Regional wall motion abnormalities and scarring in severe functional ischemic mitral regurgitation: A pilot cardiovascular magnetic resonance imaging study

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Objectives: To relate cardiovascular magnetic resonance–derived segmental wall motion and myocardial scarring and determine whether they are associated with postoperative mitral regurgitation following coronary artery bypass grafting and annuloplasty for severe functional ischemic mitral regurgitation.

Methods: From January 2001 to October 2006, 29 patients with grade ≥3+ chronic functional ischemic mitral regurgitation were studied using cardiovascular magnetic resonance. Wall motion abnormality was graded for 17 standard left ventricular myocardial segments (0 = none, 1+ = hypokinesis, 2+ = severe hypokinesis, 3+ = akinesis, 4+ = dyskinesis), as was degree of hyperenhancement (scarring). Postoperative mitral regurgitation was assessed longitudinally by 71 transthoracic echocardiograms.

Results: Wall motion abnormalities grade ≥2+ were present in most myocardial segments (median 13). Scar >25% was present in a median of 3 segments, and 44% of those were in the territory of the posterior papillary muscle. Nearly all segments (95%) with >25% scar had ≥2+ wall motion abnormality. Although 90% of patients had no mitral regurgitation at hospital discharge, by 6 months, 34% had mitral regurgitation grade ≥2+. There was little association between wall motion abnormality and recurrence of mitral regurgitation ($P > .1$). Seventy percent of patients with scar >25% in the posterior papillary muscle region exhibited postoperative mitral regurgitation of grade ≥2+ by 6 months, compared with 15% with score ≤25% ($P = .07$).

Conclusions: In a pilot study of cardiovascular magnetic resonance imaging in severe functional ischemic mitral regurgitation, severity of posterior papillary muscle region scarring correlated with decreased segmental wall motion and mitral regurgitation early after coronary revascularization and annuloplasty. Routinely assessing scar burden may identify patients for whom annuloplasty alone is insufficient to eliminate mitral regurgitation.

Supplemental material is available online.

The mechanism for persistent or recurrent regurgitation after coronary artery bypass grafting (CABG) and annuloplasty for severe functional ischemic mitral regurgitation (MR) is unclear. It is likely related to acute hemodynamic changes and continued left ventricular (LV) remodeling.[1-4] This process represents the reversible and irreversible consequences of coronary artery disease and therefore does not affect all LV myocardial segments uniformly. Preoperative assessment of segmental myocardial dysfunction and scarring with cardiac magnetic resonance (CMR) imaging may shed light on the mechanism and identify patients for whom concomitant annuloplasty alone is insufficient to eliminate MR.[5] Therefore, purposes of this pilot CMR clinical investigation were to (1) relate regional wall motion abnormalities to degree of myocardial scarring, and (2) determine if either or both play a role in return of MR following CABG and conventional mitral annuloplasty.

PATIENTS AND METHODS

Patients

From January 2001 to October 2006, 29 patients scheduled for primary CABG and mitral annuloplasty for chronic severe functional ischemic MR at Cleveland Clinic were studied by CMR imaging. All had grade 3+ or 4+ MR and a myocardial infarction that had occurred more than 30 days before operation (Table 1). Clinical data were retrieved from the prospective Cardiovascular Information Registry and follow-up echocardiographic findings from the Echocardiography Registry. These registries have been approved for use in research by the Institutional Review Board, with patient consent waived.

Regional Wall Motion and Scarring

Wall motion abnormalities and myocardial scar severity were assessed within 30 days of operation using CMR for each of 17 standard LV myocardial segments (Figure 1).[6] Images were acquired on a 1.5-T Siemens Sonata

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CMR = cardiac magnetic resonance
LAD = left anterior descending coronary artery
LCx = left circumflex coronary artery
LV = left ventricular
MR = mitral regurgitation
RCA = right coronary artery

system (Siemens Medical Solutions, Malvern, Pa) using a phased-array coil during repeated breath-holds of approximately 8 seconds.

Steady-state free precession CMR images were acquired in short-axis planes every 1 cm through the entire LV and in 3 long-axis planes. Segmental wall motion was graded as follows: 0, normal; 1, mild or moderate hypokinesia; 2, severe hypokinesia; 3, akinesia; and 4, dyskinesia.[7]

Gadolinium chelate (gadopentetate dimeglumine, 0.2 μmol $\cdot$ kg^{-1}) was administered and contrast-enhanced images acquired after 10 minutes with a segment inversion recovery technique in identical planes. Segmental gadolinium enhancement, interpreted as myocardial scar, was scored as follows: 0, 0% hyperenhanced; 1, 1% to 25% hyperenhanced; 2, 26% to 50% hyperenhanced; 3, 51% to 75% hyperenhanced; and 4, 76% to 100% hyperenhanced.[7] Previous investigators, using this scoring system, have found a high likelihood of functional improvement or recovery following revascularization in segments with <50% enhancement and low likelihood of functional improvement in segments with >50% enhancement.[7]

CMR-derived segmental wall motion and scarring data were approved for use in research by the Institutional Review Board, with patient consent waived.

Postoperative MR

Postoperative MR was assessed using all in-hospital and postdischarge transthoracic echocardiograms performed at Cleveland Clinic. Seventy-six echocardiograms were available for analysis (Figure E1, *A*). Median time of echocardiographic assessment was 3.5 months, and data were considered reliable to 2 years. Regurgitation was graded qualitatively as 0, none; 1+, mild; 2+, moderate; 3+, moderately severe; and 4+, severe.

Data Analysis

All analyses were performed using SAS statistical software (SAS v9.1, SAS Inc, Cary, NC).

Regional wall motion and scarring. Distribution of mean wall motion grade and mean scar scores was constructed for each myocardial segment. These were averaged over major epicardial coronary artery territories as follows (Figure 1): left anterior descending coronary artery (LAD) territory: segments 1, 2, 7, 8, 13, 14, and 17; right coronary artery (RCA) territory: segments 3, 4, 9, 10, and 15; left circumflex coronary artery (LCx) territory: segments 5, 6, 11, 12, and 16. They were also averaged over the regions from which the anterior papillary muscle (segment 12) and posterior papillary muscle (segments 10 and 11) typically arise, even in the setting of LV enhancement.

Correlation was determined between mean wall motion grade and mean scar score for each segment, coronary artery territory, and papillary muscle region.

Postoperative MR. We estimated the percentage of patients in each MR grade across time by longitudinal temporal decomposition. A nonlinear cumulative logit mixed model[8] was used to resolve number of temporal components and estimate-shaping parameters for each. To accommodate repeated echocardiographic assessments, each temporal component was independently modulated by a time function with a common random intercept. Because of the low-frequency occurrence of MR grade 3+ or 4+, these grades were combined with grade 2+. A focused bivariable analysis was performed to determine the association of regional wall motion abnormalities and scarring with postoperative MR.

Presentation. Continuous data are summarized by mean $\pm$ standard deviation and categorical data by frequency and percentage. Uncertainty is expressed by 68% confidence limits equivalent to $\pm$1 standard error.

TABLE 1. Preoperative characteristics and operative details of patients with chronic ischemic mitral regurgitation having cardiovascular magnetic resonance imaging (n = 29)

Variable	No. (% of 29)
Male	21 (72)
Mean age (y), mean $\pm$ SD	67 $\pm$ 8.8
New York Heart Association functional class	
I	4 (14)
II	14 (48)
III	9 (31)
IV	2 (6.9)
Coronary system disease (stenosis >50%)	
Left main	7 (24)
LAD	26 (90)
RCA	24 (83)
LCx	23 (79)
Number of systems diseased	
0 (left main)	1 (3.4)
1	2 (6.9)
2	7 (24)
3	19 (66)
Mitral regurgitation (grade)	
3+	19 (66)
4+	10 (34)
LV ejection fraction (%), mean $\pm$ SD	22 $\pm$ 8
Noncardiac comorbidities	
Diabetes mellitus (pharmacologically treated)	7 (24)
Peripheral arterial disease	18 (62)
Smoking	20 (69)
Hypertension	17 (59)
Procedure	
Graft location	
RCA	23 (79)
LAD	26 (90)
LCx	25 (86)
Number of ITA grafts used	
0	3 (10)
1	24 (83)
2	2 (6.9)
Mitral annuloplasty	
Ring size (mm)	
24	1 (3.4)
26	14 (48)
28	13 (45)
30	1 (3.5)
Complete ring	7 (24)
Tricuspid annuloplasty	4 (14)
Cardiac resynchronization	3 (10)

ITA, Internal thoracic artery; *LAD*, left anterior descending coronary artery; *LCx*, left circumflex coronary artery; *LV*, left ventricular; *RCA*, right coronary artery; *SD*, standard deviation.

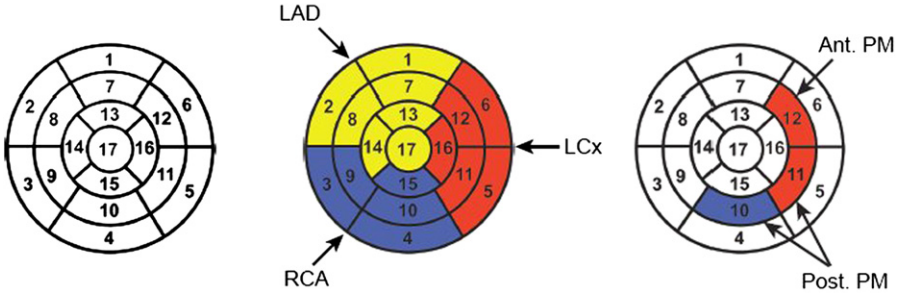

FIGURE 1. Standard myocardial segments for assessing wall motion and scarring. *Left,* Short-axis depiction of segments; outer ring contains basilar segments; middle ring, mid-myocardial segments at papillary muscle level; inner ring, apical segments. *Middle,* Superimposed are territories of the left anterior descending coronary artery *(LAD),* right coronary artery *(RCA),* and left circumflex coronary artery *(LCx). Right,* Regions of the anterior and posterior papillary muscles. *Ant. PM,* Anterior papillary muscle; *Post. PM,* posterior papillary muscle.

RESULTS

Regional Wall Motion and Scarring

Wall motion abnormalities grade ≥2+ were present in the majority of LV segments (median 13 of 17; Figure 2). In the LAD territory, the median number of segments exhibiting a wall motion abnormality was 7 of 7, with 6 of 7 being grade ≥2+. Average LAD mean wall motion grade was 2.1 ± 0.71. In the RCA territory, the median number of segments exhibiting a wall motion abnormality was 5 of 5, with all being grade ≥2+. Average RCA mean wall motion grade was 2.3 ± 0.65. In the LCx territory, the median number of segments exhibiting a wall motion abnormality was 5 of 5, with 3 of 5 being grade ≥2+. Average LCx mean wall motion grade was 1.6 ± 0.70. In the region of the anterior papillary muscle, 25 patients (90%) exhibited a wall motion abnormality, with 14 (48%) grade ≥2+; average wall motion grade was 1.4 ± 0.78. In the region of the posterior papillary muscle, 28 patients (97%) exhibited a wall motion abnormality, with 26 (90%) grade ≥2+; average of all patients' mean wall motion grade was 2.3 ± 0.83.

Scar >25% was present in a median of 3 of 17 LV segments. Distribution of scar was most varied in the LAD territory, less so in the RCA territory, and least in the LCx territory (Figure 3). In the region of the anterior papillary muscle, no patient exhibited scar >25%. In the region of the posterior papillary muscle, 8 patients (28%) exhibited scar >25%. In all, 44% of scars >25% were in the region of the posterior papillary muscle.

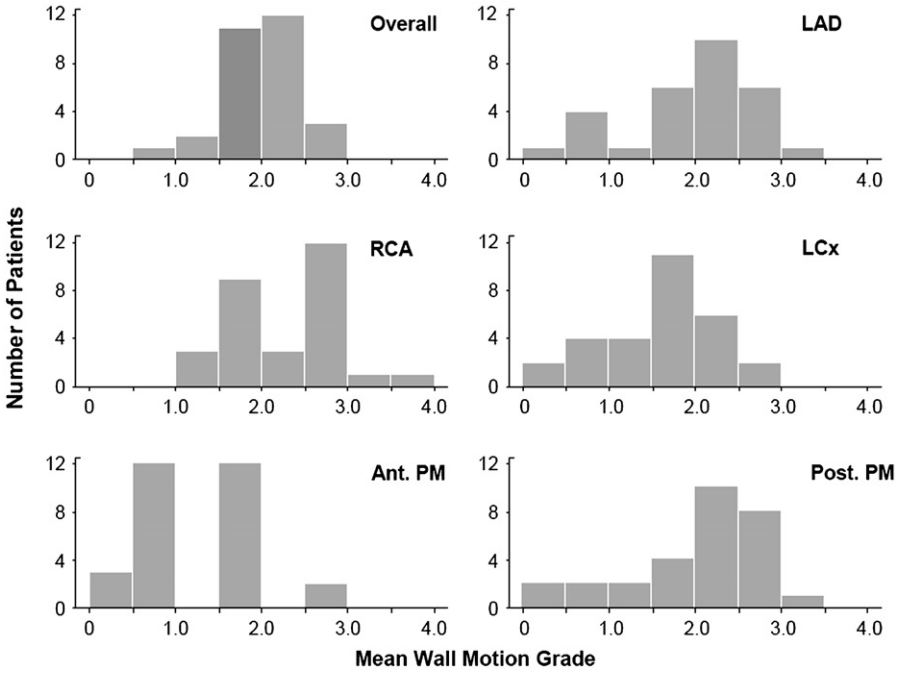

FIGURE 2. Distribution of mean wall motion grades overall and in territories of the left anterior descending coronary artery *(LAD),* right coronary artery *(RCA),* left circumflex coronary artery *(LCx),* and regions of the anterior papillary muscle *(Ant. PM)* and posterior papillary muscle *(Post. PM).*

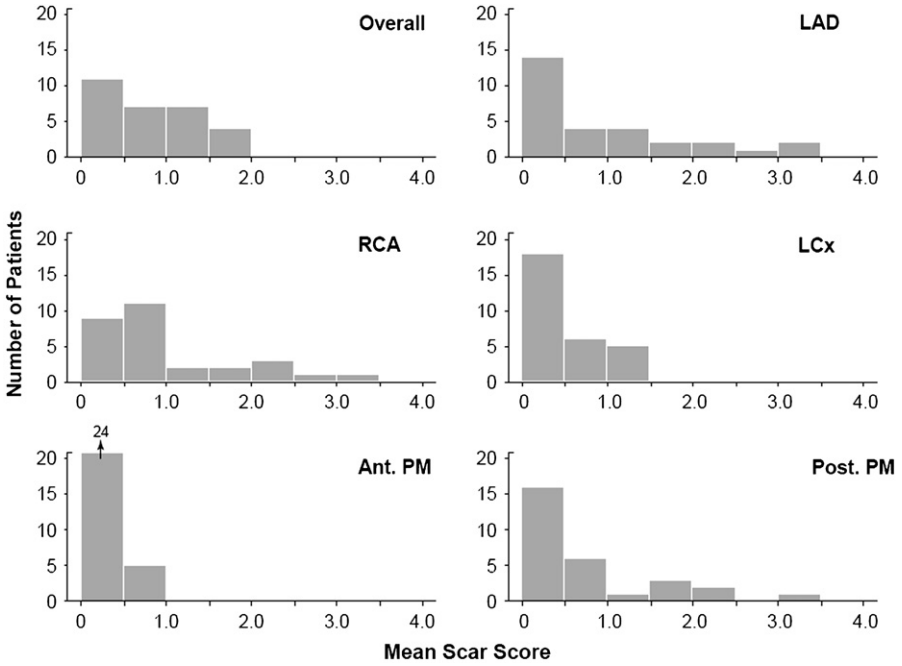

FIGURE 3. Distribution of mean scar scores overall and in territories of the left anterior descending coronary artery *(LAD),* right coronary artery *(RCA),* left circumflex coronary artery *(LCx),* and regions of the anterior papillary muscle *(Ant. PM)* and posterior papillary muscle *(Post. PM).*

If segmental wall motion was normal, generally no scarring was detected, as shown for representative segments by bubble plots (Figure 4). However, when segmental wall motion was abnormal, extent of scarring was highly variable. This resulted overall in low correlation between wall motion abnormality and scar ($r = .066$, Figure 5); however, when examined within coronary artery territories, increasing wall motion abnormality correlated modestly with increasing scar in the LAD territory ($r = .46$) and strongly in the LCx territory ($r = .68$). Correlation was strong in the region of the anterior papillary muscle ($r = .56$, $P = .001$) and modest in the region of the posterior papillary muscle ($r = .42$, $P = .02$).

Postoperative MR

The temporal pattern of postoperative MR was characterized by 2 phases: an early rapid change over the first 3 to 6 months and a constant phase thereafter (Figure E2). The percentage of patients with no MR decreased rapidly from about 90% 1 day after surgery to 19% 6 months later; the percentage of patients in MR grade 1+ increased from 10% to 49%; and the percentage of patients in MR grade 2+/3+/4+ increased from 0% to 34% (Figure 6).

Postoperative MR was unrelated to overall LV wall motion abnormality and scarring ($P \geq .5$), and the same was true for each coronary artery territory ($P \geq .2$). However, when wall motion abnormality and scarring were examined segmentally, wall motion grade ≥2+ to some extent ($P = .07$) and scar >25% ($P = .05$) in the midinferior segment (portion of the posterior papillary muscle in RCA territory) were associated with greater return of early postoperative MR. Figure 7 demonstrates the substantial impact of scar >25% on postoperative MR for the posterior papillary muscle region compared with no, or 25% or less, scarring in this same region (see Figure E1, *B* and *C* for number of patients and echocardiograms available for analysis).

DISCUSSION

Principal Finding

The main finding of this study is that extensive scarring and severe wall motion abnormalities in the region of posterior papillary muscle, identified by preoperative CMR imaging in patients with ischemic cardiomyopathy, correlate with MR after CABG and mitral annuloplasty.

Ischemic cardiomyopathy is the most common cause of heart failure in the United States. This advanced form of coronary artery disease is marked by diffuse myocardial damage causing LV remodeling. Functional ischemic MR is a common consequence of LV remodeling, with resulting decrease in mitral leaflet coaptation.[9,10] Contemporary surgical treatment consists of CABG and correction of MR by mitral annuloplasty.[11,12] Although CABG has resulted in improved survival compared with medical therapy, the efficacy of mitral annuloplasty has been disappointing because of a high rate of postoperative MR persistence or recurrence.[13,14]

We postulate that extensive scarring in the region of the posterior papillary muscle is a likely cause of failure of CABG and annuloplasty to correct functional ischemic MR. Although preoperative assessment of myocardial

viability provides important clinical information predicting outcome of coronary revascularization, it has not been used routinely as a guide in treating patients with chronic functional ischemic MR.[15]

Echocardiographic assessment of LV contractility has been demonstrated to be a useful and reliable predictor of operative risk and postoperative outcomes in patients with ischemic cardiomyopathy.[11,13] However, wall motion abnormalities can result from irreversible myocardial damage following myocardial infarction or from reversible dysfunction from ischemia or hibernation. CMR imaging has the advantages of providing information about both myocardial contractility and degree of scarring, as well as anatomic and functional assessment of the mitral valve.[15]

Patients in our study had advanced ischemic cardiomyopathy and severely depressed LV function, with diffuse regional wall motion abnormalities. Overall extent of regional wall motion abnormalities was greater than the degree of scarring, suggesting a large amount of viable, but dysfunctional, myocardium. The important finding is that even minimal scarring causes regional wall motion abnormalities, but overall extent of scarring correlates poorly with severity of wall motion abnormalities. This correlation was particularly poor in the LAD territory, which might be explained by good collateral blood supply there. The posterolateral wall, which is predominantly supplied by the LCx, has less collateral circulation in patients with diffuse 3-system coronary artery disease, making it more prone to scarring, with resulting high correlation between amount of scarring and regional wall motion abnormalities.[16]

Recent clinical and experimental studies highlight the importance of the posterior papillary muscle function in development of functional ischemic MR.[9,10,17] Ischemia or infarction in the region of the posterior papillary muscle causes apical leaflet systolic restriction, which, along with annular dilatation, causes leaflet malcoaptation in functional ischemic MR. Severe scarring in the region of the posterior papillary muscle was strongly associated with recurrent postoperative MR in our patients. A possible explanation is that undersized mitral annuloplasty, used in our patients, corrects annular dilatation but does not address apical leaflet systolic restriction caused by papillary muscle dysfunction.[11,13,14] Reversible dysfunction of ischemic posterior papillary muscle can be corrected by CABG; however, this will be ineffective if severe myocardial scarring is present.

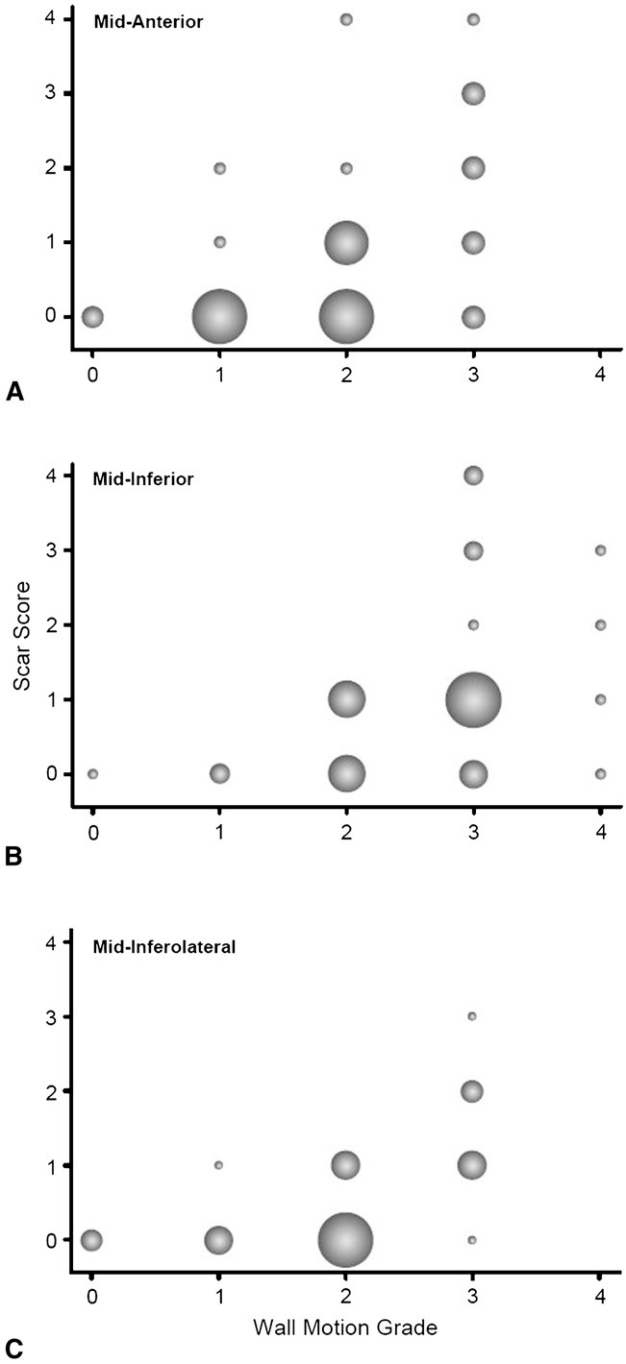

FIGURE 4. Bubble plots depicting wall motion grade and scar score in representative segments of each coronary artery territory. *A,* Midanterior segment (17) of left anterior descending coronary artery territory. *B,* Midinferior segment (10) of right coronary artery territory (and a portion of region of posterior papillary muscle). *C,* Midinferolateral segment (11) of left circumflex coronary artery territory (and a portion of region of the posterior papillary muscle).

Limitations

This is a single-institution pilot study performed during a 5-year span. CMR imaging was obtained in a small number of patients with ischemic cardiomyopathy and functional ischemic MR; thus, our findings cannot be generalized. No patient had postoperative CMR imaging, and postoperative echocardiography was performed based on clinical indications. Estimates of regurgitation were qualitative and did not include quantitative assessments such as regurgitant fraction or other volume indices. The study was not powered

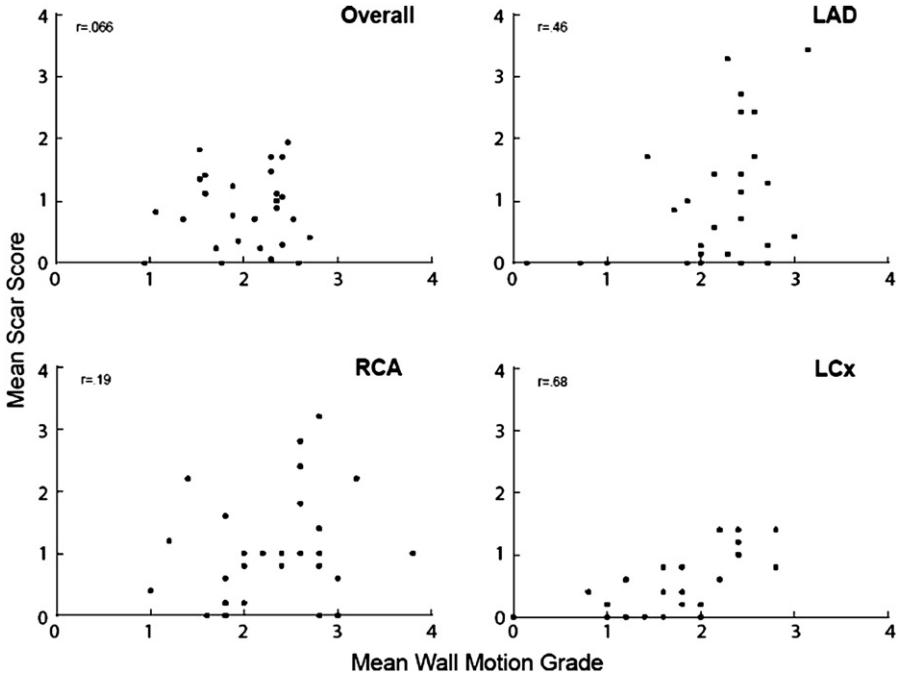

FIGURE 5. Correlation of mean wall motion grade and mean scar score overall and in coronary artery territories. *LAD,* Left anterior descending coronary artery; *RCA,* right coronary artery; *LCx,* left circumflex coronary artery.

to investigate the possible role of type of ring annuloplasty or return of MR.

Choice of operative procedures was surgeon dependent. Most patients received an undersized flexible annuloplasty band, and only a few, a complete rigid ring.

Clinical Implications

Preoperative CMR imaging should be considered for all patients with severe ischemic cardiomyopathy and functional ischemic MR. Current standard CMR protocols allow accurate assessment of LV dimensions, contractility, and scar burden, as well as mitral valve anatomy and function. Analyzing regional wall motion abnormalities and scarring is time consuming and elaborate and will require further standardization and software improvement.

CABG and concurrent mitral annuloplasty are ineffective for severe scarring in the region of the posterior papillary muscle, as detected by preoperative CMR imaging.[18-20]

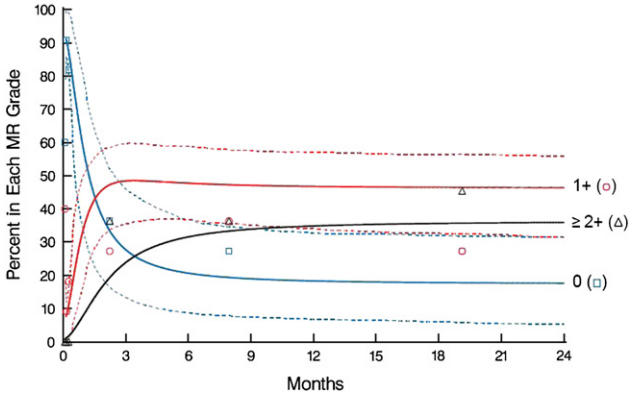

FIGURE 6. Temporal trend of postoperative mitral regurgitation *(MR)* grades across time. *Solid lines* are parametric estimates of percentages of patients in each MR grade after surgery, and *symbols* represent data grouped within unequal time intervals without regard to repeated assessment, to provide a crude verification of model fit. *Solid lines* are enclosed within 68% confidence limits obtained by bootstrap percentile method.[21]

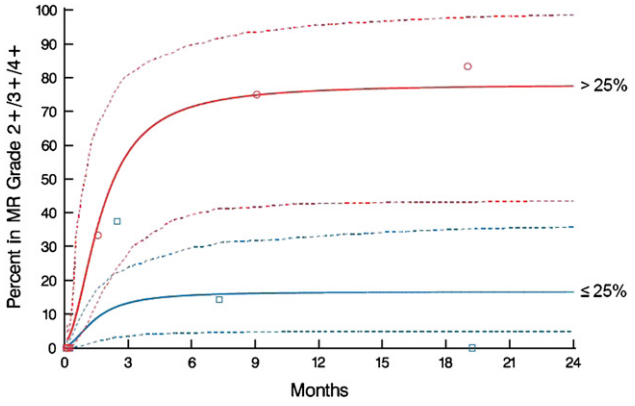

FIGURE 7. Association of postoperative mitral regurgitation *(MR)* grade ≥2+ with scar score >25% versus ≤25% in region of posterior papillary muscle. Depiction is as in Figure 6.

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Discussion

Dr R. Dion *(Genk, Belgium).* Dr Flynn, I would like to congratulate you for the quality of your presentation, and the authors and friends from the Cleveland Clinic have to be commended for an original pilot study trying to elucidate the relation between wall motion abnormality and scarring and return of MR. CMR was used, which is certainly very elaborate and time-consuming; therefore, one should not underestimate the task of applying CMR and analyzing it in 29 patients.

The main finding of this study is that extensive scarring, and severe wall motion abnormality to a lesser extent because it is less significant in the region of the posterior papillary muscle, correlates with the return of MR.

My first question concerns the preoperative myocardial infarction. All 29 patients had a history of myocardial infarction. Could you specify in which coronary territory? Was it mainly in the region of the right coronary and the circumflex, as expected, and did it always correlate with the site of scarring on CMR?

Dr Flynn. Thank you for your kind comments and your good questions. First, the most predominant area of infarction was inferior, in the right coronary territory. We did not investigate whether the degree of CMR-assessed scarring correlated with the presence of myocardial ischemia. We do not have evidence on that.

Dr Dion. I ask because the LAD mean wall motion was grade 2.1. It was grade 2.3 for the RCA and the posterior papillary muscle, but it was only grade 1.6 for the circumflex and the anterior papillary muscle. So there was more wall motion abnormality in the anterior part of the heart than in the territory of the circumflex. There was also more scar in the LAD than in LCx and in the anterior papillary muscle territory, which is a bit surprising for me, because I would have expected more scarring in the territory of the circumflex than in the LAD.

However, in the Discussion you state ''the posterolateral wall, which is predominantly supplied by the LCx, has less collateral circulation in patients with diffuse 3-system coronary artery disease, making it more prone to scarring, with resulting high correlation between amount of scarring and regional wall motion abnormalities.'' But again, the mean scar score is less than 2 in the circumflex territory. Can you elaborate on that?

Dr Flynn. Indeed. We feel that the most relevant territory is possibly that of the right coronary, and to relate this to scarring or dysfunction in the posterior papillary and the fact that it may be supplied by 2 territories, as you are aware: if there is disease or coronary disease related to both of those territories, these are the patients who are at risk and who possibly have a greater degree of scarring in the posterior papillary region. And these are possibly the patients then, as we have demonstrated here, who have a higher rate of recurrence of ischemic MR after surgery.

Dr Dion. Thank you. Forty-four percent of the patients had a scar of more than 25% in the posterior papillary muscle, but the posterior papillary was attributed 2 segments and the anterior papillary muscle, only 1 segment. Could it have influenced the results? Why did you decide that the anterior papillary muscle would be 1 segment and the posterior papillary muscle 2 segments?

Dr Flynn. Well, we know from science and nature that the posterior papillary is related to 2 coronary territories. We feel that disease involving both of those coronary territories makes the posterior papillary more at risk for infarction and a greater determinant of dysfunction.

Dr Dion. Thank you. I am surprised by the relatively high rate of recurrent MR at 6 months. It is probably explained by the fact that the choice of the procedure was left at the discretion of the surgeon, but, on the other hand, it allowed your group to perform this study with ''only'' 29 patients. What do you think about the temporal pattern of postoperative MR in 2 phases? I found it very interesting and very intriguing. Why such an increase in the first 3 months and after that, stabilization? How do you interpret that?

Dr Flynn. As you are aware, this represents a valvular approach to a ventricular problem, and this may reflect the fact that annuloplasty in these patients, particularly those who got scarring in that papillary region, may not be the appropriate approach for these patients. I think to study the overall temporal occurrence of MR was not within the remit of this study. It wasn't designed for that purpose; it wasn't powered for that purpose. So we have not studied or assessed the temporal degeneration of MR.

Dr. Dion. And finally, I found your conclusion quite severe for restrictive mitral annuloplasty. You state, ''CABG and concurrent mitral annuloplasty are ineffective for severe scarring in the region of the posterior papillary muscle.'' But even in your setup, 30% of the patients with severe scarring of the posterior papillary muscle had no recurrent MR, and 15% with little scarring in the posterior papillary muscle had recurrent MR. Don't you think that, besides the scarring and the wall motion abnormality, you should have taken into account the LV dilatation? Maybe there is a relation between the extent of scarring and the LV dilatation, which might explain that without scarring and with LV dilatation you could have recurrent MR.

Dr Flynn. I think your comments are well received. I think these are different ways of looking at very sick patients. These are different means of looking at severe LV dysfunction. Yes, indeed, LV end-diastolic diameter is 1 parameter that can be used. Our mean LV end-diastolic diameter was 62 mm, but we were unable to study whether that was a determinant of recurrence of MR or not. You will remember that our LV ejection fraction mean was 22%. They were all under 30%. So I think this is perhaps a different means of looking at a very sick patient group.

Dr Dion. Sure. But if you use CMR, it would probably be interesting as well to also look also at the dimensions: obviously you plan to extend this type of segmental analysis with CMR, which is a very time-consuming and elaborate task. And if you were able to link some of your segmental analysis to global LV dimension, which is easier to measure, it might simplify your work.

Again, I appreciate very much to review this paper and I congratulate you for an excellent presentation. I thank the Society for the privilege of discussing it.

Dr Flynn. Thank you, Professor Dion. Thank you very much.

Dr D. Adams *(New York).* Michael, that was an elegant study and it is important, and it actually correlates with some of your previous work from your institution about the importance of viable myocardium in predicting a good result after ischemic repair. So it is logical that a scar burden would also predict failure, and I think that is important, particularly in your subgroup, which I would emphasize for the audience had a very low ejection fraction. So these are difficult patients to make decisions about whether to operate and what to do. This spectrum of ischemic patients is very difficult.

My question relates to your specific ring strategy, and I think to understand any results in restrictive disease, we don't have data, we don't have randomized trials, but I just want to understand, were they downsized, were they rigid, were they complete, and did your ring strategy evolve over time? This is a relatively current study, end point 2001 to 2006, and did that make a difference? Did you see any patterns you can share with us?

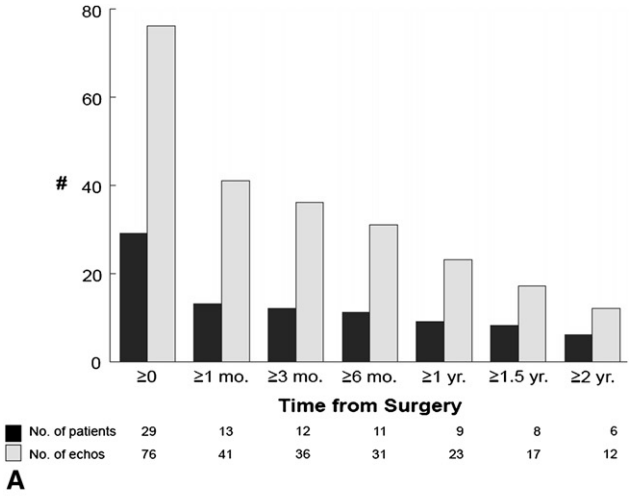
Dr Flynn. First, thank you for your comments and your very good questions. This was a very small study group. There were 7 patients who had complete rings, 22 who had partial rings. Again, this study was not designed to compare one ring to another. We found no difference in the rate of recurrence of MR between the 7 patients with a complete versus the 22 who had a partial ring. We were unable to assess that.

Your second question regarding the method of downsizing, that was surgeon-specific. There are different methods used at our institution depending upon the surgeon.

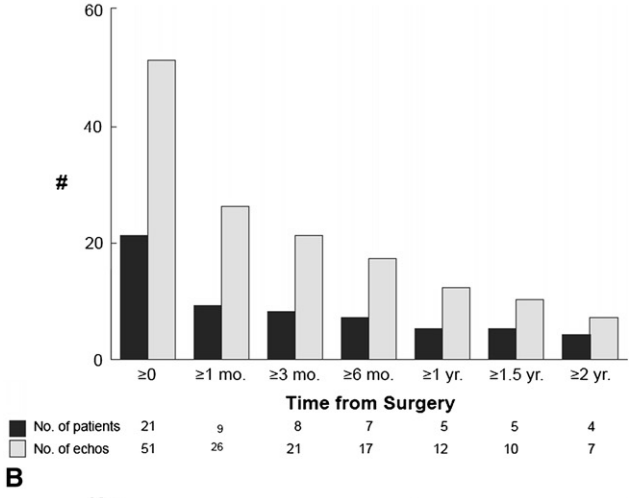
Dr L. Cohn *(Boston, Mass).* Excellent data presented beautifully. This is similar to what Dr Dor has been advocating for some time. Magnetic resonance imaging is something that cardiac surgeons should really adopt, and I suspect that you agree with that.

Any suggestions based on these data for more effective surgical therapy? Based on what you have presented to us, have you and your colleagues at the Cleveland Clinic decided on a more effective or more strategic way to treat these patients? And what are your current, shall we say, thoughts on recent surgical therapy about this now, based on the data that you presented to us?

Dr Flynn. Dr Cohn, thank you very much for your kind comments. I think this is a very difficult area and a very difficult patient group. There are various thoughts and theories. I think the thought of replacing the mitral valve in this patient group with a tissue valve is one concept, then ventricular restoration is another possibility. Again, it depends on the severity of LV dysfunction as to how one would address the ventricular problems. There are other options. None of them are ideal. As you are aware, it is a very difficult problem as to how to approach this.



A



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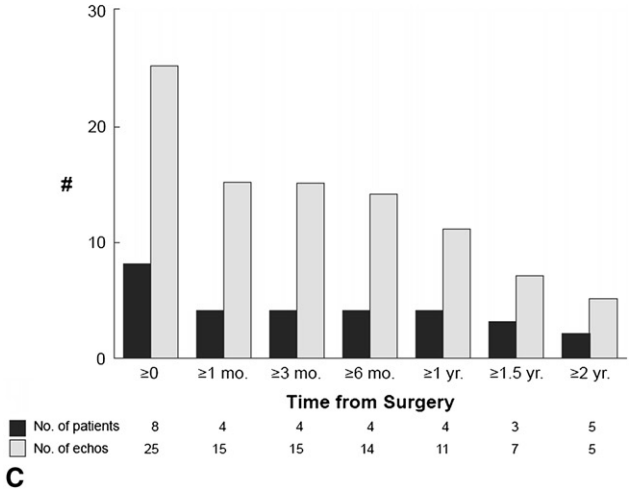

C

FIGURE E1. Number of patients with echocardiograms available at various time points across the study and number of echocardiograms available for analysis. A, All patients. B, Patients with scar score ≤25% in posterior papillary muscle region. C, Patients with scar score >25% in posterior papillary muscle region.

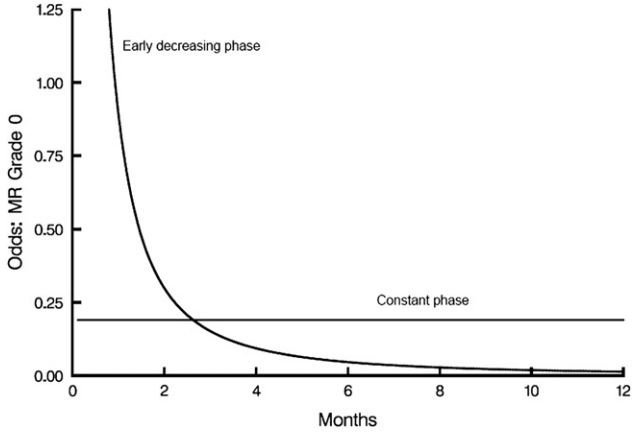

FIGURE E2. Decomposition of temporal pattern of postoperative mitral regurgitation *(MR)* in the odds domain.