

Assessment of the remodelling of the mitral valve leaflets after myocardial infarction *in vivo*

Deeksha Pharasi*, Pushpa Yadav

Pharasi D, Yadav P. Assessment of the remodelling of the mitral valve leaflets after myocardial infarction *in vivo*. Clin Cardiol J 2023;7(1):1-2.

ABSTRACT

To cure regurgitation brought on by myocardial infarction, more than 40,000 patients domestically have Mitral Valve (MV) repair surgery each year (MI). Although it is thought that ongoing MV tissue remodelling after repair has a significant role in regurgitation recurrence, it is yet unclear how the post MI condition affects MV remodelling. Our inability to forecast the remodelling of the MV both post MI and post surgery to aid surgical planning is a result of this lack of understanding. The present work was conducted to noninvasively measure the effects of MI on MV remodelling in terms of leaflet shape and deformation as a crucial first step. Real time three dimensional echocardiographic images were taken before the MI as well as at 0,4, and 8 weeks after the MI in eight adult dorset sheep. The leaflet surface at systole was scanned in both open and closed states, and the associated scans were extracted using a previously tested image based morphing workflow. We discovered that MI caused long lasting changes in leaflet dimensions in the diastolic configuration. These modifications grew over the course of four weeks before stabilising. When compared to the

current time point, MI significantly changed the MV's systolic shape, and the range of stretch that the MV leaflet experienced at peak systole was significantly decreased. Interestingly, the systolic strains remained fairly comparable throughout the post MI period when we referenced the leaflet strains to the pre MI configuration. Overall, we saw that the MV leaflet shape underwent permanent changes as a result of post MI ventricular remodeling.

This mostly had an impact on the MV's diastolic configuration, which had an impact on the leaflet's range of stretch when compared to the existing diastolic configuration. These results are in line with our earlier research, which showed that post MI leaflet deformations were more likely to be plastic (i.e., irreversible), and that this increase was entirely explained by changes in collagen fiber structure. The condition of the MV leaflet can also reveal the progression and degree of MV adaptation after MI, as we have shown through noninvasive methods, and is therefore highly relevant to the creation of new and existing patient specific minimally invasive surgical repair techniques.

Keywords: Regurgitation; Myocardial infarction; Mitral valve; Leaflet dimensions; Ventricular remodeling

INTRODUCTION

The left atrium and left ventricle's blood flow is controlled by the Mitral Heart Valve (MHV) (LV). The MV is regarded as a component of the LV functional unit because of its close anatomical integration with the LV through the annulus, chordae tendineae (MVCT), and Papillary Muscles (PMs). Ischaemic MV Regurgitation (IMR) frequently occurs after a Myocardial Infarction (MI), whose after effects alter the MV geometry through annular dilation and MVCT tethering. The severity of IMR that also occurs in the presence of LV dysfunction has been directly linked to an increased risk of early mortality. More generally, given current trends in the growth of the elderly population, it is anticipated that the societal burden of MI induced IMR will continue to rise. Undersized Ring Annuloplasty (URA), a surgical MV repair technique that physically reduces the annular orifice area, has been the most effective method of treating IMR, although this strategy is still troublesome, with around a third of repairs failing over the long term [1]. It has been proposed that the major changes in MV geometry and closing behaviour brought about by this method, including constriction and flattening of the annulus, are at least largely responsible for the failure rate of URA based repairs. Additionally, the repair does not stop the ongoing LV remodelling that occurs after a MI, which over time changes the MV's "border conditions" badly enough to result in recurrent IMR [2].

LITERATURE REVIEW

Real time, three Dimensional Echocardiography (rt-3DE) pictures that were taken before and after surgery have helped to partially unravel the reasons of MV repair failure. The posterior leaflet's pre surgical tethering angle was recently demonstrated by Bouma, et al. to be a predictor of recurrent IMR six months following URA. Our current understanding of MV function and

IMR induced remodelling thus leads us to hypothesise that, despite high short term repair success rates, URA may occasionally worsen posterior leaflet tethering by shifting the posterior annulus anteriorly, which raises the likelihood of recurrent IMR in the long run. The amount of prior research linking certain preoperative MV characteristics to the success or failure of URA emphasises the potential and urgent clinical need for noninvasive, patient specific approaches to optimise MV repair treatments based only on pre surgical data. MV development and remodelling following MI and URA also unquestionably have a significant influence in determining repair results. There is evidence of MV interstitial cell activation and matrix turnover in the MV leaflets after MI in addition to alterations in tissue level characteristics. A thorough description of tissue level deformation patterns in the post MI MV can offer significant information into the current biosynthetic state of the MV due to the proven causal relationship between tissue stretch and cell driven remodelling mechanisms. It follows that quantitative measurements of MV leaflet tissue deformation and changes therein after MI are likely to be useful, independent predictors of long term remodelling events that alter MV function and, consequently, repair outcomes. However, in both the unaltered pathological and post-surgical settings, our knowledge of how MV tissue remodels remains incredibly limited [3].

Thus, the goal of the current study was to directly measure the effects of MI on MV *in vivo* leaflet tissue deformation in order to obtain insight into the post-MI MV remodelling behaviour. In order to better understand how and how much the MV remodels post-MI, we used a recently created image based computational modelling pipeline to noninvasively quantify how the *in vivo* diastolic and systolic MV deformation patterns change after MI. Prior to attempting to optimise MV repair approaches on a patient specific basis, this understanding is essential and must be established [4].

Department of Life Sciences, Graphic Era Deemed to be University, Dehradun, India

Correspondence: Deeksha Pharasi, Department of Life Sciences, Graphic Era Deemed to be University, Dehradun, India, E-mail: Deekshapharasi998@gmail.com

Received: 22-Nov-2022, Manuscript No. PULCJ-22-5707; **Editor assigned:** 24-Nov-2022, PreQC No. PULCJ-22-5707 (PQ); **Reviewed:** 08-Dec-2023, QC No. PULCJ-22-5707; **Revised:** 17-Jan-2023, Manuscript No. PULCJ-22-5707 (R); **Published:** 24-Jan-2023, DOI: 10.37532/2753-1201.23.7(1).1-2.



This open-access article is distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC) (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits reuse, distribution and reproduction of the article, provided that the original work is properly cited and the reuse is restricted to noncommercial purposes. For commercial reuse, contact reprints@pulsus.com

RESULTS

The MV annulus significantly dilated post MI, according to preliminary analysis of rt-3DE images taken from eight ovine participants pre MI as well as 0,4, and 8 weeks post MI. This result is consistent with prior observations. Additionally, both leaflets had become quite attached after the MI. Paired t-tests demonstrated that, with average increases of 20% and 16%, respectively, at t=4 weeks and t=8 weeks, relative changes in both annular orifice and leaflet surface areas were substantially greater than their pre MI values. Dilation in both the anterior-posterior and septal lateral directions was almost equally correlated with the expansion of the annular orifice [5]. Both of the leaflets *in vivo* leaflet diastolic shape and systolic stretch patterns underwent significant modifications as a result of these MI-induced changes in MV geometry spreading throughout both leaflets over time. First, we saw that the diastolic condition had significant persistent leaflet deformations. Insofar as they manifested in the diastolic (opened), which is under little loading, these deformations were permanent. Additionally, these long lasting alterations in the MV leaflet have been noted in earlier research on post MI excised leaflets using the same animal model. They represent intrinsic changes to the MV leaflet dimensions as a result and are not linked to any additional mechanisms [6].

We used both the pre MI and the current diastolic reference configurations in our calculations based on observations of time evolving diastolic reference configurations. The directional stretches were mostly unaltered over most of the leaflet as compared to the pre MI diastolic reference configuration. Interestingly, the magnitudes of the systolic stretches showed a steady decline in amplitude during the 8 weeks period when compared to the current diastolic state. The amount of the shear angle experienced by the posterior leaflet commissural segments (P1, P3) in systole was dramatically reduced as a result of alterations in deformation brought on by post-MI shear patterns in specific leaflet areas.

DISCUSSION

We now have a much better knowledge of the MV's biomechanics and mechanobiology because to computational models of the MV. Additionally, we and others have made significant progress in clarifying how the MV tissue microarchitecture governs its organ level behaviour and how these might be thoroughly examined in diseased circumstances, such as IMR, through the combination of experimental and computational approaches. These developments in computational modelling enable a quantitative evaluation of the development of disease and remodelling caused by MI [36]. In the end, these strategies will make it possible to identify the best IMR treatments for individual patients, opening the door to individualised MV repair and stratification of patients into MV repair and replacement groups.

However, in order to enable such models, a thorough grasp of MV remodelling is necessary, and there is still a dearth of knowledge in this area. We have made progress in resolving this issue in the current study by quantifying MV leaflet deformations using our non-invasive image based computational technique. Our analysis was split into two distinct functional sections: Changes in the post MI LV, such as annular dilation and leaflet tethering, cause (1) Changes in the open (diastolic) configuration that are driven by plastic (i.e., non-recoverable) deformations, and (2) Changes in the closed (systolic) deformations that are driven by LV pressure. We looked at how these quantities changed over the course of an 8 weeks post MI period without treatment. A persistent increase in MV leaflet size was

caused by the LV in the post MI state, as shown by the increased circumferential and radial diastolic strains. While we refer to these amounts as "plastic stretches," as previously mentioned, they actually represent changes in leaflet form unrelated to any external loading. Our extensive publications on the remodelling events that occur after IMR lend credence to these observations. We specifically showed that the altered MV dimensions cause the MV leaflet stiffness to be significantly higher by 4 weeks post-MI. The MV collagen fiber structure changed along with the significant geometric and mechanical changes, but not the collagen fibre elastic modulus, which remained constant at around 200 MPa. The latter result showed that there was no obvious damage to the collagen fibres themselves and that all alterations could be fully explained by plastic modifications to the MV's unloaded configuration. These measurements were made on tissues from removed MV leaflets, therefore they can only be the result of true intrinsic changes in the leaflet and not adjustments to the boundary conditions of the diastolic state.

CONCLUSION

The modelling and analysis workflow we have used can be used to evaluate repair induced MV remodelling in addition to post MI MV assessment. In addition to recently established leaflet clipping and chord based repair devices, which increase local stress concentrations, the long term adaptive effects of annuloplasty, which modifies MV geometry worldwide, are unknown. Thus, a better comprehension of the MV remodelling process would be very beneficial for the design and improvement of such devices, as well as for the appropriate selection of them for treating a heterogeneous patient population. Given that they function more precisely as a single unit, future extensions of this study may also jointly account for the synergy between the MV and LV. The results of the current study can be used to enhance the effectiveness of post MI therapies that predominantly target the MI affected LV wall. Our findings also raise the idea of using patient specific post MI MV remodelling assessments to direct the timing of repair surgery as well as the design of MV repair techniques themselves.

REFERENCES

1. Rego BV, Khalighi AH, Lai EK, et al. *In vivo* assessment of mitral valve leaflet remodelling following myocardial infarction. Scientific Rep. 2022;12(1):18012.
2. Bartko PE, Dal-Bianco JP, Guerrero JL, et al. Effect of losartan on mitral valve changes after myocardial infarction. J American College Cardio. 2017;70(10):1232-44.
3. Bischoff J, Casanovas G, Wylie-Sears J, et al. CD 45 expression in mitral valve endothelial cells after myocardial infarction. Circu Res. 2016;119(11):1215-25.
4. Dal-Bianco JP, Aikawa E, Bischoff J, et al. Myocardial infarction alters adaptation of the tethered mitral valve. J American College Cardio. 2016;67(3):275-87.
5. Fernandez-Ruiz I. Computer modelling to personalize bioengineered heart valves. Nat Rev Cardio. 2018;15(8):440-1.
6. Marwick TH, Lancellotti P, Pierard L, et al. Ischaemic mitral regurgitation: Mechanisms and diagnosis. Heart. 2009;95(20):1711-8.