Review Article

Biomechanics raises solution to avoid geometric mitral valve configuration abnormalities in ischemic mitral regurgitation

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Abstract: Ischemic mitral regurgitation (IMR) is a form of mitral insufficiency that is characterized by papillary muscle (PM) displacement, leaflet tethering, reduced closing forces, and different degree of annular dilatation. Treatment of this condition includes mitral valve replacement or mitral valve repair with restrictive annuloplasty. Recent evidences in mitral valve repair showed that addressing only the annulus and neglecting the subvalvular apparatus provides a suboptimal operation with poor long-term results. However, the complexity of the geometrical aberrances occurring in IMR demands for more accurate analysis also involving the biomechanics underlying the failing mitral valve and subvalvular apparatus. Finite element analysis (FEA) is a powerful tool in this context and we developed a biomechanical model of mitral valve and subvalvular unit using 3D geometry of the leaflets, annulus, chordae and PM. After the application of structural properties of materials to these elements and simulation of systemic pressure loading, FEA could be used to directly determine biomechanical changes and geometry variations. We believe this approach can provide valuable information to better address the surgical treatment of IMR and answer some of the questions still pending in IMR management.

Keywords: Ischemic mitral valve regurgitation; mitral valve repair; mitral valve geometry; biomechanical model; finite element analysis (FEA)

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Introduction

Myocardial infarction (MI) currently occurs in 1 million of persons each year in USA and data reveal about 8 million of Americans with history of MI (1). The myocardial ischemic damage is cause of the dysfunction of the papillary muscles (PM) of mitral valve resulting in an ischemic mitral regurgitation (IMR). Several resources are available to health care providers describing the aetiology, pathophysiological mechanisms, treatment and prognosis of moderate to severe IMR, which has an occurrence after MI ranging between 10%, when developed acutely, to 50% in chronic cases (1). IMR is a form of mitral insufficiency that is characterized by PM displacement, leaflet tethering, reduced closing forces, and different degree of annular dilatation. Therefore, the health care providers, cardiologists and surgeons, should understand what are the common pathogenic mechanisms underlying the above-mentioned valve geometric abnormalities as well as the role played by medical or surgical treatments in the outcomes or consequences of IMR. Inappropriate diagnosis or unsuccessful surgical efforts might negatively affect the natural course of IMR. Indeed, randomized clinical evidences demonstrated that surgical attempt to mitral repair in severe IMR are associated to higher frequency MR recurrences when compared to approaches regarding the chordal-sparing replacement of the valve (2). In this context, relying on observational studies based on small series often supported by poorly geometrical investigation and scarce quality of echocardiography assessment or CT scan and reporting MR recurrence rates ranging between 5% and 20% of patients, can be misleading as underestimating or underreporting repair failure (3).

Finding answers to the current issues in ischemic mitral treatment

Definitions

IMR is a disorder of valve motion affecting activities of valvular and subvalvular apparatus of mitral valve that is due to progressive dysfunction acquired after MI. We use the term "acute IMR" to indicate structural and functional failure acquired early after MI including PM rupture, chordal injuries, malcoaptation of the leaflets often supported by an evident prolapse of leaflet (4). Conversely, we use the term "chronic IMR" to report a process of adverse left ventricular remodelling after myocardial injury culminating on enlargement of the left ventricular chamber and mitral annulus, with consequent posterior or apical and lateral vectorial migration of the PM, leaflet tethering and reduced closing forces. Morphological assessment of mitral valve, analysis of pathophysiological change in subvalvular apparatus, identification of the altered balance among closing forces and tethering forces of mitral valve and more recently biomechanics modelling by means of finite element analysis (FEA) are the determinants in answering the questions posed by the failure of treatment in IMR.

The divergent aspects of anatomy and pathophysiology of ischemic mitral disease

Mitral valve is composed by leaflets, fibrous circular annulus and subvalvular apparatus. The leaflets or cusps of MV are located anteriorly and posteriorly, uniformly attached to fibrous annulus giving to the mitral valve the appearance of a curtain that is closed during systole. Each leaflet is divides in three segments or scallops that are named A1, A2, A3 and P1, P2, P3 relating to anterior or posterior cusp, respectively. The subvalvular apparatus includes posteromedial papillary muscles (PMPM) and anterolateral papillary muscles (ALPM) from which the chordae tendinea are detached and designed to anchor on the free edge of leaflet.

Occurrence of IMR is associated to the development of several divergent phenomena stemming from the main ischemic pathological event. Indeed myocardial ischemia leads contextually to wall motion abnormality, to PM topographical displacement and to their functional dyssynchrony. In this context knowledge of anatomy of PM and its blood flow distribution is crucial to understand IMR pathophysiology and correctly address the surgical technique to be used to achieve successful repair. Anatomical studies conducted on PMs identified five segmentations and morphological types commonly classified in Type I, single uniform unit; Type II, groove with two apexes; Type III, fenestrations with muscular bridges; Type IV, complete separation in two adjacent heads and Type V, complete separation with two distant heads (5,6). A physician, cardiologist or surgeon, who provides the diagnosis and treatment of IMR, has the obligation to recognize the division of PM that can occur according to two directions corresponding to a sagittal plane or to a coronal plane. The classification of different pattern of necrosis of papillary has been described (6).

Subsequent biomechanical investigation stressed the central role of coronary blood flow distribution in the PMs as well as its different mechanical performance due to deep location in left ventricular wall (7). There is general consensus about a difference of coronary vascular distribution in the two PM with evidence of a more scarce vascularization of the PMPM among persons with a IMR [about 91% in our series (4,5)]. The evidence discussed here comes from several observational and randomized clinical study of surgical treatment of IMR suggesting that the spectrum of patients with severe impairment of right coronary blood flow distribution and inferior wall motion abnormalities is higher in IMR (2,8-10). Anterior lateral PM and all the segment of ventricular wall are rarely affected because of the perfusion provided by both the left anterior descending coronary artery and diagonal branch (4). In preliminary biomechanic studies evidence of non-homogeneous tension exerted by the chordae located in ALPM and PMPM has been provided suggesting a different distribution of dynamic stress-strain occurring at the level of PMs (11). In ALPM we observed a relatively low dynamic shear stress due to its superficial location in respect to the annulus. Conversely, the biomechanical consequences of PMPM ischemia are more eloquent because of its deep location in the left ventricle wall translating into a higher stress. Moreover, PMPM is perfused by either the right coronary or the circumflex artery, dramatically increasing its sensitivity to ischemia [reported in 91% of the cases in our patients (4,5)]. Relationship between biomechanical behaviour and PM microcirculation is confirmed by the observed segmental distribution and a well-identified arterial trunk, named Kugel's artery that perforates the PM from base to apex (7). The reliance of the two circulatory systems, morphology and position of PM within the left ventricle and presence of muscular bridging, which favours collateralization may affect the frailty of PM. Deficiency of truncal blood supply is increased in the PM Type IV–V that are more individualized from the ventricular wall favouring in this pattern a higher degree of physical stress of the apex. This variant therefore confers a predisposition to dyssynchrony, rupture or elongation. On the other end shear stress phenomena are therefore less likely to happen in other morphological patterns with multiple muscular bridges (pattern III) in which PM are protected by compensatory collateral vascularization.

Suggested surgical response to geometrical abnormalities of mitral valve

A suggested surgical approach to handle ischemic mitral valve should take into account anatomical changes imparted by LV remodelling and distortion of left ventricular geometry after MI. It is important to first ascertain the actual benefit of surgical treatment in the subgroup of patients with severe IMR in which the prognosis might be grave and ranging from 15% and 40% at 1 year (12-14). Despite the benefit of simultaneous surgical revascularization during mitral repair is undisputed, for some patients with severe IMR mitral-valve repair with an undersized annuloplasty alone has been associated with a high rate of recurrent mitral regurgitation and adverse outcomes (2,8). The most common reasons of persistence or recurrence of MR is related to anterior displacement of the posterior leaflet that promotes increased leaflet tethering. The patients develop progressive adverse global and localized left ventricular remodelling as well as significant post-repair PM dyssynchrony (9,15,16). The decision to divert in the choice of surgical treatment towards repair or replacement should be performed in the context of the heart team discussion, and factors as the individual surgical experience and preoperative echocardiographic parameters [end-diastolic diameter, end-systolic diameter, end-diastolic volume index, end-systolic volume index (ESVI), left ventricular ejection fraction, systolic sphericity index (SSI), diastolic sphericity index (DSI), WMSI, myocardial performance index, tenting area, effective regurgitant orifice area, regurgitant volume, regurgitant fraction, coaptation height, coaptation length, coaptation distance, AML tethering angle , PML tethering angle, PMPM-WMSI, and ALPM-WMSI] should be taken into account. Clinical and echocardiographic evidence, available in randomized trial are in favour of surgical correction of severe ischemic mitral valve regurgitation with chordal-sparing replacement or subvalvular repair associated to restrictive mitral annuloplasty (2,8).

The results of 2-year outcomes of The Cardiothoracic Surgical Trials Network revealed more durable correction of mitral regurgitation with favourable left ventricular remodelling in patients who underwent chordal-sparing mitral valve replacement. At 2-years rate of recurrent, moderate, or severe mitral regurgitation was significantly higher in patients who underwent isolated restrictive anuloplasty (RA) compared to those received replacement (58.8% *vs.* 3.8%, $P<0.001$). LVESVI and left ventricular ejection fraction significantly improved over baseline affecting positively long-term outcomes with relative scarce adverse consequences in using xenograft prosthetic valve (2). Clinical and echocardiographic evidence suggested that recurrence of MR might strongly affect over time LV function, quality of life and survival paving the way for a number of patients to be referred to mitral clip and transcatheter valve procedures because of the increased risks or redo operations.

Another recently recommended option in the context of surgical repair of IMR is an adjunctive subvalvular procedure in combination to standard undersizing mitral anuloplasty (3,4,9).

In our center we pioneered the technique of papillary muscle approximation (PMA) (17) and performed a randomized trial comparing the combined procedure of PMA plus undersizing annuloplasty versus RA alone in patients with moderate-severe IMR. At 5 years, there was significant improvement in regional and global left ventricular reverse remodelling in the PMA group as measured by the left ventricular end-diastolic dimension and left ventricular function. No significant difference was revealed in rate of major adverse cardiac and cerebrovascular events (MACCE). Interestingly, in the first 2 years we observed no significant difference in rate of cumulative death and MACCE between groups that became significant in the next 3 years of follow-up. The rates of major cumulative death and major adverse cardiac or cerebrovascular event was due to the proportion of patients with recurrent moderate or severe mitral regurgitation, repeat intervention and rehospitalization for heart failure that was significantly higher in the RA group than in the PMA group (8).

The results of our 5-year study are in favour of adding subvalvular repair to undersizing anuloplasty in surgical treatment of IMR because PMA significantly improved geometric parameters of mitral valve abnormalities. The evidence supporting the advantage of PMA to solve IMR includes the following observations: subvalvular repair reduce firmly leaflet tenting; improvement of PM dyssynchrony, although persisting after adjustment, and a consistent maintenance of anterior relocation of coaptation point among patient who received papillary sling procedure. These findings imply that many patients who received combined procedure had undisputed benefit regardless on the presence of preoperative symmetric and asymmetric tethering. This was related to the improved equilibrium between closing and tethering forces restored by the procedure (9). Further investigation is required to determine whether patients with baseline abnormalities in symmetric tethering and lateral wall motion, that were shown to have little further improvement during the 5 years, would benefit more from subvalvular repair than from mitral valve replacement. Today expert consensus (4,5,8,9,18-23) promotes this new frontier of surgical treatment of IMR represented by subvalvular apparatus surgery. Studies of biomechanics of ischemic mitral valve and left ventricular geometry are also under way by means of FEA.

Specific biomechanical examination

Although the geometric distortion of left ventricular chambers has been widely recognized in IMR, the heterogeneity of biomechanics events has recently become increasingly an objective of study. The importance of a comprehensive knowledge of biomechanical alteration is well accepted for prognosis of IMR but translation of new information into improved clinical treatment is just beginning. In this article, we report some recent observations on the assessment of biomechanical phenomena, understanding of geometric mitral valve disorder after MI and identification of prognostic parameters to improve the current surgical treatment.

We cannot achieve useful information for the evaluation and modelling of real-world systems without FEA. With this in mind, we applied FEA to obtain measures of area of increased leaflet tenting correlated to regions where excessive tethering force was exerted. FEA provided missing and otherwise not achievable data about the geometry of the mitral valve in patients who had IMR and in those who had suffered a MI without compromise of the mitral valve. The entire process of analysis and study comprises the following investigations: (I) development of a biomechanical model of mitral valve and subvalvular using 3D geometry of the leaflets, annulus, chordae and PM; (II) application of structural properties of materials followed by simulation of systemic pressure loading; and (III) FEA to directly determine biomechanical changes and geometry variations(11,24).

Cardiac magnetic resonance (CMR) was performed to study the geometric mitral disturbance. The procedure has been executed in order to acquire CMR images of the whole heart in the cranio-caudal direction during a single breath-hold. We obtained three-dimensional reconstruction and analysed the image to analyse to obtain quantitative determinations. We have extrapolated useful information on the geometrical characteristics of both mitral commissures, on the annulus anteroposterior diameter and on the end-systolic mitral leaflet coaptation length. In addition, 3D reconstruction using short axis images provided excellent visualization of the tips of the PM at both end-systole and end-diastole.

The geometrical variables included in the FEA actually consider the parameters normally characterizing the type and degree of MR and involved in the surgical decision-making at the time of the operation (i.e., antero-posterior diameter of mitral annulus, tenting height associated with tenting area, post-operative interpapillary distance, and PM displacement resulting from their approximation). Therefore, we investigated the application of this model to gain valuable information to better address the surgical treatment of IMR and we believe that the results of this accurate analysis can produce the answers that are still not found today.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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