Targeting the Papillary Muscles in Mitral Valve Repair for Ischemic Mitral Regurgitation

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Ischemic mitral regurgitation due to left ventricular remodeling and leaflet tethering is associated with decreased survival, and the optimal management remains unknown. Restrictive mitral annuloplasty is the current treatment of choice, but it is associated with a 15% to 30% incidence of late recurrent mitral regurgitation, which confers a poor prognosis. A pathophysiology-guided approach to surgical repair is preferable, with a goal of alleviating leaflet tethering and restoring proper subvalvular mechanics. In patients with preoperative predictors of annuloplasty failure, combining a papillary muscle repositioning technique with conventional annuloplasty repair allows for complete geometric repair of the ventriculomitral unit.

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KEY WORDS

Ischemic mitral regurgitation • Mitral annuloplasty • Papillary muscle intervention • Subvalvular repair

Carpentier type IIIb mitral valve dysfunction, which is more commonly referred to as functional or ischemic mitral regurgitation (IMR), is a common comorbidity seen in more than half of patients with ischemic cardiomyopathy.[1] It is defined as new mitral regurgitation present ≥ 1 week after a diagnosed myocardial infarction, with the following three requirements: development of a left ventricular (LV) wall motion abnormality, significant coronary artery disease in the territory of the wall motion abnormality, and structurally normal mitral valve leaflets.[2] The presence of IMR in this setting is associated with a twofold increase in mortality and new or worsening heart failure, and is commensurate to the degree of mitral regurgitation present.[3] The mechanism of IMR is centered on the complex interplay involving LV remodeling and distortion of the subvalvular apparatus. As the left ventricle dilates, there is an apicolateral displacement of the papillary muscles, which leads to chordal and leaflet tethering, with resultant leaflet malapposition and regurgitation. Chronic IMR leads to further deterioration of ventricular systolic function, worsening of the mitral regurgitation, and increased

adverse cardiovascular events and mortality.[1]

Mitral Valve Repair Versus Replacement

First popularized by Bolling and colleagues,[4] a restrictive mitral annuloplasty is the current surgical procedure of choice in the treatment of IMR, which involves reducing the septolateral diameter of the mitral annulus with an undersized annuloplasty ring.[4] The 1-year and 5-year survival has been estimated at 82% and 52%, respectively, with significant improvements reported in quality of life and LV remodeling.[5] However, there is a 15% to 30% incidence of late recurrent mitral regurgitation after annuloplasty, which increases the risk of required reoperation for clinically significant mitral regurgitation, when compared with valve replacement.[6,7] Thus, the optimal surgical approach to IMR remains controversial, with most of the reported data obtained from nonrandomized, retrospective studies.

In the only randomized trial comparing mitral valve repair versus replacement for IMR, the Cardiothoracic Surgical Trials Network allocated 251 patients with severe IMR to mitral valve repair with restrictive annuloplasty (n = 126) or chordal-sparing mitral valve replacement (n = 125).[8] The baseline comorbidities, as well as the LV ejection fraction (repair group = 42% ± 10, replacement group = 40% ± 11; $P = .10$), were similar between the cohorts, and the majority of patients underwent concomitant coronary artery bypass grafting, tricuspid valve repair, and/or atrial maze procedures. There were no differences between the surgical approaches in mortality at 30 days or 1 year, echocardiographic parameters of LV remodeling, or clinical outcomes. However, there was a significantly higher rate of recurrence of moderate to severe mitral regurgitation at 1 year in patients undergoing valve repair as opposed to replacement (32.6% vs 2.3%; $P < .001$).

Despite the reported benefits in perioperative outcomes, LV reverse remodeling, and New York Heart Association functional class in patients undergoing valve repair for IMR, no proven survival benefit has been shown over valve replacement, with a higher incidence of recurrent mitral regurgitation in repair cohorts observed at follow-up.[6-8] Thus, significant equipoise exists regarding the optimal approach to correcting severe IMR. In instances of advanced ventricular remodeling and subvalvular dysfunction, mitral valve replacement with chordal preservation may be considered, which decreases the risk of ventricular-annular disruption and LV functional impairment.[9] However, the decision to replace the mitral valve must be balanced against the risks of thromboembolic complications of metallic valves, or the long-term durability of bioprosthetic valves. Furthermore, innovative papillary muscle procedures performed at the time of annuloplasty, which aim to relieve leaflet tethering and improve the function of the subvalvular apparatus, may confer an improved durability of valve repair in IMR.

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Papillary Muscle Intervention to Improve Repair Durability in IMR

To minimize the recurrence of mitral regurgitation after valve repair for IMR, techniques aimed at the entire ventriculomitral unit may be of benefit. Restrictive mitral annuloplasty corrects annular dilatation by reducing the septolateral diameter, without addressing concomitant subvalvular dysfunction. Due to a sufficiently redundant anterior leaflet along with active leaflet remodeling processes that occur as LV function deteriorates, a 1.8-fold increase in annular size can be tolerated before mitral regurgitation develops, suggesting a greater burden from complex ventricular remodeling rather than annular dilatation in IMR.[10,11] In the trial by the Cardiothoracic Surgical Trials Network,[8] which utilized downsized rigid or semirigid complete annuloplasty rings for valve repair, the patients with recurrent mitral regurgitation had no evidence of reverse remodeling, when compared with the successful annuloplasty procedures (LV end-systolic volume index 64.1 ± 23.9 mL/m^2 vs 47.3 ± 23 mL/m^2).[8] This supports the theory that IMR is a disease of the ventricular myocardium and subvalvular apparatus, as opposed to the mitral valve itself, and continued ventricular remodeling after

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restrictive mitral annuloplasty leads to progressive displacement of the papillary muscles, which may cause valve incompetence and potential annuloplasty failure.

A pathophysiology-guided approach to surgical repair may be preferable, with the goal of alleviating leaflet tethering forces and ventricular geometric distortions that contribute to annuloplasty failure. One such target has been the reestablishment of physiologic papillary muscle positioning through several innovative subvalvular techniques that can be performed at the time of annuloplasty repair. Such procedures include papillary muscle approximation or elevation, as well as commissural plication and chordal base fixture (Table 1).[12-19] Combining annuloplasty with a papillary muscle intervention results in reduced septolateral annular dilatation, moves the anterolateral papillary muscle closer to the annulus, and corrects both lateral displacement and apical restriction of the posterior papillary muscle.[20,21] Furthermore, these techniques may help attenuate the augmented posterior leaflet tethering that often occurs after restrictive annuloplasty, which itself is associated with the development of recurrent mitral regurgitation.[22,23] In patients with preoperative echocardiographic predictors of annuloplasty failure (Table 2), combining annuloplasty repair with a papillary muscle procedure allows for a complete geometric repair of the ventriculomitral unit (Figures 1 and 2).[24]

Combining annuloplasty with a papillary muscle intervention results in reduced septolateral annular dilatation, moves the anterolateral papillary muscle closer to the annulus, and corrects both lateral displacement and apical restriction of the posterior papillary muscle.

TABLE 1

Adjunctive Papillary Muscle Surgical Techniques With Mitral Annuloplasty

Study	N	LVEF	Surgical Technique	Outcomes
Fattouch K et al[12]	115	43%	PM elevation with sutures from both PM heads through the ipsilateral mitral annulus	91% survival and 97% freedom from > 2+ MR at 5 y
Hvass and Joudinaud [13]	37	30%	PM approximation with 4-mm interpapillary muscle Gore-Tex[a] sling; CABG	None/trivial MR in 84% and 95% survival at 5 y
Roshanali F et al[14]	31	28%	PM approximation with 4-mm interpapillary muscle Gore-Tex sling	Mean MR grade 1+ and mean NYHA 1 at 6 mo
Langer F et al[15]	30	37%	Transventricular suture of posterior PM through the intervalvular fibrosa ("Ring + String")	94% freedom from MR > 2+, and 89% survival at 2 y
Santana O et al[16]	19	23%	PM approximation using 4-mm interpapillary muscle Gore-Tex sling	None/trivial MR at 3 mo, 0% 30-d mortality
Kron IL et al[17]	18	N/A	Posterior PM elevation with suture from PM tip to the right mitral annular fibrous trigone; CABG	None/trivial MR and 0% mortality at 2 mo
Ishikawa S et al[18]	15	48%	Commissural PM plication and chordal base fixture ("Sandwich plasty"); AVR (n = 14) and David procedure (n = 1)[b]	83% freedom from MR and 100% survival at 2 y
Rama A et al[19]	8	36%	PM approximation with suture reinforced by autologous pericardium; CABG	Less than 1+ MR and mean LVEF 59% at 11 mo

AVR, aortic valve replacement; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; N/A, not available; NYHA, New York Heart Association; PM, papillary muscle.

[a]Gore-Tex® is manufactured by WL Gore, Newark, DE.

[b]David procedure, aortic valve-sparing root replacement.

TABLE 2

Transthoracic Echocardiographic Predictors of Annuloplasty Failure

Measurement	Value	Sensitivity (%)	Specificity (%)
Mitral valve tenting area	≥ 2.5 cm^2	64	90
Mitral valve tenting height	≥ 11 mm	81	84
Interpapillary muscle distance	> 20 mm	96	97
Anterior leaflet tethering angle	≥ 39.5°	98	97
Posterior leaflet tethering angle	≥ 45°	100	95
Left ventricular end-systolic volume	≥ 145 mL	90	90
Left ventricular sphericity index	≥ 0.7	100	100

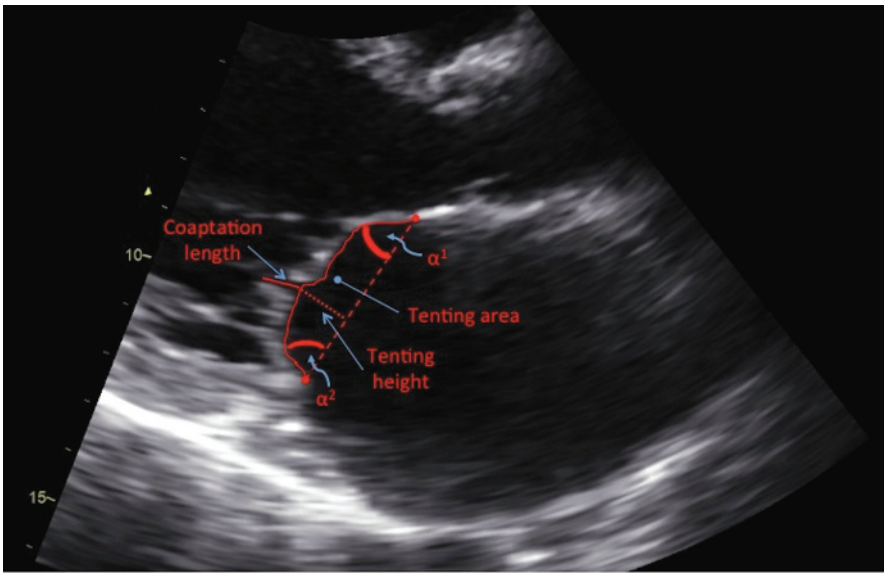

Figure 1. Parasternal long-axis view of the mitral valve in mid-systole on transthoracic echocardiogram. α1, anterior leaflet tethering angle; α2, posterior leaflet tethering angle; tenting area, area enclosed by the mitral leaflets and annular plane.

Should Moderate IMR be Treated?

To date, there have been four randomized controlled trials comparing revascularization with coronary artery bypass graft (CABG) surgery alone versus CABG plus mitral valve repair utilizing a restrictive annuloplasty in patients with coronary artery disease and moderate IMR.[25-28] The studies yielded equivocal results, with two trials reporting improved functional capacity, LV reverse remodeling, pulmonary hemodynamics, and less mitral regurgitation recurrence with concomitant valve repair,[25,26] whereas two later trials found no difference in clinical outcomes or incidence of significant recurrent mitral regurgitation (Table 3).[27,28] However, several important limitations were noted among these trials, including lack of consistency in defining IMR, suboptimal analysis of the impact of recurrent mitral regurgitation on functional status and survival, heterogeneity in the types of annuloplasty rings utilized, and limited follow-up of 1 year in three of the four trials.

In patients undergoing isolated CABG with moderate preoperative IMR, up to 50% will have persistence or worsening of the mitral regurgitation grade after revascularization alone, which portends a poor prognosis.[29,30] Several preoperative predictors of persistent or worsened mitral regurgitation after isolated CABG have been identified, which can help risk stratify patients and select candidates who may benefit from combined CABG and mitral valve repair. These include (1) extensively infarcted myocardium with ≤ 5 viable myocardial segments; (2) infarcted myocardium subtending or adjacent to one or both papillary muscles; (3) dyssynchronous papillary muscles, defined as > 60 ms by echocardiographic tissue Doppler imaging; and (4) exercise intolerance

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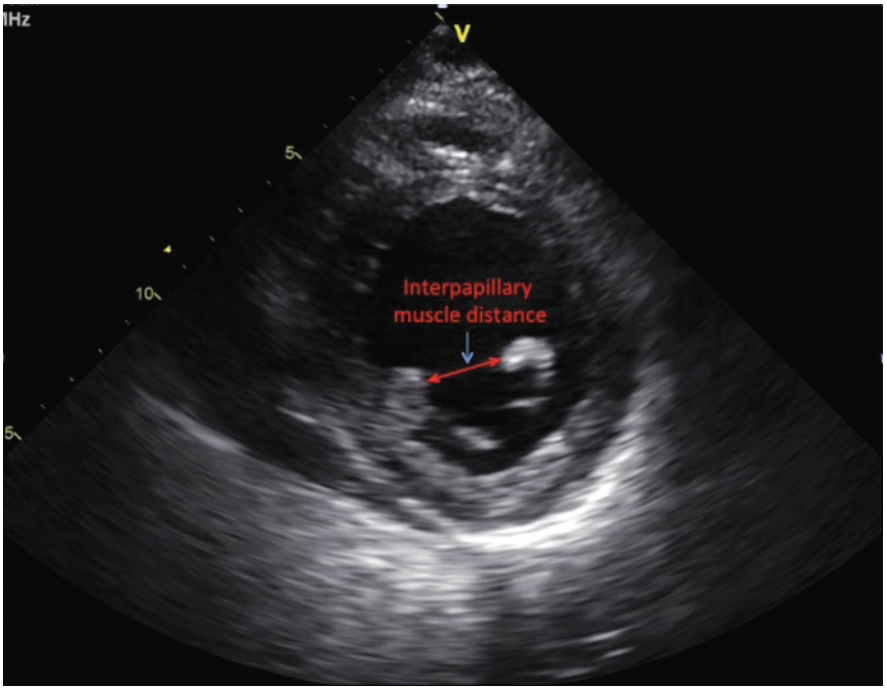

Figure 2. Parasternal short-axis view at the level of the papillary muscles at end-systole on transthoracic echocardiogram.

or worsening mitral regurgitation on exercise stress testing.[8,25,30-34] A concomitant papillary muscle intervention may be considered in these patients.

Conclusions

In the 2014 American College of Cardiology/American Heart Association, and the 2012 European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines for the management of valvular heart disease, surgical correction holds a class IIb recommendation for patients with symptomatic severe IMR refractory to optimal guideline-directed management of ischemic heart disease and heart failure.[35,36] This reflects the uncertainty regarding the optimal surgical approach to treating IMR. Addressing the mechanisms underlying IMR is critical to applying the optimal surgical strategy. Techniques aimed at restoring proper anatomic papillary muscle alignment appear to improve ventricular geometry and the durability of valve repair in the setting of IMR in patients with preoperative echocardiographic predictors for annuloplasty failure. However, most reports are from small, single-center experiences with short-term follow-up. Randomized trials and multicenter registries are needed to validate the efficacy and long-term outcomes of these promising procedures. ■

TABLE 3

Summary of Randomized Clinical Trials Comparing CABG Versus CABG + MVr in Moderate IMR

Study	N	LVEF, %	Prior MI, %	LV Size	Follow-up	Summary of Outcomes	Recurrent > 2+ MR, %
Fattouch K et al[25]	102	43	95	LVEDD 59 mm	32 ± 18 mo	Improved MR grade, NYHA functional class, PASP, LV remodeling, and LA size in CABG + MVr group	CABG 60 CABG + MVr 0
Chan KM et al[26]	73	40	73	LVEDD 57 mm	1 y	Improved peak oxygen consumption, LV remodeling, NYHA functional class, and BNP level in CABG + MVr group	CABG 50 CABG + MVr 4
Bouchard D et al[27]	31	44	68	LVEDD 57 mm	1 y	No difference in LV remodeling, MR grade, or functional capacity	CABG 14 CABG + MVr 14
Smith PK et al[28]	301	40	67	LVESVI 58 mL/m^2	1 y	No difference in LV remodeling, major adverse clinical events, or functional capacity	CABG 31 CABG + MVr 11

BNP, brain natriuretic peptide; CABG, coronary artery bypass graft surgery; IMR, ischemic mitral regurgitation; LA, left atrial; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESI, left ventricular end-systolic volume index; MI, myocardial infarction; MR, mitral regurgitation; MVr, mitral valve repair; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure.

MAIN POINTS

- Ischemic mitral regurgitation (IMR) is a common comorbidity seen in more than half of patients with ischemic cardiomyopathy. Chronic IMR leads to further deterioration of ventricular systolic function, worsening of the mitral regurgitation, and increased adverse cardiovascular events and mortality.
- Restrictive mitral annuloplasty is the current surgical procedure of choice in the treatment of IMR. The 1-year and 5-year survival has been estimated at 82% and 52%, respectively, with significant improvements reported in quality of life and left ventricular (LV) remodeling. However, there is a 15% to 30% incidence of late recurrent mitral regurgitation after annuloplasty, which increases the risk of required reoperation for clinically significant mitral regurgitation, when compared with valve replacement.
- The decision to replace the mitral valve must be balanced against the risks of thromboembolic complications of metallic valves, or the long-term durability of bioprosthetic valves.
- Innovative papillary muscle procedures performed at the time of annuloplasty, which aim to relieve leaflet tethering and improve the function of the subvalvular apparatus, may confer an improved durability of valve repair in IMR.
- Techniques aimed at restoring proper anatomic papillary muscle alignment appear to improve ventricular geometry and the durability of valve repair in the setting of IMR, in patients with preoperative echocardiographic predictors for annuloplasty failure. Several preoperative predictors of persistent or worsened mitral regurgitation after isolated coronary artery bypass grafting (CABG) have been identified, which can help risk stratify patients and select candidates who may benefit from combined CABG and mitral valve repair.

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