REVIEW ARTICLE

Ischemic mitral regurgitation
Clinical Review Emphasizing the Surgical Treatment

Vojáček J., Hlubocký J., Burkert J., Telekeš P., Špatenka J., Pavel P.
Cardiac Surgery, 2nd Medical Faculty, Charles University and University Hospital Motol, Prague, Czech Republic

SUMMARY

Ischemic mitral regurgitation (IMR) is a relatively frequent complication of myocardial infarction. The presence of IMR negatively influences imminent mortality after myocardial infarction and the long-term survival of the patients. IMR is a functional, not morphological impairment of mitral valve and is caused by a change in the geometry of the left ventricle. In the review article, the authors deal with the origin and pathophysiology of chronic IMR and with current possibilities for surgical treatment of this serious complication of ischemic heart disease.
Key words: ischemic mitral regurgitation, mitral valve repair, coronary artery disease.

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Ischemic mitral regurgitation (IMR) is a frequent complication of coronary artery disease (CAD). In most cases it develops as consequence of myocardial infarction. The presence of IMR worsens the prognosis of the patients after myocardial infarction - even after myocardial revascularization - and increases the late mortality more than twofold (1, 2).

PATHOPHYSIOLOGY

With the sole exception of papillary muscle rupture (PM), IMR is a functional rergurgitation characterized by structurally normal cusps and chordae tendineae.

Formerly, the creation of IMR was explained by so-called papillary muscle dysfunction. It was defined as a loss of the ability of the papillary muscle to contract during systole, which was supposed to be the cause of prolaps of mitral valve leaflet. Acute ischemia of papillary muscle really exists and causes its dysfunction, but in view of the fact that the systolic-diastolic difference in the length of this muscle is only 2–4 mm, this dysfunction cannot be the cause of mitral regurgitation (3, 4).

On the contrary, some experiments on sheep provide evidence that acute ischemia of the papillary muscle and its dysfunction (loss of contractility) may alleviate the severity of ischemic mitral regurgitation in cases of inferobasal myocardial ischemia (5). Loss of contractility of the papillary muscle actually leads to its prolongation during acute ischemia, which may paradoxically decrease the restrictive motion of the mitral leaflet caused by displacement of the base of papillary muscle apart from the mitral annulus (Fig. 1). Thus papillary muscle dysfunction does not participate in the etiopathogenesis of ischemic mitral regurgitation, and therefore this term should not be used in this context.

Mitral valve function, its ability to close during systole, is based on the geometry and function of the left ventricle: during systole, the base of the papillary muscle approaches towards the mitral annulus. In cases of myocardial ischemia adjacent to the base of papillary muscle, this part of myocardium does not contract during

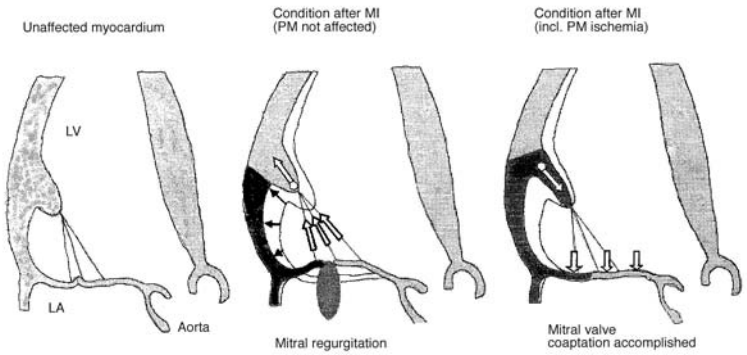


Fig. 1. Acute ischemia of papillary muscle disables the contractility which causes muscle prolongation. Paradoxically, it may decrease the restrictive motion of the mitral leaflet, caused by displacement of the papillary muscle base apart from the mitral annulus (5)

Address for correspondence:
Jan Vojáček, MD.
Cardiac Surgery, 2nd Medical Faculty, Charles University and University Hospital Motol
155 00 Prague 5, V Úvalu 84
Czech Republic
E-mail.: j.vojacek@fnmotol.cz

systole. This results in restrictive motion of one or both leaflets of the mitral valve and, consequently, it may lead to the incomplete leaflet closure. It is the condition when the coaptation zone of the anterior and posterior leaflet shifts apart from the mitral annulus to the heart apex. On echocardiogram, this shift manifests itself as tenting (Fig 2). If this shift continues, mitral regurgitation occurs, and is classified as type IIIb (Carpentier classification).

Under physiologic conditions, the area of mitral valve is double of that of mitral orifice and the only restrictive motion of mitral leaflets caused by myocardial ischemia rarely leads to regurgitation without a dilation of mitral annulus. The annulus dilates, its geometry and function change together with the left ventricle. Ischemic cardiomyopathy with marked remodelling and dilatation of the left ventricle may lead to IMR even without restrictive leaflet motion, due to the central regurgitation of dilated and dysfunctional mitral annulus. This type of regurgitation is denoted as Type I according to the Carpentier classification. Concurrent change of left ventricle geometry and dilation of mitral annulus are the main cause of ischemic mitral regurgitation. Lowered transmitral force closing the mitral valve during systole may contribute to IMR. This is caused by the deteriorated systolic function of the left ventricle (LV) (6).

ACUTE ISCHEMIC MITRAL REGURGITATION

Papillary muscle rupture

Papillary muscle rupture is less frequent than the significant functional acute IMR. Affliction of the posteromedial papillary muscle is about twice as frequent as rupture of the anterolateral papillary muscle. It is the early complication of acute MI, it may appear as early as the first day from the onset of MI but almost always up to the seventh day, most frequently during the 3rd or 4th day.

The papillary muscle rupture leads to severe mitral regurgitation. This results in left ventricular volume overload, i. e. enlargement of end-diastolic volume, increase of end-diastolic pressure of LV and strong increase of pressure in non-dilated left atrium. Postcapillary pulmonary hypertension appears with possible right heart failure. Effective cardiac output depends on the area of regurgitation orifice, on afterload and left atrial pressure. In cases of massive mitral regurgitation occurring in papillary muscle rupture, the heart output is critically lowered, and cardiogenic shock develops.

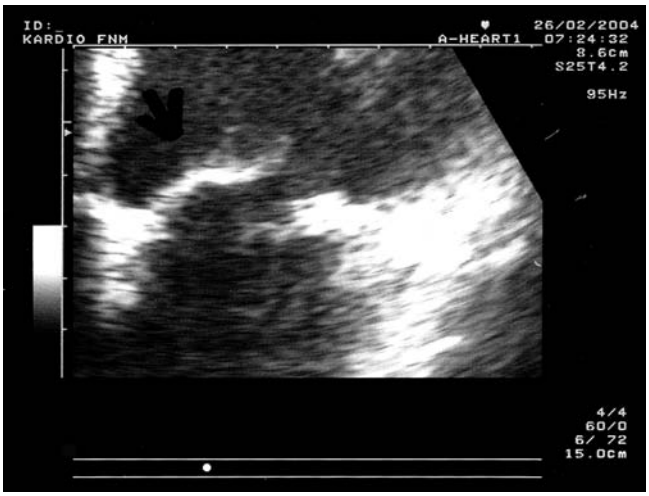


Fig. 2. Echocardiogram of tenting of the anterior leaflet of mitral valve
The arrow shows the place of attachment of secondary (paramedial) chordae, which by their tension (tethering) contribute to the incomplete leaflet closure of mitral valve.

The symptoms resemble those of vast MI, i. e. signs of pulmonary congestion or even pulmonary oedema with signs of low cardiac output. Holosystolic murmur is present. Final diagnosis may be established by means of echocardiographic examination. Prognosis of non-surgically treated patients with papillary muscle rupture is catastrophic, with one-day mortality up to 70% and 48-hour mortality up to 95% (7). Therefore in these patients urgent CABG + mitral valve replacement is indicated. Preservation of the subvalvular apparatus of mitral valve is essential to prevent further systolic dysfunction of LV. Intraaortic balloon counterpulsation (IABP) may be indicated before surgery in order to hemodynamically stabilize the patient. IABP decreases afterload as well as regurgitation volume and improves the perfusion of the ischemic myocardium. Incomplete rupture of papillary muscle is linked with lower mortality.

Functional acute ischemic mitral regurgitation

Acute functional IMR occurs as a complication of myocardial infarction. Valvular leaflets and subvalvular apparatus are not damaged, and the regurgitation arises in consequence of restrictive motion of mitral cusps, which results in incomplete leaflet closure. If early reperfusion after acute MI is achieved, regurgitation may diminish or disappear. Generally, though, this phenomenon is difficult to predict. The marked acute functional mitral regurgitation might clinically manifest itself as papillary muscle rupture.

FUNCTIONAL CHRONIC ISCHEMIC MITRAL REGURGITATION

The etiopathogenesis of chronic IMR, like acute IMR, is based on restrictive motion of the mitral leaflets. This is caused by left ventricle remodelling and segmental disorders of kinetics, i. e. by a change in the mutual position of papillary muscles and in their position to mitral annulus. Fibrotization and atrophy of ischemic papillary muscle also play a role. It leads to shortening of papillary muscles, which also contributes to the restrictive motion of mitral valve. Dilation of mitral annulus caused by ischemic cardiomyopathy and lowered myocardium contractility, i. e. the strength with which the mitral valve during systole is closed, here plays an even more important role than in postinfarction IMR. All these factors may occur in combination or individually.

ISCHEMIC MITRAL REGURGITATION FROM THE SURGICAL POINT OF VIEW

What optimal procedure in patients with ischemic mitral regurgitation has been recommended? If we scrutinize the contemporary literature, we ascertain that there is no ”state-of-the-art” study available, i. e. randomized trials that compare the results of various therapeutic procedures (conservative treatment vs. CABG, CABG vs. CABG + MVR/R, mitral valve repair vs. mitral valve replacement). Our experience with IMR is based on observational retrospective or prospective studies, the results of which are often contradictory; their interpretation is unclear and does not provide clear rules on how to proceed in particular situations.

In context with chronic ischemic mitral regurgitation, these questions are to be asked:

1. Does the presence of IMR negatively influence the patient’s prognosis? If so, what degree of IMR is considered significant?
2. Does surgical myocardial revascularization improve the negative prognosis of the patients with significant IMR?
3. Is it necessary to complete aortocoronary bypass graft by concomitant mitral valve surgery?

4. What are the results of surgical intervention on mitral valve in case of IMR, and does mitral valve repair have better long-term results than valvular replacement?

Does the presence of IMR negatively influence the patient's prognosis? If so, what grade of IMR is considered significant?

Prognostic significance in ischemic mitral regurgitation remained unclear. The data obtained from trials dealing with the treatment of acute MI using fibrinolysis show that the presence of moderate or severe IMR negatively influences the patients' prognosis with one-year 52% mortality (2).

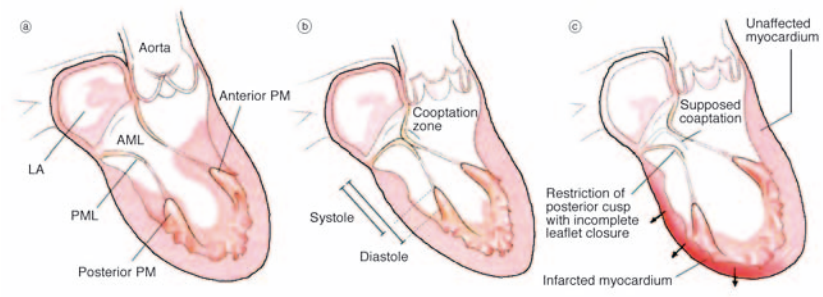


Fig. 3. Schematic representation of the origin of ischemic mitral regurgitation

SAVE study (Survival and Ventricular Enlargement) proves that even the presence of moderate and mild IMR worsens the patients' prognosis (1). The study encompassed 727 patients with recent acute MI (up to 16 days from the onset of AMI), with EF less than 40% and with mild or moderate IMR. Multivariate analysis showed that the presence of such IMR is the significant independent factor influencing mid-term mortality.

A recent study from the Mayo Clinic (8) deals with chronic IMR (more than 16 days from the onset of AMI). The study encompassed patients with MI older than 16 days in whom the presence of IMR was detected on echocardiogram (the 16-day criterion has been chosen because only patients with onset of acute MI up to 16 days were included in the SAVE study). This group of patients was compared with the control group of the patients (corresponding EF, age, comorbidities) without IMR. The degree of regurgitation was quantified by means of PISA method (Proximal Isovelocity Surface Area) that determined the effective regurgitant orifice (ERO) and regurgitant volume (RVol). The results of the study demonstrate that the presence of IMR clearly worsens five-year survival in comparison with the control group (38% vs. 61%). Quantificative evaluation of IMR degree shows that the greater IMR, the worse the prognosis. Patients with ERO greater than 20 mm^2 and RVol greater than 30 ml have significantly worse five-year survival than patients with lower degree of regurgitation (Graph 1). There is crucial difference between IMR and other cases of organic mitral regurgitation in which the significant values of ERO and RVol are considered values over 40 mm^2 and 60 ml, respectively. This higher value demonstrably worsens the long-term prognosis of the patients with IMR. Thus if we compared quantification mitral regurgitation grade (ERO and RVol) with IMR determined by Doppler method, then mild or mild to moderate IMR could be considered the significant value!

Does surgical myocardial revascularization improve the negative prognosis of the patients with significant IMR?

Trichon et al. from the Duke University Medical Center processed the prospectively acquired data from 2,757 patients with CAD and IMR (9). Ischemic mitral regurgitation was defined as MR grade ≥2 in presence of CAD (at least one-vessel disease with stenoses 75% or greater) and without primary mitral valve disease. The patients were divided into 4 groups on the basis of the selected therapeutic strategy. 1,305 were treated conservatively, 537 underwent percutaneous coronary intervention (PCI), 687 underwent CABG, and in the remaining 228 patients CABG + MVR/R were performed. Graph 2 depicts differences in long-term survival among treatment groups after performing risk stratification. The patients from the conservatively treated subgroup had the worst long-term results; on the contrary, patients with CABG had the best

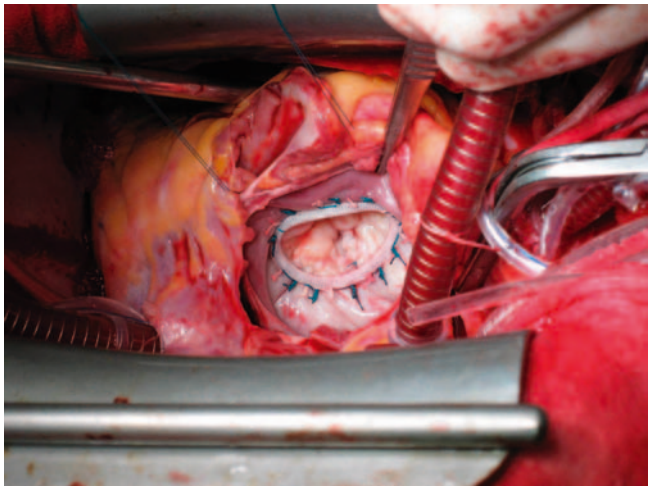


Fig. 4. Mitral valve after a mitral ring implantation

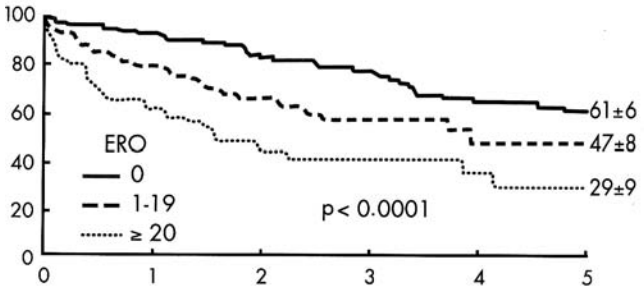
results. The results of the study show that myocardial revascularization (CABG or PCI) improves the negative prognosis of the patients with ischemic mitral regurgitation! Concomitant MVR/R does not contribute to further improvement of the prognosis. It is important that in the group CABG + MVR/R there is the highest representation of moderate or severe IMR, on the contrary, the lowest representation of mild IMR. It can be only supposed that in the group MVR/R where the rate of serious MR is the highest, the long-term results would be worse if only myocardial revascularization was performed without concomitant mitral surgery.

Is it necessary to complete CABG with concomitant mitral valve surgery?

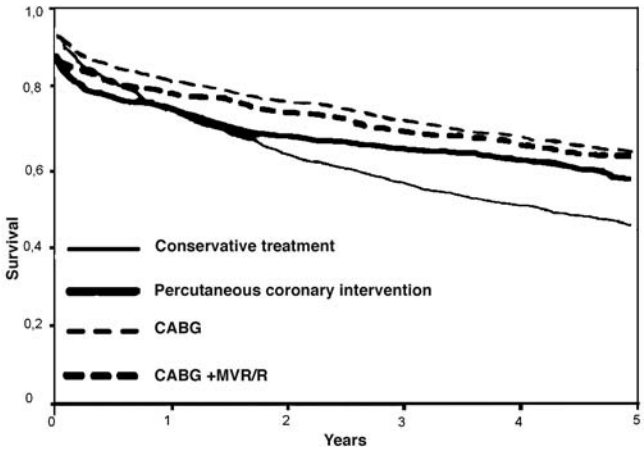
Again, we have no randomized studies comparing the results of surgical myocardial revascularization in patients with IMR with or without concomitant mitral valve surgery.

Duarte et al. present 10-year results of myocardial revascularization alone in 58 patients with moderate mitral regurgitation (9). This group was compared to the control group of patients who underwent operations during the same period but without MR. Five-year and 10-year survival were almost identical in both groups. Nevertheless, the results of the study are biased by the fact that more than 25% of the patients from the IMR group did not have pure IMR but had coincidence of CAD and degenerative or rheumatic affection of mitral valve. Most of the patients also had good EF (mean EF=53%) and only 10% patients had symptoms of advanced congestive heart failure.

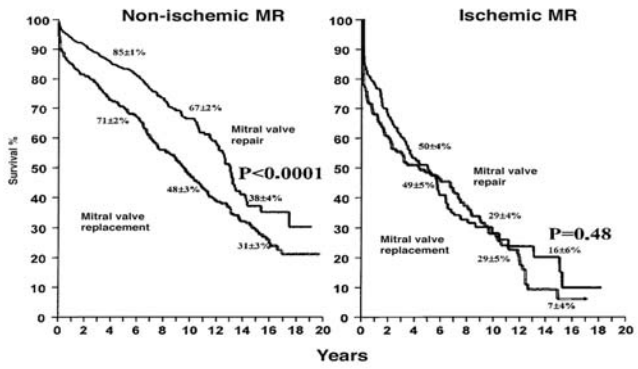
Aklog et al. try to answer the question as to the further course of IMR after surgical revascularization of myocardium (10). They processed retrospectively obtained data of 269 patients with CAD, who had moderate IMR. Mean EF was 38%, and 63% of patients had symptoms of heart failure NYHA III-IV. In all patients, CABG without concomitant mitral surgery was performed. The early mortality was 2.9%. The mean preoperative, intraoperative, and postoperative MR grades were 3.0±0.0, 1.4±1.0, and 2.3±0.8, respectively (p<0.001).



Graph 1. Five-year survival of the patients after myocardial infarction depending on the presence or absence of chronic ischemic mitral regurgitation
It is apparent that the prognosis of the patients with ERO over 20 mm² is worse than in patients with lower degree of regurgitation (8)
(ERO = effective regurgitant orifice)



Graph 2. Five-year survival of patients with ischemic mitral regurgitation according to a different therapeutic strategy - conservative treatment vs. myocardial revascularization (9)



Graph 3. Comparison of patients' survival after mitral valve repair and replacement in dependence on etiology (ischemic vs. organic non-ischemic etiology)
It is apparent from the graph that in case of ischemic mitral regurgitation the advantage of mitral valve repair as opposed to its replacement is statistically non-significant (16)

On postoperative TTE, 40% of patients had at least moderate MR (3+ to 4+), 51% improved somewhat to mild MR, and only 9% had resolution of their MR. The results show that in most patients with moderate IMR there was no or only mild improvement after CABG. CABG alone without concomitant mitral valve surgery may not be the optimal therapy for most patients with IMR because it leaves many patients with significant residual regurgitation. This is why concominant mitral valve surgery in these patients seems to be logical and convenient.

What are the results of mitral valve surgery in IMR, and does mitral valve repair have better long-term results than mitral valve replacement?

As opposed to organic valvulopathies, left ventricle dysfunction is not consequence, but the cause of this functional valvular disorder. It determined the seriousness of IMR and its negative influence on immediate and late outcomes of the operated patients (CABG + MVR/R), which are significantly worse in comparison with degenerative affection of mitral valves. Five-year survival of these patients may reach only 50% (11). On the contrary, 10-year survival of patients after mitral valve repair performed due to degenerative affection of the valve may reach up to 85% (12).

The factors that unfavourably influence survival are: age, advanced congestive heart failure NYHA III and IV, systolic dysfunction of LV, extent of coronary disease and the presence of residual regurgitation after mitral valve repair (13).

MITRAL VALVE REPAIR

As already mentioned, IMR is the functional valvular affliction without pathological damage of the leaflets. In these cases, mitral valve repair is generally performed by implantation of mitral ring (so called mitral valve annuloplasty). The aim is to keep the annulus in systolic shape, to diminish the area of the mitral orifice and thus to accomplish the optimal coaptation of the leaflets and diminishing or even eliminating mitral regurgitation. In some cases, mitral valve repair is performed together with chordal cutting of secondary chords that cause so-called tethering and thus contribute to the restrictive motion of mitral leaflets (14). The left ventricular restoration (resection of left ventricular aneurysm) may also decrease IMR.

It has not been unequivocally proved that mitral valve repair in case of IMR is more convenient than replacement. Retrospective studies comparing long-term results of mitral valve repair and replacement in the patients with IMR provide almost comparable results (Graph 3). Nevertheless, early mortality is lower in case of mitral valve repair (15-17).

CONCLUSION

Ischemic mitral regurgitation is a significant negative prognostic factor in patients with coronary artery disease. In contrast to cases of organic regurgitation, there are no unambiguous rules about therapeutic approaches in these patients. This especially refers to mild or moderate IMR. In the light of the available information, we assume (with respect to the proved negative influence of even mild IMR) that concomitant mitral valve surgery is indicated in these patients in selected cases. This mainly refers to patients with systolic dysfunction of LV and advanced congestive heart failure. Randomized studies will be necessary to confirm the justification of more radical pro-

cedure and to specify the indications.

Quantification of IMR by means of PISA method with determination of ERO and RVol seems convenient. Both these values, even though burdened with measurement error, render clinical equivalents relating to the patient's prognosis. In patients with mild or moderate IMR, PISA may be used as one of the main criteria on which indication of concomitant mitral valve surgery is based.
Even though mitral valve surgery fails to show convincingly better long-term results than mitral replacement, there is lower early mortality than in mitral valve replacement, and so it should be preferred.

Surgical treatment of ischemic mitral regurgitation remains the complicated and still continuing challenge. The etiopathogenesis of IMR is complex, as is its treatment (myocardial revascularization, mitral valve repair, left ventricular restoration and eventually chordal cutting).

Abbreviations

AMI - acute myocardial infarction
AML - anterior papillary muscle
CABG - coronary artery bypass grafting
CAD - coronary artery disease
EF - ejection fraction
ERO - effective regurgitant orifice
IABP - intraaortic balloon counterpulsation
IMR - ischemic mitral regurgitation
LA - left atrium
LV - left ventricle
MI - myocardial infarction
MR - mitral regurgitation
MVR/R - mitral valve repair or replacement
PCI - percutaneous coronary intervention
PISA - Proximal Isovelocity Surface Area
PM - papillary muscle
PML - posterior papillary muscle
RV - right ventricle
RVol - regurgitant volume

REFERENCES

1. **Lamas, G. A., Mitchell, G. F., Flaker, M. D. et al.:** for Survival and Ventricular Enlargement Investigators. Clinical significance of mitral regurgitation after acute myocardial infarction. Circulation,1997, 96, pp. 827-833.
2. **Tcheng, J. E., Jackman, J. D., Nelson, C. L. et al.:** Outcome of patients sustaining acute ischemic mitral regurgitation during myocardial infarcion. Ann. Intern. Med., 1992, 117, pp. 18-24.
3. **Hirakawa, S., Sasayama, S., Tomoike, H. et al.:** *In situ* measurement of papillary muscle dynamics in the dog left ventricle. Am. J. Physiol. (Heart Circ. Physiol.), 1977, 2, p. H384.
4. **Gorman, R. C., McCaughan, J. S., Ratcliffe, M. B. et al.:** A three-dimensional analysis of papillary muscle spatial relationships in acute postinfarction mitral insufficiency. Surg. Forum. 1994, 45, p. 330.
5. **Messas, E., Guerrero, L. G., Handschumacher, M. D. et al.:** Paradoxic decrease in ischemic mitral regurgitation with papillary muscle dysfunction. Insights from three-dimensional and contrast echocardiography with strain rate measurement. Circulation, 2001, 104, pp. 1952-1957.
6. **Kaul, S., Spotnitz, W., Glasheen, W. P. et al.:** Mechanism of ischemic mitral regurgitation: an experimental evaluation. Circulation, 1991, 84, pp. 2167-2180.
7. **Wei, J. Y., Hutchins, G. M., Bulkley, B. H. et al.:** Papillary muscle rupture in fatal acute myocardial infarction: a potentially treatable form of cardiogenic shock. Ann. Intern. Med., 1979, 90, pp. 149-152.
8. **Grigioni, F., Sarano, M. E., Kenton, J. Z. et al.:** Ischemic Mitral Regurgitation. Long-term outcome and prognostic implication with quantitative Doppler assessment. Circulation, 2001, 103, pp. 1759-1764.
9. **Trichon, B. H., Glower, D. D., Shaw, L. K. et al.:** Survival after coronary revascularization, with and without mitral valve surgery in patients with ischemic mitral regurgitation. Circulation, 2003, 108 (Suppl. II), pp. II-103 – II-110.
10. **Duarte, I. G., Shen, Y., MacDonald, M. J. et al.:** Treatment of moderate mitral regurgitation and coronary disease by coronary bypass alone: late results. Ann. Thorac. Surg., 1999, 68, pp. 426-430.
11. **Aklog, L., Filsoufi, F., Flores, K. Q., Chen, R. H. et al.:** Does coronary artery bypass grafting alone correct moderate ischemic mitral regurgitation? Circulation, 2001, 104 (Suppl.), pp. I-68 – I-75.
12. **Gilinov, A. M., Wierup, P. N., Blackstone, E. H. et al.:** Is repair preferable to replacement for ischemic mitral regurgitation? J. Thorac. Cardiovasc. Surg., 2001, 122, pp. 1125-1141.
13. **Kuwaki, K., Kiyofumi, M., Tsukamoto, M. et al.:** Early and late results of mitral valve repair for mitral valve regurgitation. J. Cardiovasc. Surg., 2000, 41, pp. 187-192.
14. **Dahlberg, P. S., Orszulak, T. A., Mullany, C. H. J. et al.:** Late outcome of mitral valve surgery for patients with coronary artery disease. Ann. Thorac. Surg., 2003, 76, pp. 1539-1548.
15. Chordal cutting. In: A new therapeutic approach for ischemic mitral regurgitation. Messas, E, Guerrero, J. L., Handschumacher, M. D. et al. Circulation, 2001, 104, pp. 1958-1963.
16. **Sarano, M. E., Schaff, H. V., Frye, R. L.:** Mitral Regurgitation. What causes the leakage is fundamental to the outcome of valve repair. Circulation, 2003, 108, pp. 253-256.
17. **Thourani, V. H., Weintraub, W. S., Guzton, R. A. et al.:** Outcomes and long-term survival for patients undergoing mitral valve repair versus replacement: effect of age and concomitant coronary artery bypass grafting. Circulation, 2003, 108, pp. 298-302.

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