Perspective

Analysing the reasons of failure of surgical mitral repair approaches—do we need to better think in biomechanics?

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Abstract: The failure of mitral valve repair procedures revealed in the outcomes of the recent randomized studies is suggesting the necessity for a better understanding of the biomechanical mechanisms underlying the failure of the surgical approaches. Use of biomechanical modelling and finite element analysis (FEA) in cardiovascular research is an important aid in this context. In our group we developed a biomechanical model taking into account all the component of the mitral valve functional unit including the valve leaflets, the annulus, the papillary muscles, the chordae tendinea and the ventricular geometry. The two-dimensional mathematical model was capable to predict some of the actual geometrical and mechanical features of the valvular and subvalvular apparatuses in physiological and pathological conditions providing the engineering quantitative relations between closing and tethering forces and the mechanisms governing the mitral valve unit function. This model might further become patient-specific by means of 3D reconstruction of clinical imaging. Images are first converted in a standard vector format (DICOM, etc.), then automatically translated in a "structural" finite element model and finally implemented in a finite element code. This allows for in silico simulations to virtually explore the effects of different surgical approaches at an early stage after the procedure, to help the operative decision processes, or to optimize the design of surgical implants.

Keywords: Mitral valve repair; papillary muscle approximation (PMA); restrictive annuloplasty; finite element analysis (FEA); patient-specific modelling

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General surgical perspectives in ischemic mitral regurgitation (IMR)

Since the publication of the "French correction" (1), Carpentier had identified the radical benefit of adding restrictive mitral-valve repair in patients with moderate and severe IMR. Clinical evidences demonstrated reduced rate of perioperative morbidity and death after annuloplasty, as well as the advantage of preserving the subvalvular apparatus to guarantee left ventricular systolic function (2-4). Recently, guidelines pointed out as IMR may not be mitigated by the only restrictive annuloplasty (RA) and several questions still remain unresolved (5). Indeed the isolated undersizing procedure reduces the degree of mitral regurgitation but does not prevent further adverse remodelling and recurrent moderate or severe mitral regurgitation overtime.

In our randomized studies (2,3,6,7) we observed in the RA group limited improvement of LV contractility, global LV dyssynchrony, papillary muscle dyssynchrony and altered mitral systolic annular contraction, which are expressions of alteration of the "closing forces". In addition, RA does not intervene directly on the abnormal posterior or apical and lateral displacement of the papillary muscle, which causes persistently augmented leaflet tethering for the anterior displacement of the posterior leaflet. Therefore, to circumvent this issue we performed a single center randomized study comparing an approach using a single row suture and one using a double row of overlapping sutures to undersize the mitral posterior annulus during RA in patients with severe IMR (3). At 18 months follow-up, we showed a lower risk of MR recurrence in patients who received the double row procedure (3). We observed a durable reduction of the anteroposterior diameter and permanent increase in the coaptation length due to the anterior relocation of the coaptation point (3,8). Nevertheless, long-term follow up at five years would be needed to demonstrate its clinical benefit.

Specific surgical perspectives in IMR

Given the high rate of recurrent mitral regurgitation in patients after RA-repair, surgeons have to consider chordal-sparing mitral-valve replacement or combined procedure with subvalvular repair and undersizing mitral annuloplasty to solve ischemic mitral disorder (9-14). The results of the two-years randomized trial in patients with moderate and severe IMR by the Cardiothoracic Surgical Trials Network (CTSN) imposed the need to revise the surgical dogma regarding the superiority of mitral valve repair over replacement (9,10). Moreover, we reported the results of a randomized study in patients with severe IMR who received a combined procedure of subvalvular repair [papillary muscle approximation, (PMA)] and undersizing mitral annuloplasty compared to restrictive annuloplasty alone. All patients had complete surgical revascularization which is an undisputable pillar of treatment of IMR in presence of high-grade proximal lesion of coronary arteries and of ischemic viable myocardium. In our study, subvalvular repair showed better long-term correction of mitral regurgitation when was compared to RA alone. We observed significant between-group differences in left ventricular reverse remodeling as measured by LVEDD, LVESD, LV function and wall motion score index. Rate of death and major adverse cardiac or cerebrovascular events differ significantly at two-year follow-up among the treatments groups, with worse outcomes in the RA alone group. This difference was related to the significantly higher recurrence of moderate or severe mitral regurgitation, repeat re-intervention and hospitalization in patients who received the isolated RA repair procedure. Interestingly, the ratio of patients with failed mitral repair was significantly higher in isolated undersized repair than in combined subvalvular surgery at 5-years follow-up (2,7). Lack of moderate or severe regurgitation in patients who underwent PMA is due to a geometrical improvement in the equilibrium between closing and tethering forces (2,4,6,7).

The combined procedure provided considerably more durable correction of the altered symmetric and asymmetric tethering forces in IMR, which have an important effect on anterior and posterior leaflet tethering. In the asymmetrical pattern of tethering, in which we have a predominant posterior tethering vector, PMA significantly improved traction on chordae of both leaflets. In addition, the benefit of subvalvular repair is sustained by a persistent anterior relocation of the coaptation point that is normally dragged more posteriorly, parallel to the posterior wall, after a myocardial infarction. In the symmetrical tethering configuration, there was little further improvement after the combined procedure (7). This deficiency could be determined by the higher degree of dilation of the left ventricular chamber and the more difficult achievement of anterior relocation after apical or lateral vectorial migration in this type of IMR. Similarly, in the symmetrical pattern, there were few additional deaths, which were equally allocated between the two groups (PMA *vs.* RA) and related to more significant impairment of the lateral wall (7). A little improvement in lateral wall motion score index and reverse left ventricular remodeling after revascularization are indicative of a different biomechanical impairment that results in a more difficult recovery of the optimal geometric conditions. Successful revascularization, known to facilitate the restoration of mitral valve function in patients with IMR in virtue of the expected decrease in left ventricular size, increase in mitral-valve closing forces, improvement in papillary-muscle synchrony, and enhanced contractility of subjacent myocardium, does not seem to be a decisive factor in cases of compromised function the lateral wall (7).

Our previous findings on subvalvular surgery demonstrated a significant improvement of the dyssynchrony of the left ventricle posteromedial and anterolateral papillary muscles in both symmetrical and asymmetrical patterns, but the results of the study need to be compared with 3D geometric investigations that further elucidate the biomechanical mechanisms of mitral valve disorder.

In this context, geometrical abnormalities of mitral valve might be misleading as underestimating or underreporting repair failure. The failure of mitral valve repair procedures revealed in the outcomes of the recent randomized studies is suggesting the necessity for a better understanding of the biomechanical mechanisms underlying the failure of the surgical approaches. Assessment of these issues with finite element analysis (FEA) in cardiovascular research is an exciting avenue to find biomechanical solutions having impact on the postoperative results.

Specific biomechanical considerations

To approach the problem at hand from the biomechanical standpoint, we hence proceeded in two steps.

In the first one, we identified all the key geometrical parameters playing a crucial role in the dynamics of the system, relating morphological features, shape details and relevant kinematics to the corresponding stresses (forces per unit cross sectional areas), then separately recognizing tethering forces as responsible of annular dilatation, enlargement of the left ventricular chamber and possible abnormal displacement/migration of the papillary muscles and (reduced) closing forces as stress loads mainly involved in altered annular contraction and LV and papillary dyssynchrony phenomena. Given that all the biological structures of the district are physiologically forced to experience large deformation regimes and exhibit to both time-dependent mechanical (viscoelastic) and biological (remodeling) behaviours, a first biomechanical model was constructed by combining the hyperelastic responses of the tissues with the most significant rheological features (stress-relaxation processes). In this way, the two-dimensional mathematical (parametric) model was capable to predict some of the actual updated geometrical and mechanical features of the valvular and subvalvular apparatuses in physiological and pathological conditions, so furnishing the engineering quantitative relations between closing and tethering forces and the mechanisms governing the interlaced kinematics of mitral leaflet, chordae tendineae and moving sites where the papillary muscles are attached.

This first parametric model—which integrates geometry and mechanics of the system in a relatively simple scheme to give key information to support/orient some relevant surgery choices—was successively thought to become specialized (patient-specific). This second stage can be in fact obtained by means of a 3D image reconstruction of the whole system which is first converted in a standard vector format (DICOM, etc.), then automatically translated in a "structural" finite element model (with ad hoc routines for generating mesh with the needed accuracy for faithfully replicating the actual geometry of any anatomic site of interest and avoiding mechanical errors), and finally implemented in a FE code. By uploading initial and boundary conditions (applied constraints, forces, pressures and dynamic loads) the biomechanical model can be utilized for conducting, essentially in real time, in silico simulations to virtually explore the effects of different surgical choices/decisions at an early stage of clinical follow up, paving the way for envisaging new perspectives in which integrated medical-engineering strategies could help the operative decision processes, guide optimization and design of surgical implants and significantly improve life expectancy in cardiac diseases.

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Footnote

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

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