(19):1692-1698.
3. Stevenson LW, Fowler MB, Schroeder JS, et al: Poor survival of patients with idiopathic cardiomyopathy considered too well for transplantation. Am J Med 1987;83(5):871-876.
4. Junker A, Thayssen P, Nielsen B, et al: The hemodynamic and prognostic significance of echo-Doppler-proven mitral regurgitation in patients with dilated cardiomyopathy. Cardiology 1993;83(1-2):14-20.
5. Grigioni F, Enriquez-Sarano M, Zehr KJ, et al: Ischemic mitral regurgitation: Long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation 2001;103(13):1759-1764.
6. Boltwood CM, Tei C, Wong M, et al: Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: The mechanism of functional mitral regurgitation. Circulation 1983;68(3):498-508.
7. Kono T, Sabbah HN, Rosman H, et al: Left ventricular shape is the primary determinant of functional mitral regurgitation in heart failure. J Am Coll Cardiol 1992;20(7):1594-1598.
8. Hendren WG, Nemec JJ, Lytle BW, et al: Mitral valve repair for ischemic mitral insufficiency. Ann Thorac Surg 1991;52(6):1246-1251 (discussion 1251-1252).
9. Chandraratna PA, Aronow WS: Mitral valve ring in normal vs dilated left ventricle. Cross-sectional echocardiographic study. Chest 1981;79(2):151-154.
10. Rosario LB, Stevenson LW, Solomon SD, et al:. The mechanism of decrease in dynamic mitral regurgitation during heart failure treatment: Importance of reduction in the regurgitant orifice size. J Am Coll Cardiol 1998;32(7):1819-1824.
11. Fann J, Ingels N, Miller D: Pathophysiology of mitral valve disease and operative indications. In Edmunds L (ed): Cardiac Surgery in the Adult. McGraw-Hill: New York, 1997, pp. 959-990.
12. Bach DS, Bolling SF: Early improvement in congestive heart failure after correction of secondary mitral regurgitation in end-stage cardiomyopathy. Am Heart J 1995;129(6):1165-1170.
13. Bolling SF, Deeb GM, Brunsting LA, et al: Early outcome of mitral valve reconstruction in patients with end-stage cardiomyopathy. J Thorac Cardiovasc Surg 1995;109(4):676-682 (discussion 682-683).
14. Bach DS, Bolling SF: Improvement following correction of secondary mitral regurgitation in end-stage cardiomyopathy with mitral annuloplasty. Am J Cardiol 1996;78(8):966-969.
15. Bolling SF, Pagani FD, Deeb GM, et al: Intermediate-term outcome of mitral reconstruction in cardiomyopathy.

J Thorac Cardiovasc Surg 1998;115(2):381-386 (discussion 387-388).
16. Chen FY, Adams DH, Aranki SF, et al: Mitral valve repair in cardiomyopathy. Circulation 1998;98(19 Suppl):II124-II127.
17. Pitarys CJ, II, Forman MB, Panayiotou H, et al: Long-term effects of excision of the mitral apparatus on global and regional ventricular function in humans. J Am Coll Cardiol 1990;15(3):557-563.
18. Pinson CW, Cobanoglu A, Metzdorff MT, et al: Late surgical results for ischemic mitral regurgitation. Role of wall motion score and severity of regurgitation. J Thorac Cardiovasc Surg 1984;88(5 Pt 1):663-672.
19. Phillips HR, Levine FH, Carter JE, et al: Mitral valve replacement for isolated mitral regurgitation: Analysis of clinical course and late postoperative left ventricular ejection fraction. Am J Cardiol 1981;48(4):647-654.
20. Gallino A, Jenni R, Hurni R, et al: Early results after mitral valvuloplasty for pure mitral regurgitation. Eur Heart J 1987;8(8):902-905.
21. Rankin JS, Feneley MP, Hickey MS, et al: A clinical comparison of mitral valve repair versus valve replacement in ischemic mitral regurgitation. J Thorac Cardiovasc Surg 1988;95(2):165-177.
22. Akins CW, Hilgenberg AD, Buckley MJ, et al: Mitral valve reconstruction versus replacement for degenerative or ischemic mitral regurgitation. Ann Thorac Surg 1994;58(3):668-675 (discussion 675-676).
23. Alvarez JM, Deal CW, Loveridge K, et al: Repairing the degenerative mitral valve: Ten- to fifteen-year follow-up. J Thorac Cardiovasc Surg 1996;112(2):238-247.
24. Sarris GE, Cahill PD, Hansen DE, et al: Restoration of left ventricular systolic performance after reattachment of the mitral chordae tendineae. The importance of valvular-ventricular interaction. J Thorac Cardiovasc Surg 1988;95(6):969-979.
25. David TE, Uden DE, Strauss HD: The importance of the mitral apparatus in left ventricular function after correction of mitral regurgitation. Circulation 1983;68(3 Pt 2):II76-II82.
26. Goldman ME, Mora F, Guarino T, et al: Mitral valvuloplasty is superior to valve replacement for preservation of left ventricular function: An intraoperative two-dimensional echocardiographic study. J Am Coll Cardiol 1987;10(3):568-575.
27. Tischler MD, Cooper KA, Rowen M, et al: Mitral valve replacement versus mitral valve repair. A Doppler and quantitative stress echocardiographic study. Circulation 1994;89(1):132-137.
28. Hueb A, Jatene F, Moreira L, et al: Ventricular remodeling and mitral valve modifications in dilated cardiomyopathy: New insights from anatomic study. J Thorac Cardiovasc Surg 2002;124(6):1216–1224.
29. McCarthy P: Does the intertrigonal distance dilate? Never say never. J Thorac Cardiovasc Surg 2002;124(6):1078-1079.
30. Bitran D, Merin O, Klutstein MW, et al: Mitral valve repair in severe ischemic cardiomyopathy. J Card Surg 2001;16(1):79-82.
31. Bishay ES, McCarthy PM, Cosgrove DM, et al: Mitral valve surgery in patients with severe left ventricular dysfunction. Eur J Cardiothorac Surg 2000;17(3):213-221.
32. Akasaka T, Yoshida K, Hozumi T, et al: Restricted coronary flow reserve in patients with mitral regurgitation improves after mitral reconstructive surgery. J Am Coll Cardiol 1998;32(7):1923-1930.