Therapy Principles in Ischemic Mitral Regurgitation

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ABSTRACT
Mitral regurgitation is a result of the ischemic cardiac disease, with two forms, acute and chronic. The main occurring mechanism is left ventricle dysfunction resulting from acute myocardial infarction with negative remodeling, displacement of papillary muscles, dilation of mitral ring and tethering of mitral valves. The treatment of the chronic form is complete surgical myocardial revascularization associate with mitral annuloplasty with “undersizing” prosthetic ring or mitral prosthesis. Taking into account the high frequency of residual mitral regurgitation, surgical techniques have been developed to address mitral subvalvular floor, whose efficiency remains to be proved in time.

Key words: acute myocardial infarction, ischemic mitral regurgitation, coronary by-pass, left ventricle
Ischemic mitral regurgitation (IMG) is the mitral regurgitation that is determined by the ischemic coronary disease and must be differentiated from the mitral regurgitation, which coexists with ischemic coronary disease. It appears secondary to acute myocardial infarction with angiographic or echocardiographic signs of contraction anomaly of left ventricle in a region vascularized by a critically stenosed coronary artery (1-3).

Ischemic mitral regurgitation is determined by an excess of tethering of one or both mitral valves, as a result of displacement of one or both papillary muscles. All patients have anterior acute myocardial infarction with regional anomaly of left ventricle wall contraction. Statistically, approximately 80% display posterior infarction and 20% anterior infarction (4).

Mitral ischemic regurgitation occurs in 13-50% of the cases after acute myocardial infarction, has poor long term prognostic, and becomes an independent risk factor for cardiac insufficiency occurrence, for survival rate and for atrial fibrillation, proportionally with the level of mitral regurgitation (2, 5-7).

Under medical treatment only, mitral ischemic regurgitation has a reserved prognostic, the survival rate at 1 year is 52-87%, and at 5 years is 22-54% (5, 8).

Morphologically, mitral ischemic regurgitation has 2 forms, acute and chronic.

The acute form occurs by:
- rupture of papillary muscles
- papillary muscles necrosis

**Rupture of papillary muscles**

In 1/3 of the cases, complete rupture occurs, affecting both mitral cusps, and resulting in mitral prolapse, and in 2/3 of the cases, the rupture of one or more ends of papillary muscles occurs. In about 75% of the cases, postero-medial papillary muscle rupture occurs, and in 25% of the cases, the antero-lateral is affected (9-11), and accordingly, patients develop acute infero-posterior myocardial infarction in 75% of the cases. The acute myocardial infarction can be subendocardial or transmural, with different dimensions depending on coronary collateral circulation. Rupture of intraventricular septum or free wall of left ventricle may also occur (10, 12).

**Papillary muscles necrosis**

Is present in about 50% of the cases and determines papillary muscle dysfunction (10, 12).

Chronic mitral ischemic regurgitation is mainly defined as follows (1, 2, 8):
- acute myocardial infarction at least 16 days old;
- more than 70% of at least one coronary artery stenosis
- presence of abnormal movement of left ventricle wall;
- presence of myocardial infarction with mechanism I/IIb (Carpenter classification)

Chronic IMG has the following main causes (9, 12):
- ischemic dysfunction of papillary muscle;
- papillary muscle scar;
- asynergy of the adjacent wall of the left ventricle;
- left ventricle remodeling.

It may be localized on antero-lateral or postero-medial commissure, or may display central regurgitation.

The pathophysiological mechanism of occurring of IMG is only partially known; remodeling of left ventricle affecting left atrium and development of atrial fibrillation occur in 5-23% of the cases (13).

The ischemic distress determines left ventricle dysfunction with negative remodeling, papillary muscle displacement (one or both), mitral ring dilation, tethering of mitral valves with peripheral or central regurgitation jet. The remodeling determines most frequently the displacement of posterior papillary muscle. The mitral ring dilation occurs when the ventricle is significantly dilated. The local (regional) and global remodeling of left ventricle with asymmetric or symmetric tethering occurs (13, 14).

Local remodeling typically occurs in inferior myocardial infarction with posterior papillary muscle displacement (asymmetric tethering). The regurgitated jet is eccentric at postero-medial commissure (13, 14)

Global remodeling of left ventricle occurs when both papillary muscles are displaced toward apex, with restrictive movement of both mitral valves (symmetric tethering). The regurgitation jet is central (13, 14)

The understanding of the pathophysiological mechanism allows the choice for treatment strategy (4). Ischemic mitral regurgitation as a result of acute myocardial infarction - affecting left ventricle structure and function - raises the diastolic distress,
determining eccentric hypertrophy and dilation of the left ventricle, and phenomena of cardiac insufficiency.

The telesystolic and telediastolic diameters and volumes increase, left ventricle performances decrease and left atrium diameter increases (2, 15).

Clinically, ischemic mitral regurgitation may occur in first hours to 14 days (with a peak in frequency of 2-7 days) after acute myocardial infarction (4).

Ultrasound (trans-thoracic and trans-esophageal) is crucial for corroborating the diagnostic, being able to differentiate rupture from papillary muscle dysfunction, indicating also any movement anomaly of the left ventricle (1).

The investigation needs to assess the following: inter-commissural and septo-lateral distance in systole and diastole, the rate of the septo-lateral distance comparative to the inter-commissural distance (in systole), the length of anterior valve, tenting area, co-opting depth, co-opting length, telesystolic volume, ejection fraction of left ventricle (EFLV), sphericity index (1, 17).

Regurgitation level has been assessed through the effective regurgitating orifice (ERO) (1):
- ERO > 20 mm² – severe IMG
- 10 – 19 mm² – moderate IMG
- 1 – 9 mm² – light IMG

There are certain cardiac ultrasound indicators for the surgeon which corroborate the reversibility of mitral regurgitation: co-opting depth, level of displacement of papillary muscles, the angle between posterior or anterior mitral valve and mitral plan (18). Furthermore, if echocardiographically the telesystolic diameter of left ventricle (TSDLV) is over 65 mm, excision of the post-infarction scar of the left ventricle is mandatory (18). When posterior valve angle is over 45 degrees, mitral prosthetic is recommended, this indicator being an important predictor for residual mitral regurgitation secondary to plasty (19). Another investigation that brings up precious information is cardiac ultrasound under dobutamine (20). Gadolinium MRI highlights myocardial scar area and papillary muscle dysfunction (9, 16).

In case of total rupture of papillary muscle with acute ischemic mitral regurgitation, the survival rate in first 24 hours is about 25%, and in case of partial rupture, surgical patients have a survival rate of 70% at 24 h and 50% at 1 month (13). In the absence of papillary muscle rupture, natural evolution is uncertainly defined.

Severe mitral ischemic regurgitation occurs in 3-19% of the patients with acute myocardial infarction without papillary muscle rupture and is a predictor of cardiovascular mortality at 1 year (13).

Best strategy to ameliorate the reshaping of left ventricle after acute myocardial infarction is immediate myocardial perfusion. However, the success of myocardial perfusion does not decrease the risk of ischemic mitral regurgitation occurrence and has mortality risk of 40-55% at 5 years (21).

Taking into account that mortality at 1 year in severe ischemic mitral regurgitation is about 40%, complete myocardial reperfusion combined with mitral valve plasty or prosthesis is recommended (22).

**Therapy principles**

In the acute form, surgical intervention comes as an emergency, usually needing aortic counter pulsation balloon or pulmonary percutaneous by-pass, followed by complete surgical myocardial revascularization combined with mitral valve plasty with prosthetic ring (usually 2 numbers smaller than valve surface), or mitral valvular prosthesis with mechanic or biological prosthesis; it is preferable to preserve the mitral valves (both or only the posterior one). When hemodynamic status becomes stable, the operation may be temporized between 2 weeks and 2 months. In case of complete papillary muscle rupture, valvular prosthesis is mandatory (11).

For the chronic form, the usual approach consists in complete surgical myocardial revascularization, associated with prosthetic “undersizing” ring plasty or mitral prosthesis (14, 23). When the chronic ischemic mitral regurgitation is preoperatively variable and intraoperatively not worse than moderate, and the signs and symptoms of myocardial ischemia are predominant, ischemic mitral regurgitation may be left untreated (24). For severe chronic ischemic mitral regurgitation the association with complete myocardial revascularization of the plasty or mitral prosthesis is always mandatory (23).

In patients with left ventricle ejection fraction (EF) under 20% and severe ischemic mitral regurgitation, resynchronization therapy can be applied. Also, mitral prosthesis is preferred to plasty, since the persistence of residual ischemic mitral regurgitation results in poor postoperative evolution (21).

Mitril anuloplasty with restrictive prosthetic
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ring was introduced by Bolling in 1995, and can be applied with complete or incomplete rings, rigid or flexible, with similar postoperative results, according to the mainstream (14).

American Heart Association recommends mitral annuloplasty with ring like in surgical procedure (even if optimal operation is still controversial - 2008 ACC / AHA JACC Guidelines) (23).

Medical guides recommend class I surgical treatment for severe ischemic mitral regurgitation, but do not specify the type of intervention - plasty or prosthesis (13, 25).

The main objectives of the surgical treatment are as follows (14):

a. complete surgical myocardial revascularization;

b. complete ring, rigid or semirigid (preferably to not use flexible bands);

c. restrictive ring (twice smaller than the mitral valve surface, in order to accomplish a valvular co-optation surface bigger than 5-9 mm;

d. postoperative cardiographic control to highlight no more than rank I residual mitral regurgitation.

The treatment of ischemic mitral regurgitation must address all the following elements: annular dilation and flattering, dysfunction and displacement of papillary muscles, valvular tethering and inadequate adaptation, dilation and dysfunction of LV (1).

It is generally considered that restrictive annuloplasty of mitral valve combined with myocardial revascularization needs to be performed in the first 30 days after acute myocardial infarction, in order to accomplish the reversibility of the remodeling of LV (26).

The mitral annuloplasty ring is intended especially for ischemic etiology cases and has a specific 3D form (GEOFORM ring) (25). Comparative to the classical ring, this ring has the same intertrigonal dimension, with a smaller septo-lateral area and with a posterior to superior indentation, in order to pull upwards after implantation the middle scallop (P2) of the mitral valve, improving valvular co-opting. This ring - by pulling the posterior mitral ring anterior and superior - diminishes the tethering forces of LV remodeling. It is exclusively used in asymmetric tethering.

The greater than rank 2 residual mitral regurgitation, resulted after restrictive annuloplasty, has a frequency of up to 30% and is unacceptable (27, 28). In order to prevent its occurrence, the nickel-titanium deformable annuloplasty ring has been introduced, that allows the reduction of septo-lateral diameter. This is a complete rigid ring, with a diameter between 28 and 36 mm; by using radio-frequency energy, the nitinol stem can modify its diameter and shape at septo-lateral area from 0.5 to 3 mm and the intercommissural from 1 to 3.5 mm. The change becomes irreversible. Radiofrequency does not induce thermic distress or adjacent tissue necrosis, or changes of blood constituents (25, 28).

Both complete and incomplete rings are used, and no significant differences have been noticed so far as regards the efficiency and durability of the plasty (29).

However, complete ring is superior in ischemic etiology cases, decreasing the risk of main complications occurrence, but also decreasing the survival rate (8).

Its superiority has been proved regarding the occurrence of recurrent ischemic mitral regurgitation (21% vs. 10% at 30 days and 34% vs. 30% at 6 months). Pathophysiologically, the complete ring has the ability to maintain the aular diameter, the intertrigonal and septo-lateral distance, resulted from geometry change of the subvalvular apparatus. The study shows a greater frequency in residual ischemic mitral regurgitation occurrence after using the incomplete ring, because it allows an unknown dilation of anterior mitral ring (despite what is presently known). However, other recent studies refute this (8, 29). This is why the incomplete ring cannot maintain a fixed septo-lateral distance. Other occurring mechanisms of residual ischemic mitral regurgitation are the displacement of posterior papillary muscle and valvular tethering (13, 30).

Previous studies supported the usage of the incomplete ring in order to prevent the occurrence of "systolic anterior motion” (SAM), which appears more frequently by using the complete ring, because of the anterior displacement of the valvular co-option point (the mechanism is applicable only in degenerative etiology) (8).

All the patients whose preoperative cardiac ultrasound showed ERO greater than 10 mm² were recommended mitral plasty, whose purpose was to obtain a co-opting length of 5-8 mm, accepting a longer than 25 mm anterior mitral valve (8, 31).

In case of asymmetric displacement of the mitral
valve, it is preferable that the specific ring for ischemic etiology to be used, in order to compensate the valvular tethering in P2, P3 and commissural P (Pc). This type of ring does not imply “undersizing”. If the classical ring is used, "undersizing" is necessary (14).

In case of global left ventricle affecting, symmetrical dilation of mitral ring occurs. In this case, only the “undersizing” classical ring is used (14).

Residual ischemic mitral regurgitation occurs in 10-30% of the cases, 6 months postoperatively after mitral valve restrictive annuloplasty (27, 32).

The following predictive factors are used in order to assess the occurrence of residual ischemic mitral regurgitation after restrictive annuloplasty (33):
- LV ejection fraction (LVEF) under 35%;
- telediastolic diameter of LV over 65 mm;
- postoperative severe ischemic mitral regurgitation
- co-opting index (CI) \( \leq 6 \) mm;
- co-opting depth > 10 mm;
- posterior valve angle \( \geq 45^\circ \).

Taking into account the increased frequency of residual ischemic mitral regurgitation occurrence after “undersizing” annuloplasty, new surgical techniques that address the mitral subvalvular apparatus or the infarction scar area have been developed. All these techniques are applied when severe tethering occurs (cardiac ultrasound displays over 10 mm tethering) and are associated with prosthetic ring annuloplasty corresponding with valve surface number wise (33).

All these additional techniques have as outcome the diminishing of the mitral regurgitation degree, the telesystolic volume of left ventricle, the telediastolic volume of left ventricle and the improvement of left ventricle ejection fraction (34).

The following techniques have been developed:

**Sectioning of the secondary tendinous cords**

Sectioning of the secondary tendinous cords determines valvular tethering decrease. Left ventricle remodeling with valvular tethering prevents fair valvular co-opting. Secondary tendinous cords contribute as well.

The technique is applicable to anterior or posterior mitral valve, or for commissures, and addresses to secondary tendinous cords of one or both papillary muscles (affected by the myocardial infarction areas).

The sectioning of the secondary tendinous cords results in a better valvular mobility. Usually the tendinous cords emerging from posterior papillary muscle on ventricular insertion on scallop A2 are sectioned and transferred on the free margin of scallop A3.

This maneuver decreases the valvular tethering and increases the valvular mobility, restoring the curve toward left atrium (20, 34-36).

**Posterior valvular extension with pericardium**

It is usually applied on P2-P3 scallops in order to reduce the degree of mitral regurgitation. Anterior mitral valve extension can be performed as well, in cases when its length is under 25 mm. It is always combined with the sectioning of secondary tendinous cords (4, 13, 36, 37).

**Relocation of the posterior papillary muscle**

Relocation of the posterior papillary muscle on the corresponding to P3 scallop mitral ring. This way, co-opting depth significantly changes the aular level, reducing the height and tenting area. The displacement of papillary muscle with negative reshaping of the left ventricle is also prevented.

The relocation is performed with GORETEX thread number 4 or PROLENE thread 3/0 (KRON technique) which is passed through the papillary muscle body and then through the mitral ring posterior to the right fibrous trine. Both papillary muscle can be relocated.

The anterior papillary muscle is relocated only anterior, since it offers tendinous cords only to anterior mitral valve, while the posterior papillary muscle offers tendinous cords also to posterior valve (P1, P3) (38).

After papillary muscles relocation, positive remodeling of left ventricle has been acquired, regarding the telesystolic and telediastolic diameter, and also the tenting area and co-opting depth have been improved (13, 17, 37).

**Papillary muscles sling**

It is performed by passing the threads through the base of papillary muscles and through the in-between left ventricle wall, which brings them near (11, 13, 37, 47).

**External folding of myocardial infarction area**

It reduces the distance between the two papillary muscles and their apical shift (16, 39). In the presence of post infarction scar of the posterior wall
of left ventricle, a longitudinal incision parallel with the posterior descendant coronary artery can be performed, together with scar excision and longitudinal suture with separate threads in "U" (16, 36).

All these procedures need to restore the conical shape of left ventricle and a volume of left ventricle over 60 ml/m² (39).

**“Edge to edge” technique**

MITRACLIP percutaneous procedure can be performed. It may reduce with 2 degrees the rank of the ischemic mitral regurgitation in about 85% of the cases (40), it increases the ejection fraction and improves NYHA rank.

This technique is used in patients with very high operative risk, resulting in left ventricle modeling reversibility (13, 41).

Prosthetics with mechanical or biological prosthesis with preservation - whenever possible - of both mitral valves or of only posterior mitral valve is the alternative to mitral valve plasty (29, 48-51).

Restrictive annuloplasty determines a certain degree of functional mitral stenosis, its gradient being parallel with the amount of effort, but not limiting its functional capacity.

The technique fixes the posterior valve, unaltering the subvalvular apparatus, and restricts the systolic-diastolic movement of mitral valve (1, 33).

It appears that hemodynamic performances in restrictive mitral annuloplasty are poorer than in mitral prosthesis, because the first one is not affecting subvalvular tethering.

The success of mitral valve plasty is assessed by cardiac ultrasound, by measuring a greater than 0.8 valvular co-opting and a bigger than 2 cm² surface area (32). Complete surgical myocardial revascularization associated with "undersizing" annuloplasty improves left ventricle remodeling, increases functional capacity, reduces mitral regurgitation severity and decreases the level of natriuretic peptide (15, 31).

Comparative studies regarding complete surgical myocardial revascularization associated with plasty of mitral valve prosthesis show that early postoperative mortality is comparable (3.3 - 5%); main risk factors are age over 70, over 12 EUROSCOR, and prolonged extracorporeal circulation or clamping time (13, 14).

Mitrail prosthesis is recommended in cases where the left ventricle telediastolic diameter is over 65 mm (14, 42); the plasty or the prosthesis improves left ventricle function in 33% of the cases, worsens it in 16-20%, and shows no change in 18% of the cases (14, 20).

An improvement of left ventricle function is shown in about 50% of the cases by postoperative positive remodeling (14, 43). The conclusions are that the plasty is not superior to prosthesis as regards early and late survival rate, and left ventricle performances. In both groups, NYHA improved at 3 and 12 months, the effort test was similar, and BNP (brain natriuretic peptide) was similar at 3 months.

There are comparative studies as well regarding the effect on chronic ischemic mitral regurgitation in patients who underwent surgical myocardial revascularization versus patients who underwent both surgical myocardial revascularization and "undersizing" annuloplasty (24, 31).

Both groups showed a decrease of the effective regurgitation orifice (ERO), jet area, regurgitated volume and regurgitation fraction at 3 and 12 months, but less decrease in diameters and volumes of left ventricle and ejection fraction for the group with associated annuloplasty (1).

In 2009 (34) first randomized study on this subject was published, with comparisons up to 32 months. The degree of the residual ischemic mitral regurgitation was 0.8 for coronary by-pass combined with annuloplasty and was 1.7 for coronary by-pass alone.

The combining of the annuloplasty reduces the degree of the mitral regurgitation, reduces the dimensions of left atrium and the pulmonary artery pressure in a better percentage.

In acute form with papillary muscles rupture, postoperative early mortality is 18-22%, and at 5 years is 65-68% (22). For the chronic form, mortality rate is 29% at 2 years (44). The main risk factors for postoperative mortality are the following: left ventricle reduced ejection fraction, tricoronary ischemic disease, advanced age, renal insufficiency, anemia, above 65 mm telediastolic diameter of left ventricle, prolonged cardio-pulmonary by-pass, increased need for inotropic support (14).

The main risk factors for recurrent ischemic mitral regurgitation occurrence after surgical myocardial revascularization with mitral annuloplasty are as follows (12, 14, 21):
- mitral regurgitating flux over 35%;
- age over 70;
- reduced ejection fraction of left ventricle;
- over 65-70 mm telesystolic diameter of left ventricle;
- NYHA class over III;
- arrhythmia;
- echocardiographically: posterior mitral valve angle over 45°, anterior mitral valve angle over 25°, co-opting distance over 10 mm, telediastolic distance between the two papillary muscles over 20 mm, and systolic sphericity index of left ventricle over 0.7.

Mitral valve plasty combined with coronary bypass may result in positive reshaping of left ventricle, which can be echocardiographically assessed by: increase of the valvular co-opting height, decrease of tenting area, decrease of telesystolic and telediastolic diameters of left ventricle, improvement of ejection fraction, increase of the shortening fraction, decrease of the pulmonary artery pressure (14, 45 - 51). Reversible reshaping of left ventricle in “undersizing” plasty and in mitral prosthesis are comparable at 1 year after surgery (26).

CONCLUSIONS

Ischemic mitral regurgitation is a result of the ischemic coronary disease secondary to acute myocardial infarction and has 2 forms: acute, severe and chronic. The surgical treatment of choice is complete surgical myocardial revascularization, usually combined in moderate to severe forms with mitral annuloplasty with “undersizing” prosthetic ring or mitral prosthesis. The occurrence of severe mitral regurgitation in significant percentage (about 30%) after mitral plasty with “undersizing” prosthetic ring determined the development of several new combined surgical techniques which address to the mitral subvalvular floor. The efficiency of all these techniques remains to be proven in time.

REFERENCES

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