

Review

The Role of Echocardiography in the Surgical Management of Secondary Mitral Regurgitation

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REZUMAT

Rolul ecocardiografiei în managementul chirurgical al regurgitării mitrale secundare

Regurgitarea mitrală (RM) secundară este mai frecventă, asociază un prognostic mai sever și pune mai multe probleme de diagnostic și tratament față de RM primară. RM secundară apare secundar remodelării ventriculului stâng în contextul unor foite mitrale indemne morfologic. Tratamentul chirurgical al RM secundare severe constă fie în reparația fie în protezarea valvulară mitrală. Tehnica de reparație valvulară cea mai frecvent utilizată este reprezentată de implantarea unui inel mitral subdimensionat. Această tehnică chirurgicală prezintă un risc mai mic operator însă se asociază cu o rată mai mare a recurenței RM postoperator, comparativ cu înlocuirea valvulară mitrală. Ecocardiografia oferă o serie de parametri legați de modificarea geometrică a aparatului mitral, capabili să prezică succesul sau insuccesul reparației valvulare mitrale și astfel să selecteze strategia chirurgicală cea mai potrivită pentru fiecare pacient în parte. Ne propunem să trecem în revistă, parametrii de ecocardiografie bidimensională care s-au dovedit a avea valoare predictivă înaltă pentru recurența RM secundare după intervenția de reparație valvulară mitrală.

Cuvinte cheie: ecocardiografie, chirurgia insuficienței mitrale secundare

ABSTRACT

Secondary mitral regurgitation (MR) is more frequent, portends a worse prognosis and its diagnostic and management are more difficult in comparison with primary MR. The mechanism of secondary MR is linked to the left ventricle remodeling, while the valve morphology is normal. Surgical treatment of severe secondary MR consists either in mitral valve replacement or in mitral valve repair. The most commonly used repair technique is represented by undersized mitral annuloplasty. This surgical technique implies lower surgical risk but associates a higher rate of postoperative MR recurrence, compared to mitral valve replacement. Echocardiography provides geometric parameters related to mitral apparatus deformation, which are able to predict the success or failure of mitral valve repair and thus helps in selecting the best surgical strategy for each patient. In this paper we try to make an inventory of the echocardiographical parameters which proved predictive power for unsuccessful mitral valve repair techniques.

Key words: ecocardiography, surgery for secondary mitral regurgitation

INTRODUCTION

Secondary mitral regurgitation (MR) also known as functional mitral regurgitation is more common, portends a worse prognosis than primary MR and its management is more difficult and less sustained by evidence. [1]The etiology of secondary MR may be ischemic or non-ischemic such as in idiopathic dilative cardiomyopathy. The prognosis of patients with secondary MR is worse with increasing severity of MR.[2]

The mechanism of secondary MR is linked to the left ventricle (LV) geometrical remodeling with secondary tethering of the mitral leaflets, while the valve morphology is normal. [3][4]

The therapeutic approach of severe secondary MR consists in surgical repair, surgical replacement or percutaneous edge-to-edge repair. While the percutaneous techniques are reserved for high surgical risk patients, for the other patients a surgical approach is recommended. Choosing between mitral valve (MV) repair and MV replacement in each individual case is a difficult decision taking into accounts the advantages and disadvantages of each procedure, as well as the conflicting results of the clinical trials.

Specifically MV repair is associated with lower surgical risk but with a higher rate of postoperative recurrence when compared to MV replacement. The high MR recurrence rate after MV repair techniques can be easily explained by the fact that these procedures usually address only to mitral annulus dilatation which is only one of the several morphological changes associated to secondary MR. In this specific type of MR, the mitral apparatus undergoes complex geometrical alterations consisting in mitral annulus flattening, tethering of the leaflets, posterior and lateral displacement of the papillary muscles; these alterations are accompanied by local and global LV remodeling.

Echocardiography can offer valuable information regarding the morphology of the mitral apparatus in each patient. Previous studies have identified several echocardiography predictors of unsuccessful valve repair. In patients in whom these parameters are present, MV replacement is more suitable than MV repair.

But most importantly, echocardiography can depict the specific pattern of MV remodeling in each patient, thereby suggesting other repairing techniques associated to annuloplasty such as cutting chordae, Alfieri stitch or ventricular reconstruction techniques.

More recently, three-dimensional (3D) echocardiography added important missing information related to the pathophysiology of secondary MR.[5][6][7][8]. This imaging technique might offer in the future new predictors of surgical success and new insights into the field of MV repair. Furthermore, 3D echocardiography plays an essential role in guiding the percutaneous procedures of MV repair.

In this paper we try to make an inventory of the echocardiography parameters which proved predictive power for unsuccessful mitral valve repair techniques.

Echocardiographic assessment of secondary MR severity

The first step in the echocardiographic evaluation of secondary MR is to determine its severity. This is of capital importance since only severe secondary MR should be treated surgically or percutaneously. The transthoracic echocardiographic examination provides important information regarding mitral apparatus morphology and severity of the regurgitation while the transoesophageal echocardiography may provide complementary information, having the advantage of a better visualization of the mitral valve structures and mobility. The disadvantage of transoesophageal echocardiography is that it is usually performed under sedation with drugs lowering the afterload, which results in underestimation of secondary MR. This is due to modified hemodynamics. It is not uncommon that secondary MR quantified as severe before the intervention to be found intraoperative under general anesthesia as being moderate or even mild.

Assessment of secondary MR severity is often difficult because it is a dynamic valvulopathy par excellence. The dynamic character of secondary MR refers to three instances: 1. the regurgitant flow which varies according to the different phases of the cardiac cycle; 2. the severity of the regurgitation which worsens or improves during the physical effort; 3. secondary MR which improves under treatment and worsens in the context of acute ischemia. Therefore secondary MR severity assessment is a difficult chapter of cardiovascular imaging, with many unknowns and possibilities for improvement in the future.

MR severity assessment methods have certain particularities for secondary MR. Currently, the recommended methods of quantification of secondary MR are represented by measuring the vena contracta width (VCW), the regurgitant volume and the effective regurgitant orifice area using the proximal isovelocity surface area (PISA) method and the volumetric method [9]. Using the last method, one can calculate the regurgitant volume as the difference between mitral and aortic valve stroke volumes. Severe secondary MR is defined as a regurgitant volume greater than 30 ml or an effective regurgitant orifice area greater than 20 mm² [9].

However, using the above mentioned echocardiography methods for secondary MR quantitation implies several geometrical assumptions which can, sometimes, be very different from reality. For example, measuring VCW assumes that the regurgitant orifice is perfectly circular, assumption inappropriate in the context of secondary MR, in which case the regurgitant orifice shape is complex and often asymmetrical. Two-dimensional echocardiography cannot provide an accurate picture of the regurgitant orifice shape, due to the inability to obtain

the perfect alignment with the orifice.

Similarly, 2D PISA method cannot be very accurate for the secondary MR quantitation, given the characteristics of the regurgitant jet. The PISA radius varies in size during systole, being larger in early and late systole and lower in mid-systole. Ideally, the value of PISA radius should be an average of several values measured during systole. Moreover, the physical concept underlying the calculation method PISA implies a perfect hemispheric convergence zone, but most times, in the context of secondary MR the convergence zone is flattened, leading to underestimation of MR severity. Furthermore, in case of multiple regurgitant jets, this method cannot be used.

3D echocardiography has added major improvements in the quantification methods of secondary MR, providing a more realistic assessment of this complex pathology. Studies have shown that the use of 3D echocardiography leads to similar results to cardiac magnetic resonance imaging, regarding secondary MR quantitation. [10][11]

Furthermore 3D echocardiography demonstrated superiority over 2D echocardiography in evaluating LV volumes, localizing and assessing the extent of mitral valve deformation, and determining the shape of the regurgitant orifice. [12]

Echocardiography parameters used in defining mitral valve apparatus geometry

Echocardiography offers several parameters by which one observer can describe the geometry of mitral valve apparatus. These parameters are usually classified into 3 groups: 1) mitral valve deformation parameters, 2) papillary muscles displacement parameters and 3) global left ventricle (LV) remodeling parameters.

1) Mitral valve deformation parameters consist of mitral annulus diameters and area, coaptation distance, coaptation length, tenting area, posterolateral angle. Mitral annular diameters are usually measured in the parasternal long-axis, 4-chamber, and 2-chamber views, from which mitral annular area may be calculated, using ellipsoid assumption. The coaptation distance is defined as the shortest distance between the coaptation point and the annular plane. The coaptation length is measured as the length of systolic leaflet contact. The tenting area is measured as the area enclosed by the mitral leaflets and the annular plane. The postero-lateral angle is defined as the angle between the annular plane and posterior leaflet and is regarded as a measure of the mobility of posterior leaflet. [13]

2) Papillary muscle displacement can be quantified by means of interpapillary muscle distance, posterior papillary-fibrosa distance, lateral and posterior papillary muscle displacement and lateral wall motion abnormalities. Interpapillary muscle distance is measured in parasternal short axis while posterior papillary-fibrosa distance is measured in the long-axis view being regarded

as a measure of the apical displacement of the posterior papillary muscle.

3) Global LV remodeling can be quantified by end-diastolic and end-systolic diameters, end-diastolic and end-systolic volumes and systolic sphericity index.

The importance of tethering patterns

Agricola et al. defined two patterns of mitral tethering in chronic ischemic MR: symmetric and asymmetric. [14] The symmetric one appears due to predominant apical tethering of both mitral leaflets such as in severe LV dilation secondary to large myocardial infarctions, while the asymmetric pattern appears secondary to predominant posterior tethering of both leaflets, as in inferior myocardial infarctions. Since each papillary muscle supplies chordae to both leaflets, consequently a posterior displacement of only one papillary muscle invariably exerts traction on both leaflets. This explains the finding that in the setting of inferior myocardial infarction, the posterior leaflet appears retracted, but also the body of the anterior leaflet is retracted creating the seagull appearance. All indexes of global LV remodeling are significantly higher in the symmetric than asymmetric group, such as the posterior and lateral displacement of the anterior papillary muscle, the papillary muscle separation and the anterior papillary muscle wall motion index. The direction of the regurgitant jet is different between the two patterns, being central in the symmetric pattern whereas the jet direction is usually posterior in the asymmetric pattern. [14]

The tethering pattern has important prognostic value, but also can help in choosing the most suitable surgical procedure. Taking into account that the degree of LV dilatation and dysfunction are paramount indexes of worse prognosis, we may think that the symmetric tethering pattern portends worse prognosis compared to the asymmetrical pattern. Agricola et al. suggest different surgical approaches for mitral valve reconstruction in each type of tethering pattern: in patients with asymmetric tethering with regurgitant jet arising from the medial commissure, they suggest a commissural Alfieri stitch with undersized annuloplasty squashed in the region of medial commissure, whereas in the symmetric tethering they suggest a central Alfieri stitch with undersized annuloplasty centrally squashed. [14]

Echocardiography predictors of unsuccessful mitral valve repair

Restrictive mitral annuloplasty which seeks to increase mitral leaflet coaptation by reducing mitral annular diameter is the most frequently used surgical approach. The mechanism of secondary MR is complex and usually implies alterations of the LV or mitral valve apparatus (mitral annular dilatation and tethering of mitral leaflets). However, the restrictive annuloplasty procedure focuses only on the mitral annulus enlargement. As expected, the

rate of MR recurrence after this type of surgical repair is high during follow-up mainly due to continued LV remodeling and persistent leaflet tethering. [15] Several studies tried to identify the preoperative echocardiographical parameters which could predict the postoperative MR recurrence.

The European Society of Echocardiography recommendations for the assessment of valvular regurgitation define the predictors of successful valve repair for secondary MR. [9] According to this document, high probability of MR recurrence is defined by a coaptation distance >1 cm, a systolic tenting area $>2,5$ cm², a posterior leaflet angle $>45^\circ$, a central regurgitant jet, the presence of complex jets originating centrally and posteromedially and a severe LV enlargement. However, recent studies identified other parameters such as anterior leaflet tethering indexes to have better predictive value.

Gelsomino et al. analyzed the echocardiography predictors of ischemic MR recurrence in 230 patients who underwent undersized mitral ring annuloplasty associated with complete revascularization by coronary artery bypass grafting (CABG). [16] Early follow-up was performed at 6 months while late follow-up was performed at 33 months. MR severity was quantified using the volumetric method (RV is the difference between mitral valve and aortic valve stroke volumes) and the PISA method. The patients were divided into 2 groups: patients with or without late recurrent MR. In the late recurrent MR group, preoperative echocardiography identified a central or anterior jet direction in most patients while in the recurrence free patients the jet was oriented posterior in most cases, the tethering pattern being asymmetric, with a prevalent restriction of the posterior leaflet excursion. Furthermore, patients with recurrent MR had greater preoperative posterior and lateral displacement of the anterior papillary muscle, a wider interpapillary distance and a larger wall motion score index of the segments underlying the anterior papillary muscle. Moreover, tenting area and coaptation height were higher, while coaptation length was lower in patients with recurrent MR. Patients without postoperative MR had a more pronounced posterior leaflet tethering, with prevalent restriction of the posterior leaflet excursion, while patients with postoperative MR had a more accentuated anterior leaflet tethering and a more symmetric tethering. At postoperative control, in patients with no recurrent MR at discharge, indexes of posterior and lateral displacement of papillary muscles, as well as the interpapillary distance were reduced significantly. In group with recurrent MR all indices of papillary muscle displacement showed a non significant reduction at discharge. These parameters remained stable at early control while increasing significantly at late examination. Multivariable regression analysis identified an anterior tethering angle of 39.5 or greater, an anterior/posterior

tethering angle ratio of 0.76 or greater, an anterior leaflet excursion angle of 35 or less, and a coaptation height of 11 mm or greater as independent predictors of recurrent MR. As authors conclude, their study showed that recurrent MR is more frequent in patients with preoperatively greater local remodeling of the left ventricular segments underlying the anterior papillary muscle, a greater lateral and posterior displacement of the anterior papillary muscle, and a wider papillary muscle separation. [16] In fact, this was the first study to demonstrate that patients with predominant tethering of the anterior leaflet had a higher likelihood of postoperative recurrent MR after reductive annuloplasty.

As expected, the group of patients with postoperative recurrent MR in this study is similar to the symmetric tethering pattern group described by Agricola et al. [14], with prevalent posterior and lateral displacement of anterior papillary muscle, and greater wall motion score index of the regions supporting the anterior papillary muscle.

Gelsomino et al, suggest that in patients with strongly tethered anterior mitral leaflet or with less tethered anterior leaflets not long enough to ensure a postoperative coaptation length of 8 mm or greater, MR presumably cannot be eliminated by means of ring annuloplasty. In these patients a technique directly addressing left ventricular remodeling or a chordal sparing mitral valve replacement should be considered. [16]

The undersized mitral anuloplasty results in even more restriction of the posterior leaflet, without affecting the anterior leaflet. [17] In this situation, the anterior leaflet has the central role in the mitral valve closure.

Lee et al. analyzed 104 patients with idiopathic dilated cardiomyopathy who underwent annuloplasty for functional MR. [13] In their study, the anterior leaflet tethering was defined using two distinct parameters: basal and distal tethering of the anterior leaflet. The tethering of basal anterior leaflet was assessed by measuring the angle between the annular plane and the basal portion of anterior leaflet while the tethering of distal anterior leaflet was assessed by measuring the angle between the annular plane and a line that joins the anterior annulus and coaptation point. Preoperative distal anterior leaflet tethering correlated strongly ($\rho=0.66$, $P<0.001$) with postoperative MR. Preoperative basal anterior leaflet tethering ($\rho=0.44$, $P<0.001$), coaptation depth ($\rho=0.47$, $P<0.001$), tenting area ($\rho=0.36$, $P<0.001$), VCW ($\rho=0.35$, $P=0.001$), LVEDV ($\rho=0.38$, $P<0.001$), LVESV ($\rho=0.33$, $P=0.002$), and LVEF ($\rho=-0.22$, $P=0.04$) had moderate correlation with postoperative MR. The best preoperative predictor of significant MR recurrence was preoperative distal tethering of the anterior leaflet, followed by coaptation depth and basal tethering of the anterior leaflet. Postoperative posterolateral angle showed a weak correlation with MR recurrence ($\rho=-0.24$, $P=0.02$).

As chordae originating from the posterior papillary muscle inserted on the base of the anterior leaflet, tethering of the basal chordae is more severe with predominant posterior displacement of the papillary muscles. This might be also because they are farther away from the papillary muscles than the distal anterior leaflet. If apical displacement is predominant, both leaflets are tethered apically, and a restricted motion of the distal anterior leaflet is also seen.

Ciarka et al. identified the echocardiography predictors of recurrent MR after mitral annuloplasty in patients with heart failure (HF) of both ischemic and non-ischemic etiology. Mitral regurgitation preoperative severity, mitral annular area, and LV volume and dimension were similar among patients with and without recurrent MR. In contrast, patients with recurrent MR had increased preoperative posterior and anterior leaflet angles, tenting height, tenting area and LV sphericity index compared to the patients without recurrent MR. Of the different parameters of mitral and LV geometry, the distal mitral anterior leaflet angle and posterior leaflet angle were independent determinants of recurrent MR. [18]

Hung et al. demonstrated that recurrent MR in patients after ring annuloplasty relates to continued LV remodeling. They showed that the only independent predictor of late postoperative MR was LV sphericity index at end-systole. In their study, the degree of MR increased from mild to moderate, on average, from early to late postoperative stages, without significant change in LV ejection fraction. In contrast, changes in MR paralleled increases in LV volumes and sphericity index at end-systole and end-diastole.

In summary, the symmetric tethering pattern is a consequence of a more severe LV remodeling and is a predictor for failure of MV repair surgery. The tethering of the anterior mitral leaflet seems to be more important in predicting procedural success than the tethering of the posterior leaflet.

Novel parameters of mitral valve geometry are obtainable through 3D echocardiography: mitral leaflet size, annulus area, intercomisural distance, annulus perimeter and height and annulus dynamics, posterior and anterior leaflet area, coaptation indexes, leaflet coaptation area, tenting volume, tenting area, PISA shape and regurgitant orifice geometry. [12] Whether these parameters are better predictors of unsuccessful MV repair and may improve the selection of patients and minimize procedural failure remains to be demonstrated.

Mitral valve reconstruction or replacement?

Surgery for secondary MR may consist of valve replacement with metal or biological prosthesis or mitral apparatus reconstruction techniques consisting in implantation of an undersized prosthetic ring with or without resection of the chordae or ventricular reconstruction

procedures. In case of primary MR we clearly know that valve repair is preferable to valve replacement, while in case of secondary MR experts opinions are divided regarding superiority of one technique over the other, each having advantages and disadvantages.

Recurrent MR is frequent after undersized mitral annuloplasty. Despite its initial elimination in all patients, moderate or greater MR recurs in 15% to 25% of patients at 6 to 12 months, increasing to 70% at 5 years. [19]

In recent years, the proportion of mitral repairs increased in the detriment of valvular replacement, a strategy supported by the literature data which reported better results of mitral repairing procedures. However, the study of Acker et al. published at the beginning of 2014 comes to contradict the previous data, showing no difference between the two techniques at 1 year follow-up in terms of the degree of LV reverse remodeling and mortality; furthermore MR recurrence at 1 year was 32.6% in the patients with annuloplasty and only 2.3% in the mitral prosthesis patients. [20]. In this context, it is obvious that mitral repair techniques can be improved, most likely by associating ventricular and mitral subvalvular apparatus reconstruction techniques, taking into account that simple undersized ring implantation alone cannot solve this complex pathology.

CONCLUSIONS

In conclusion, several geometrical parameters are obtainable by echocardiography, which can predict the failure or success of MV repair surgery. Most of these parameters point to the anterior mitral leaflet tethering and continued LV remodeling as the most important mechanisms involved in the postoperative MR recurrence. A complete echocardiography must include all these parameters in order to help the heart team in selecting the most suitable surgical strategy for each patient. Whether the new 3D echocardiographic parameters will improve the selection process will have to be demonstrated by future studies.

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REFERENCES

1. A. W. Asgar, M. J. Mack, and G. W. Stone, "Secondary Mitral Regurgitation in Heart Failure Pathophysiology, Prognosis, and Therapeutic Considerations," *J. Am. Coll. Cardiol.*, vol. 65, no. 12, pp. 1231-1248, 2015.
2. L. A. Piérard and B. A. Carabello, "Ischaemic mitral regurgitation: pathophysiology, outcomes and the conundrum of treatment," *Eur. Hear. J.*, Dec. 2010.
3. T. H. Marwick, P. Lancellotti, and L. Pierard, "Ischaemic mitral regurgitation: mechanisms and diagnosis.," *Heart*, vol. 95, no. 20, pp. 1711-1718, 2009.

4. R. A. Levine and E. Schwammenthal, "Ischemic mitral regurgitation on the threshold of a solution: from paradoxes to unifying concepts.," *Circulation*, vol. 112, no. 5, pp. 745–758, 2005.
5. W. Tsang and R. M. Lang, "Three-dimensional Echocardiography Is Essential for Intraoperative Assessment of Mitral Regurgitation," *Circ.*, vol. 128, no. 6, pp. 643–652, 2013.
6. K. Yoshida and K. Obase, "Assessment of Mitral Valve Complex by Three-Dimensional Echocardiography: Therapeutic Strategy for Functional Mitral Regurgitation," *J. Cardiovasc. Ultrasound*, vol. 20, no. 2, pp. 69–76, 2012.
7. M. Vergnat, A. S. Jassar, B. M. Jackson, L. P. Ryan, T. J. Eperjesi, A. M. Pouch, S. J. Weiss, A. T. Cheung, M. A. Acker, J. H. Gorman, and R. C. Gorman, "Ischemic Mitral Regurgitation: A Quantitative Three-Dimensional Echocardiographic Analysis," *Ann. Thorac. Surg.*, vol. 91, no. 1, pp. 157–164, 2011.
8. N. Watanabe, Y. Ogasawara, Y. Yamaura, T. Kawamoto, E. Toyota, T. Akasaka, and K. Yoshida, "Quantitation of mitral valve tenting in ischemic mitral regurgitation by transthoracic real-time three-dimensional echocardiography.," *J. Am. Coll. Cardiol.*, vol. 45, no. 5, pp. 763–769, 2005.
9. P. Lancellotti, L. Moura, L. A. Pierard, E. Agricola, B. A. Popescu, C. Tribouilloy, A. Hagendorff, J.-L. Monin, L. Badano, and J. L. Zamorano, "European Association of Echocardiography recommendations for the assessment of valvular regurgitation. Part 2: mitral and tricuspid regurgitation (native valve disease).," *Eur. J. Echocardiogr.*, vol. 11, no. 4, pp. 307–32, 2010.
10. N. A. Marsan, J. J. M. Westenberg, C. Ypenburg, V. Delgado, R. J. van Bommel, S. D. Roes, G. Nucifora, R. J. van der Geest, A. de Roos, J. C. Reiber, M. J. Schalij, and J. J. Bax, "Quantification of Functional Mitral Regurgitation by Real-Time 3D Echocardiography: Comparison With 3D Velocity-Encoded Cardiac Magnetic Resonance," *JACC Cardiovasc. Imaging*, vol. 2, no. 11, pp. 1245–1252, 2009.
11. M. Shanks, H.-M. J. Siebelink, V. Delgado, N. R. L. van de Veire, A. C. T. Ng, A. Sieders, J. D. Schuijff, H. J. Lamb, N. Ajmone Marsan, J. J. M. Westenberg, L. J. Kroft, A. de Roos, and J. J. Bax, "Quantitative Assessment of Mitral Regurgitation: Comparison Between Three-Dimensional Transesophageal Echocardiography and Magnetic Resonance Imaging," *Circ. Cardiovasc. Imaging*, vol. 3, no. 6, pp. 694–700, 2010.
12. P. Lancellotti, J.-L. Zamorano, and M. A. Vannan, "Imaging Challenges in Secondary Mitral Regurgitation: Unsolved Issues and Perspectives," *Circ. Cardiovasc. Imaging*, vol. 7, no. 4, pp. 735–746, 2014.
13. A. P.-W. Lee, M. Acker, S. H. Kubo, S. F. Bolling, S. W. Park, C. J. Bruce, and J. K. Oh, "Mechanisms of Recurrent Functional Mitral Regurgitation After Mitral Valve Repair in Nonischemic Dilated Cardiomyopathy: Importance of Distal Anterior Leaflet Tethering," *Circ.*, vol. 119, no. 19, pp. 2606–2614, 2009.
14. E. Agricola, M. Oppizzi, F. Maisano, M. De Bonis, A. F. L. Schinkel, L. Torracca, A. Margonato, G. Melisurgo, and O. Alfieri, "Echocardiographic classification of chronic ischemic mitral regurgitation caused by restricted motion according to tethering pattern," *Eur. Hear. J. - Cardiovasc. Imaging*, vol. 5, no. 5, pp. 326–334, 2004.
15. E. C. McGee Jr, A. M. Gillinov, E. H. Blackstone, J. Rajeswaran, G. Cohen, F. Najam, T. Shiota, J. F. Sabik, B. W. Lytle, P. M. McCarthy, and D. M. Cosgrove, "Recurrent mitral regurgitation after annuloplasty for functional ischemic mitral regurgitation," *J. Thorac. Cardiovasc. Surg.*, vol. 128, no. 6, pp. 916–924, 2014.
16. S. Gelsomino, R. Lorusso, S. Cacioli, I. Capecci, C. Rostagno, M. Chioccioli, G. De Cicco, G. Billè, P. Stefano, and G. F. Gensini, "Insights on left ventricular and valvular mechanisms of recurrent ischemic mitral regurgitation after restrictive annuloplasty and coronary artery bypass grafting," *J. Thorac. Cardiovasc. Surg.*, vol. 136, no. 2, pp. 507–518, 2015.
17. G. R. Green, P. Dagum, J. R. Glasson, J. F. Nistal, G. T. Daughters II, N. B. Ingels Jr, and D. C. Miller, "Restricted posterior leaflet motion after mitral ring annuloplasty," *Ann. Thorac. Surg.*, vol. 68, no. 6, pp. 2100–2106, 2015.
18. A. Ciarka, J. Braun, V. Delgado, M. Versteegh, E. Boersma, R. Klautz, R. Dion, J. J. Bax, and N. Van de Veire, "Predictors of Mitral Regurgitation Recurrence in Patients With Heart Failure Undergoing Mitral Valve Annuloplasty," *Am. J. Cardiol.*, vol. 106, no. 3, pp. 395–401, 2010.
19. C. A. Milano, M. A. Daneshmand, J. S. Rankin, E. Honeycutt, M. L. Williams, M. Swaminathan, L. Linblad, L. K. Shaw, D. D. Glower, and P. K. Smith, "Survival prognosis and surgical management of ischemic mitral regurgitation.," *Ann. Thorac. Surg.*, vol. 86, no. 3, pp. 735–744, 2008.
20. M. A. Acker, M. K. Parides, L. P. Perrault, A. J. Moskowitz, A. C. Gelijns, P. Voisine, P. K. Smith, J. W. Hung, E. H. Blackstone, J. D. Puskas, M. Argenziano, J. S. Gammie, M. Mack, D. D. Ascheim, E. Bagiella, E. G. Moquete, T. B. Ferguson, K. A. Horvath, N. L. Geller, M. A. Miller, Y. J. Woo, D. A. D'Alessandro, G. Ailawadi, F. Dagenais, T. J. Gardner, P. T. O'Gara, R. E. Michler, and I. L. Kron, "Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation," *N. Engl. J. Med.*, vol. 370, no. 1, pp. 23–32, 2013.