Paradoxic Decrease in Ischemic Mitral Regurgitation With Papillary Muscle Dysfunction

Insights From Three-Dimensional and Contrast Echocardiography With Strain Rate Measurement

Emmanuel Messas, MD, MSc; J. Luis Guerrero, BS; Mark D. Handschumacher, BS;
Chi-Ming Chow, MD; Suzanne Sullivan, BS; Ehud Schwammenthal, MD, PhD; Robert A. Levine, MD

Background—Ischemic mitral regurgitation (MR) was first ascribed to papillary muscle (PM) contractile dysfunction. Current theories include apical leaflet tethering caused by left ventricular (LV) distortion, but PM dysfunction is still postulated and commonly diagnosed. PM contraction, however, parallels apical tethering, suggesting the hypothesis that PM contractile dysfunction can actually diminish MR due to ischemic distortion of the inferior base alone.

Methods and Results—We therefore occluded the proximal circumflex circulation in 7 sheep while maintaining PM perfusion, confirmed by contrast echocardiography. By 3D echocardiography, we measured the tethering distance between the ischemic medial PM tip and anterior annulus and LV ejection volume to give MR (by subtracting flowmeter LV outflow). In 6 sheep without initial MR, inferior ischemia alone produced PM tip retraction with restricted leaflet closure and mild-to-moderate MR (regurgitant fraction, $25.2\pm2.8\%$). Adding PM ischemia consistently decreased MR and tethering distance (5.2 ± 0.3 to 1.4 ± 0.3 mL; $+3.8\pm0.5$ mm to -2.2 ± 0.7 mm axially relative to baseline; $P<0.001$) as PM strain rate decreased from $+0.78\pm0.07$ per second (contraction) to -0.42 ± 0.06 per second (elongation, $P<0.001$) and leaflet tenting decreased. In one sheep, prolapse and MR resolved with inferior ischemia and recurred with PM ischemia.

Conclusions—PM contractile dysfunction can paradoxically decrease MR from inferobasal ischemia by reducing leaflet tethering to improve coaptation. This emphasizes the role of geometric factors in ischemic MR mechanism and potential therapy. (*Circulation*. 2001;104:1952-1957.)

Key Words: mitral valve ■ regurgitation ■ remodeling ■ myocardial infarction ■ echocardiography

Mitral regurgitation (MR) is a common complication of ischemic heart disease and myocardial infarction, doubling the risk of late death.[1,2] Since its initial recognition by Burch and De Pasquale,[3–5] ischemic MR has been attributed, in both name and mechanism, to dysfunction of the papillary muscles (PMs), impairing their normal support of effective coaptation.[3–7] Early experimental studies refined this concept by suggesting that to produce important MR required damaging not only the PMs but also the underlying myocardium[8–11]; MR, however, also frequently developed in the chronic phase of ethanol injection into the PMs.[8] More recently, Kisanuki et al[7] showed that patients with diminished PM shortening had the most severe MR, perpetuating the term "PM dysfunction," which remains common in clinical parlance and echocardiographic interpretation. The goal of

this study is to reassess the role of PM dysfunction in ischemic MR.

Prevailing explanations for such MR have focused on two factors: (1) ischemic distortion of ventricular geometry, displacing the attachments of the mitral leaflets to the PMs and annulus and restricting their ability to close effectively at the annular level,[12–19] and (2) decreased left ventricular (LV)-generated force acting to close the leaflets,[11] particularly when they are under increased tension.[18] Both factors would produce the apically tented or tethered leaflet configuration referred to as incomplete mitral leaflet closure.[6] Nevertheless, a potential contributory role of PM contractile dysfunction has remained within the range of proposed mechanisms. This persistent notion is particularly problematic when we consider the following reasoning: If, in fact,
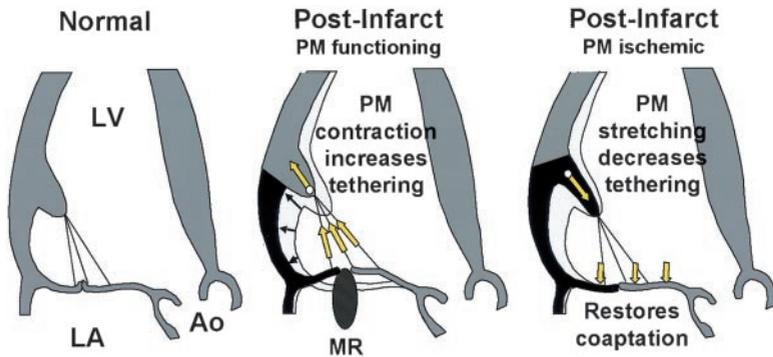
Figure 1. Hypothesis: How PM dysfunction can decrease ischemic MR. Left, Baseline configuration of LV with normal mitral leaflet closure. Middle, Inferobasal infarction with PM still functioning, causing MR by outward distortion of the inferior base. Right, Extension of ischemic zone to include PM can paradoxically diminish MR by reducing tethering so that leaflets can seat better at annular level. Ao indicates aorta.

ischemic MR results from a net imbalance of apically directed forces—increased tethering and diminished LV contraction—then normal PM contraction, which is also directed toward the apex, should in principle increase apical tethering and augment MR. Conversely, we can propose the hypothesis that in the presence of MR caused by increased tethering, for example, from ischemia with outward distortion of the inferior base of the heart (but not involving the PMs), adding contractile dysfunction of the PMs can paradoxically diminish MR by allowing the leaflets to seat better and approach the annular level more closely to close more effectively. Tethering may also be reduced by possible stretching of the ischemic papillary muscle toward the annulus by LV force transmitted through the leaflets and chords (Figure 1). Testing this hypothesis is important not only to sharpen our understanding of mechanism but also practically because abnormal tethering can potentially be addressed mechanically,[1,2,20] but restoring PM contractile function may not be possible.

We tested this hypothesis in an experimental model that allows us to separate ischemic dysfunction of the PMs from that of the inferoposterior wall between the insertion of the PMs and the mitral annulus. Three-dimensional echocardiography was used to quantify the relations between components of the mitral apparatus; contrast echocardiography to confirm PM perfusion; and Doppler strain rate to measure longitudinal PM contraction noninvasively, without PM instrumentation.

Methods

Experimental Model

To separate ischemia and perfusion of the inferoposterior base from that of the more apically positioned PMs, we used a technique similar to the salvage perfusion used in angioplasty. The aim was to infarct a proximal (basal) portion of the left circumflex (LCX) coronary artery territory while maintaining perfusion of the more distal (apical) papillary muscles. An 8F wide-bore cannula was advanced from the left carotid artery to the ostium of the left main coronary artery, and a smaller 6F perfusion catheter was inserted through it with its tip placed within the circumflex, just before the origin of the second obtuse marginal branch (Figure I; can be found Online at http://www.circulationaha.org); the guiding catheter was then withdrawn. The perfusion catheter had a side-hole entry port at the aortic root level. Therefore, ligatures could be placed around the proximal LCX, near its origin and before the second obtuse marginal, to produce ischemia of the inferior base; at the same time, the perfusion catheter would continue to convey blood from the aortic root to the more distal LCX territory to maintain PM perfusion. Subsequently, the proximal LCX ligatures could be closed and the 6F perfusion catheter withdrawn to produce ischemia of both the inferior base and the medial PM within the center of the ischemic

territory.[15–17] (The apex, anterolateral wall, and majority of the septum still contract in this sheep model,[16] unlike more extensive changes that can develop in the dog.[13])

Protocol

This approach was applied in 7 Dorsett hybrid sheep anesthetized with thiopental (0.5 mL/kg), intubated, and ventilated at 15 mL/kg with 2% isoflurane and oxygen and given glycopyrrolate (0.4 mg IV), with procainamide (15 mg/kg IV) and lidocaine (3 mg/kg IV followed by 2 mg/min) infused 10 minutes before coronary ligation.[15,16] After left thoracotomy and pericardial incision were performed, hemodynamic monitoring devices were inserted (left atrial [LA] and LV Millar catheters and aortic root Transonic flow probe). After baseline imaging and hemodynamic measurements were performed, including assessment of PM contraction (see below), the PM perfusion catheter was placed and the proximal LCX ligatures were tied to produce ischemia of the inferior base; after 30 minutes (the typical time for wall distortion and ischemic MR to develop), imaging and hemodynamics were repeated, and PM perfusion was confirmed by contrast echocardiography (see below). In the final stage, the proximal LCX ligatures were closed and the perfusion catheter was removed, producing combined inferior and PM ischemia.

Three-Dimensional Echocardiography

Thirty rotated LV apical views were acquired (5 MHz, epicardial, Agilent Sonos 5500) with suspended respiration as previously described and validated against sonomicrometry.[17] Three-dimensional LV volumes were obtained through endocardial borders from 9 views.[21] MR stroke volume was calculated as LV ejection volume minus aortic outflow volume directly measured by flowmeter,[22] and MR orifice area was calculated from regurgitant stroke
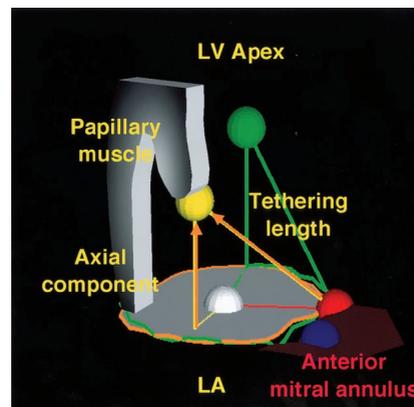

Figure 2. Tethering lengths between PM and anterior mitral annulus. Tethering length over which mitral leaflets are stretched between PM tips and anterior annulus was measured as well as axial component of this tethering length in the direction of PM longitudinal contraction.
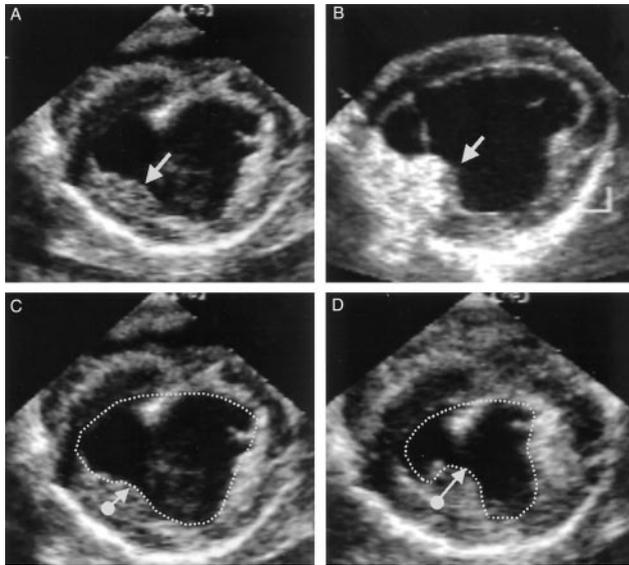
Figure 3. PM perfusion and function assessment. A and B, Contrast echocardiographic image (B; A shows baseline) showing preserved PM perfusion with inferobasal defect. C and D, Short-axis views showing preserved PM thickening despite inferobasal ischemia during diastole (C) and systole (D).

volume and LV-LA pressure gradient (Yellin-modified Gorlin equation).[17]

The least-squares plane of the mitral annular hinge points (confirmed by cineloop review) was established as the reference frame[23]; projecting the annulus onto this plane gave annular area. Mitral geometry was analyzed at mid-systole (time of closest leaflet–annulus approach).[6,24] The PMs were traced, and their most basal and anterior tips were identified from several adjacent images.

The tethering length over which the valve is stretched between the PMs and the relatively fixed fibrous portion of the annulus (Figure 2) was measured from each PM tip to the medial trigone of the aortic valve (medial junction of aortic and mitral annuli); this point was selected because the line connecting it with the mitral annular centroid roughly bisected the line connecting the PM tips, so that symmetric outward PM displacements appear symmetric in this reference frame.[17] Tethering length was used because it has previously emerged as the strongest predictor of ischemic MR.[17] Three-dimensional echocardiography was used because it relates multiple structures in multiple views, establishes annular and trigonal references, and optimizes PM tip selection. Three-dimensional echocardiography also allowed us to select the component of tethering length parallel to the LV long axis, which should express the major effect of PM inactivation with loss of its longitudinal contraction (compare Figure 1).

PM Assessment

PM perfusion was confirmed when ischemia was limited to the inferobasal wall by injecting 3 mL of agitated saline echo contrast into the 6F perfusion catheter at its carotid entry port (Figures 3A and 3B). Three complementary measures assessed PM contraction: (1) cross-sectional mid-PM thickening (Kaul et al,[11] Figures 3C and 3D); (2) M-mode thickening from endocardial to PM interfaces by epicardial probe over the PM; and (3) longitudinal contraction by strain rate. The rate of change of the length between PM insertion and tip equals the difference in the velocity of these two points; dividing by initial length gives strain rate. This was measured with the low-pass filter of an ATL HDI 5000 scanner, with velocity components parallel to the PM long axis used to assess longitudinal contraction.

Statistical Analysis

Hemodynamic and geometric measures were compared among stages and sheep by 2-way ANOVA. Significant ANOVAs were explored by 2 paired *t* tests (inferobasal ischemia versus baseline and versus combined inferior and PM ischemia), with significance at $P<0.01$ (Bonferroni-corrected).

Results

Mitral Regurgitation

Six of the 7 sheep studied had no or only trace MR at baseline and are analyzed together; the seventh had mitral valve prolapse and moderate MR at baseline and was studied with the same protocol but reported separately.

In the 6 sheep without baseline prolapse, ischemia of the inferior base alone with preserved PM perfusion outwardly distorted the affected wall, retracting the PM tip away from the annulus and causing apical tenting of the mitral leaflets with mild to moderate MR (Figure 4). In all animals studied, adding PM ischemia consistently decreased the MR despite greater degrees of LV systolic dysfunction and annular dilation (Table). Images showed improved seating of the leaflets at the annular level with PM ischemia; the inactivated medial PM appeared to elongate, and its tip moved closer to the annulus, as quantified below. Although the MR driving pressure ($=LV-LA$ pressure) trended toward lower values with the larger ischemic territory, the MR orifice area, which factors out the driving pressure, also decreased considerably with added PM ischemia. Moreover, MR stroke volume and orifice area decreased despite a trend (not significant) toward lower mitral valve closing force$=(LVP-LAP)\times$mitral annular area.

Quantitative Geometric Analysis

The mid-systolic PM-to-anterior annular tethering length for the medial PM (its axial component, expressing the major effect of PM inactivation and loss of its longitudinal contraction) increased with ischemia limited to the inferobasal wall as that akinetic wall remodeled away from the anterior annulus, displacing the PM along with it. This value returned toward normal and actually decreased relative to baseline when PM ischemia was added and the apical vector of PM contraction was lost (Figure II; also see the Table). Moreover, there was a nonlinear relation between MR and tethering length, with a steeper rise in MR as tethering increased, suggesting that a normal excess of leaflet area is being used up (Figure II).

PM Assessment

Contrast echocardiography demonstrated preserved PM perfusion in the stage with inferobasal ischemia in all animals. Similarly, PM contraction was preserved in that stage but was lost in the final stage. The normal peak systolic strain rate corresponding to longitudinal PM contraction was 0.78 ± 0.07 per second (average$\pm$SD in 5 beats) versus 0.75 ± 0.03 per second with inferobasal ischemia but normal PM perfusion (no significant difference) and -0.42 ± 0.06 per second with combined inferior and PM ischemia ($P<0.001$); this negative strain rate, indicating that the velocity of motion toward the apex is lower at the PM tip than at its insertion, corresponds to PM elongation.
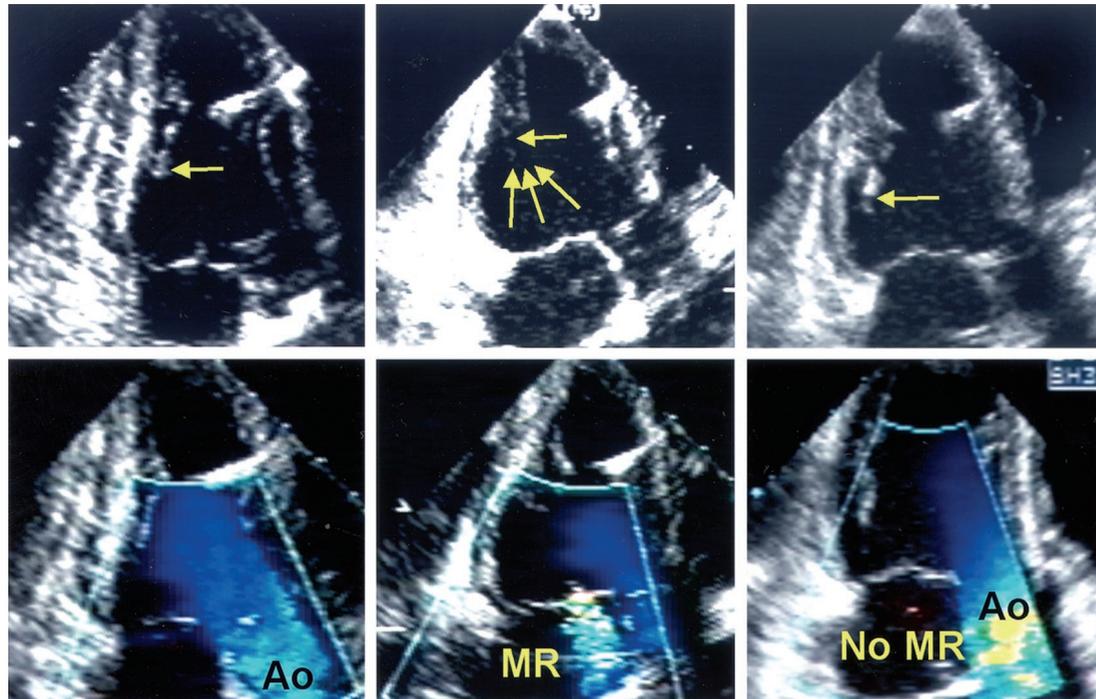
Figure 4. Results in mid-systolic apical 2D echo images with Doppler color flow mapping. Left, Baseline, with normal mitral coaptation. Arrow indicates PM tip. Middle, Apically tented leaflets and MR with ischemia of the inferior base alone; upward arrows indicate direction of tethering to displaced PM tip. Right, Resolution of MR and improved mitral coaptation with added PM ischemia; PM is elongated and its tip (arrow) is closer to the annulus.

Prolapse

In the sheep with posterior leaflet prolapse and significant baseline MR, inferobasal ischemia actually reduced MR, with an increase in tethering length retracting the leaflets into the LV and eliminating prolapse. With PM ischemia, prolapse and MR recurred in a pattern parallel to that observed in the other sheep, with PM ischemia normalizing the augmented tethering imposed on the leaflets by inferobasal remodeling (Figure III).

Discussion

After nearly 4 decades, ischemic MR in the absence of PM rupture is still widely referred to as PM dysfunction in both clinical and echocardiographic practice. Although the concept has been broadened to include ischemic ventricular distortion with displacement of the PMs along with their underlying myocardium, a role for PM contractile dysfunction is still supported by clinical and experimental observations.[7,8] Such a role is difficult to test directly because contractile dysfunction of the PMs frequently accompanies geometric changes of their adjacent walls. The experimental model in this study effectively separates these two factors. The results show that ischemic distortion of the inferior wall restricts leaflet closure and causes MR but that adding PM contractile dysfunction actually decreases MR stroke volume and orifice area despite a larger ischemic territory. This results from normalization of the 3D tethering relations between the PM tips and mitral annulus.[25] Normal PM contraction toward the apex acts to augment leaflet tethering; reducing PM contraction allows the leaflets to seat better at the annular level with less apical tenting and MR. The finding of a negative strain rate,

indicating PM elongation that allows the PM tip to approach closer to the annulus, is consistent with Gam's experimental observations that ischemic papillary muscles are elongated in situ by the force exerted on them through the mitral leaflets and chordae.[26]

Implications

Mechanistically, these results emphasize the central role of geometric changes and tethering in causing ischemic MR.[27] Practically, they lend further support to therapeutic efforts directly targeting the fundamental tethering imbalance that restricts leaflet closure, either by plicating distorted infarct regions[19,28] or by resecting myocardium between the PMs.[1,29] Such interventions aim to overcome the variable, often frustrating results of annuloplasty techniques that only incompletely address tethering at the annular end.[1,2,20,30] The benefit of preventing ischemic distortion can also be a factor in decisions regarding thrombolysis in acute inferior infarctions despite their often limited size.[31] The results of this study can help us understand the dynamic relation between leaflets and ventricle, for example, the diminution of mitral valve prolapse in occasional patients whose left ventricles dilate,[32] as in our seventh sheep. Finally, from a technical point of view, the terminology "PM dysfunction" as an explanation for ischemic MR with incomplete mitral leaflet closure or apical tenting in echocardiographic reports should be replaced with a term such as "PM displacement."

Limitations and Prior Literature

The clinical spectrum of ischemic MR includes widely varying location and chronicity of ischemia, PM tip geometry, and

Hemodynamic, LV, Mitral Valve, and PM Measurements

	Baseline (1)	Inferior Ischemia (2)	Inferior+PM Ischemia (3)
Heart rate, bpm	118±3.3	120.5±10.8	122±3.1
LVP, mm Hg	83.3±2.5	77.5±2.1*	68.3±2.1
LAP, mm Hg	12.2±0.83	19.7±1.7*	16.2±1.5
LVP-LAP, mm Hg	71.2±2.6	57.8±2.7*	52.2±2.2
LV dp/dt, mm Hg/s	1533±55.8	1266±42.1*	1200±25.8
LVEDV, mL	45.2±0.8	52.2±1.1*	52.7±1.1
LVESV, mL	18.5±0.4	29.6±1.0*	32±1.3
EF, %	59±1.4	43±2.1*	39±2.7
MR stroke volume, mL	1.3±0.3	5.2±0.3*	1.4±0.3†
MR regurgitation fraction, %	4.9±1	25.2±2.8*	7±1.5†
MR orifice area, mm^2	1.9±0.5	9.2±0.8*	2.4±0.5†
Tethering length, axial component (medial PM, mm)	15.4±0.7	19.2±0.5*	13.2±0.7†
MA area, cm^2	5.6±0.2	6.2±0.3	6.5±0.3
Closing force, mm Hg/cm^2	404.3±23.6	360.4±13.8	336.8±14.1
PM % thickening (SAX)	49.6±5.2	47.2±3.1	7.2±2†
PM % thickening (M-mode)	34.3±3.4	37.0±3.3	7.5±2†
Strain rate, s^{-1}	0.78±0.07	0.75±0.03	−42±0.06†

LVP indicates LV pressure; LAP, LA pressure; LVED, LV end-diastolic volume; LVES, LV end-systolic volume; tethering length, distance of PM from mitral annulus (MA); and SAX, short axis. All 2-way ANOVAs but one (heart rate) were significant ($P<0.01$). Significant changes ($P<0.01$, Bonferroni) are indicated for 2-way comparisons.

*Baseline vs inferior ischemia, †inferior ischemia vs inferior+PM ischemia.

potentially leaflet length. The purpose of this study, however, was specifically to explore a model that could separate changes in PM contractile function from increased tethering caused by ischemic distortion of the underlying wall. In our mechanistic studies, therefore, a relatively localized initial ischemic insult was specifically induced, sufficient to produce MR but not so great that PM ischemia and elongation could no longer restore effective coaptation. The PM dysfunction was also acute to avoid superimposed PM scarring and retraction that could by itself introduce fixed tethering and preclude elongation, a potential explanation for why ethanol injections into the PMs, which failed to produce MR acutely, did so after several weeks in the study of Hider et al.[8]

These considerations are therefore helpful when we consider this study in the perspective of the prior literature. The concept that "failure of the PM to contract may actually compensate for the altered spatial relationships... so that the valve leaflets come into better apposition" was actually advanced as an explanation for a decrescendo murmur of ischemic MR by Burch et al.[5] Despite this, Kisanuki et al[7] correlated PM contractile dysfunction with ischemic MR; however, this dysfunction was also accompanied by more widespread LV dysfunction in their clinical series, with the potential for more severe tethering. Our study used a model of inferobasal ischemia resembling the pattern seen in many patients with ischemic MR to test the hypothesis that ischemic MR can actually be diminished by PM contractile dysfunction. It is reasonable to suppose, however, that with more severe LV dilation and tethering, ischemic MR is likely to persist regardless of PM inactivation.

The study design precluded consistent histologic confirmation of ischemic zone because two stages (with and without PM perfusion) needed to be successively studied in the same animal. Contrast echocardiography was therefore used to confirm PM perfusion; the basic infarct territories defined by LCX branch occlusions have been reported by Llaneras et al.[15,16] Future quantitative 3D reconstruction could potentially be facilitated by voxel and real-time 3D echocardiography.[33,34] Because of the difficulties in measuring PM contraction without implanted markers that may disturb the muscles, we used several complementary techniques, including strain-rate measurement, as well as the demonstration of perfusion and the published technique of Kaul and colleagues[11] of measuring cross-sectional thickening (used to confirm MR with global ischemia and maintained PM perfusion[11]). Although LV-unattached PM length may be greater in some patients,[35] that would in fact favor ischemic PM elongation, decreasing MR as observed.

Conclusions

Papillary muscle contractile dysfunction can paradoxically decrease MR caused by ischemic distortion of the inferior base of the left ventricle; it does so by reducing leaflet tethering to promote more effective leaflet closure. Three-dimensional, contrast, and Doppler strain rate echocardiographic techniques provide physiological tools to support this conclusion, which emphasizes the importance of geometric factors in the mechanism and potential therapy of this complication of ischemic heart disease.

References

1. Rankin JS, Hickey MSJ, Smith LR, et al. Ischemic mitral regurgitation. *Circulation*. 1989;79(suppl I):I-116–I-121.
2. Frater RWM, Cornelissen P, Sisto D. Mechanisms of ischemic mitral insufficiency and their surgical correction. In: Vetter HO, Hetzer R, Schmutzler H, eds. *Ischemic Mitral Incompetence*. New York, NY: Springer-Verlag;1991:117–130.
3. Burch GE, De Pasquale NP, Phillips JH. Clinical manifestations of papillary muscle dysfunction. *Arch Intern Med*. 1963;59:508–520.
4. Phillips JH, Burch GE, De Pasquale NP. The syndrome of papillary muscle dysfunction. *Ann Intern Med*. 1963;59:508–520.
5. Burch GE, De Pasquale NP, Phillips JH. The syndrome of papillary muscle dysfunction. *Am Heart J*. 1968;75:399–415.
6. Godley RW, Wann LS, Rogers EW, et al. Incomplete mitral leaflet closure in patients with papillary muscle dysfunction. *Circulation*. 1981;63:565–571.
7. Kisanuki A, Otsuji Y, Kuroiwa R, et al. Two-dimensional echocardiographic assessment of papillary muscle contractility in patients with prior myocardial infarction. *J Am Coll Cardiol*. 1993;21:932–938.
8. Hider CF, Taylor DEM, Wade JD. The effect of papillary muscle damage on atrioventricular valve function in the left heart. *Q J Exp Physiol*. 1965;50:15–22.
9. Tsakiris AG, Rastelli GC, Amorim D, et al. Effect of experimental papillary muscle damage on mitral valve closure in intact anesthetized dogs. *Mayo Clin Proc*. 1970;45:275–285.
10. Mittal AK, Langston M Jr, Cohn KE, et al. Combined papillary muscle and left ventricular wall dysfunction as a cause of mitral regurgitation: an experimental study. *Circulation*. 1971;44:174–180.
11. Kaul S, Spotnitz WD, Glasheen WP, et al. Mechanism of ischemic mitral regurgitation: an experimental evaluation. *Circulation*. 1991;84:2167–2180.
12. 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;68:498–508.
13. Gillam LD, Levine RA, Guyer DE, et al. Echocardiography. In: Eagle KA, Haber E, DeSanctis RW, et al, eds. *The Practice of Cardiology*. Boston, Mass: Little Brown; 1989:1512–1513.
14. Kono T, Sabbah HN, Rosman H, et al. Mechanism of functional mitral regurgitation during acute myocardial ischemia. *J Am Coll Cardiol*. 1992;19:1101–1105.
15. Llaneras MR, Nance ML, Streicher JT, et al. Pathogenesis of ischemic mitral insufficiency. *J Thorac Cardiovasc Surg*. 1993;105:439–443.
16. Llaneras MR, Nance ML, Streicher JT, et al. Large animal model of ischemic mitral regurgitation. *Ann Thorac Surg*. 1994;57:432–439.
17. Otsuji Y, Handschumacher MD, Schwammenthal E, et al. Insights from three-dimensional echocardiography into the mechanism of functional mitral regurgitation: direct in vivo demonstration of altered leaflet tethering geometry. *Circulation*. 1997;96:1999–2008.
18. He S, Fontaine AA, Schwammenthal E, et al. An integrated mechanism for functional mitral regurgitation: leaflet restriction vs coapting force-in vitro studies. *Circulation*. 1997;96:1826–1834.
19. Liel-Cohen N, Guerrero JL, Otsuji Y, et al. Design of a new surgical approach for ventricular remodeling to relieve ischemic mitral regurgitation: insights from three-dimensional echocardiography. *Circulation*. 2000;101:2756–2763.
20. David TE. Techniques and results of mitral valve repair for ischemic mitral regurgitation. *J Card Surg*. 1994;9:274–277.
21. Handschumacher MD, Lethor J-P, Siu SC, et al. A new integrated system for three-dimensional echocardiographic reconstruction: development and validation for ventricular volume with application in human subjects. *J Am Coll Cardiol*. 1993;21:743–753.
22. Blumlein S, Bouchard A, Schiller NB, et al. Quantification of mitral regurgitation by Doppler echocardiography. *Circulation*. 1986;74:306–314.
23. Levine RA, Handschumacher MD, Sanfilippo AJ, et al. Three-dimensional echocardiographic reconstruction of the mitral valve, with implications for the diagnosis of mitral valve prolapse. *Circulation*. 1989;80:589–598.
24. Schwammenthal E, Chen C, Benning F, et al. Dynamics of mitral regurgitant flow and orifice area in different forms of mitral regurgitation: physiologic application of the proximal flow convergence method. *Circulation*. 1994;90:307–322.
25. Miller GE Jr, Cohn KE, Kerth WJ, et al. Experimental papillary muscle infarction. *J Thorac Cardiovasc Surg*. 1968;56:611–626.
26. Gam E, Hagl S, Heimisch W, et al. Influence of papillary muscle function on the mitral valve and left ventricular mechanics. In: Vetter HO, Hetzer R, Schmutzler H, eds. *Ischemic Mitral Incompetence*. New York, NY: Springer-Verlag; 1991:35–48.
27. Yiu SF, Enriquez-Sarano M, Tribouilloy C, et al. Determinants of the degree of functional mitral regurgitation in patients with systolic left ventricular dysfunction: a quantitative clinical study. *Circulation*. 2000;102:1400–1406.
28. Schwarz ER, Speakman MP, Kloner RA. A new model of ventricular plication: a suturing technique to decrease left ventricular dimensions, improve contractility, and attenuate ventricular remodeling after myocardial infarction in the rat heart. *J Cardiovasc Pharmacol Ther*. 2000;5:41–49.
29. Batista RJV, Santos JLV, Takeshita N, et al. Partial left ventriculectomy to improve left ventricular function in end-stage heart disease. *J Card Surg*. 1996;11:96–97.
30. Carpentier A, Chauvaud S, Fabiani JN, et al. Reconstructive surgery of mitral valve incompetence: ten-year appraisal. *J Thorac Cardiovasc Surg*. 1980;79:338–348.
31. Tenenbaum A, Leor J, Motro M, et al. Improved posterobasal segment function after thrombolysis is associated with decreased incidence of significant mitral regurgitation in a first inferior myocardial infarction. *J Am Coll Cardiol*. 1995;25:1558–1563.
32. Karkal SS, Kramer-Fox R, Devereux RB. Masking of echocardiographic mitral valve prolapse during evolution of dilated cardiomyopathy. *Am Heart J*. 1993;126:242–246.
33. Shiota T, McCarthy PM, White RD, et al. Initial clinical experience of real-time three-dimensional echocardiography in patients with ischemic and idiopathic dilated cardiomyopathy. *Am J Cardiol*. 1999;84:1068–1073.
34. Pandian NG, Nanda NC, Schwartz SL, et al. Three-dimensional and four-dimensional transesophageal echocardiographic imaging of the heart and aorta in humans using a computed tomographic imaging probe. *Echocardiography*. 1992;9:677–687.
35. Gorman JH III, Gorman RC, Jackson BM, et al. Distortions of the mitral valve in acute ischemic mitral regurgitation. *Ann Thorac Surg*. 1997;64:1026–1031.

Circulation

American Heart Association®

Paradoxic Decrease in Ischemic Mitral Regurgitation With Papillary Muscle Dysfunction: Insights From Three-Dimensional and Contrast Echocardiography With Strain Rate Measurement

Emmanuel Messas, J. Luis Guerrero, Mark D. Handschumacher, Chi-Ming Chow, Suzanne Sullivan, Ehud Schwammenthal and Robert A. Levine

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circ.ahajournals.org/content/104/16/1952

Data Supplement (unedited) at:

http://circ.ahajournals.org/content/suppl/2001/09/24/104.16.1952.DC1