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Tricuspid Valve Regurgitation Decreases after MitraClip Implantation: Fluid Structure Interaction Simulation

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Abstract

Untreated tricuspid valve regurgitation (TR) is associated with increased rates of mortality, morbidity, and hospitalization. Current pharmacological and surgical treatment options for TR are limited. MitraClip (MC), an edge-to-edge percutaneous intervention, has been reported to be effective for treatment of TR. The goal of this study was to examine the effects of MC position on TR, using a multiphysics fluid-structure-interaction (FSI) analysis.

The computational set up included the tricuspid valve (TV), the chordae tendineae, the blood particles, and a tube that surrounded the leaflets and blood particles. The leaflets and chordae were modeled as hyperelastic materials, and blood was modeled using smoothed particle hydrodynamics. FSI analysis was conducted for blood flow through the closed valve for multiple simulations that account for normal, diseased, and treated conditions of the TV. To simulate the diseased TV, a group of chordae between septal and pulmonary leaflets were removed from the normal TV, which produced increased regurgitation. Four MC treated scenarios were considered: i) one MC near the annulus, ii) one MC approximately midway between the annulus and leaflet tip, iii) one MC near the leaflet tip, iv) two MCs: one approximately midway between the annulus and leaflet tip, and one close to the leaflet tip.

The TR increased in diseased TV (7.5%) compared to normal TV (2.5%). All MC treated scenarios decreased TR. The MC located near the midway point between the annulus and leaflet tip led to largest decrease in TR (75.2% compared to the untreated condition). The MC located near the leaflet tip was associated with lowest reduction in TR (2.2% compared to the untreated condition). When two MCs were used, reduction in TR was relatively high (68.7%), but TR was

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Conflict of Interest

Dr. Guccione is a consultant for, and Jiang Yao is an employee of, Dassault Systèmes Simulia Corporation (Johnston, RI, USA)

not improved compared to the optimal single MC. MC caused high stresses in the vicinity of the clipping area in all conditions; the highest occurred when the MC was near the leaflet tips.

Using a quantitative computational approach, we confirm previous clinical reports on the efficacy of MC for treatment of TR. The results of this study could lead to the design of more efficient MC interventions for TR.

Graphical Abstract

Keywords

MitraClip; Tricuspid Valve; Regurgitation; FSI; Finite Element

1. Introduction

Tricuspid valve regurgitation (TR) is a high-risk disease with limited treatment options. There are approximately 1.6 million patients with TR in the US alone [1–3]. Higher risk of mortality and morbidity, and higher rates of hospitalization are reported as consequences of severe TR if untreated [4–7].

Despite the need for viable treatment options for TR, pharmacological and surgical strategies remain limited, although several are under development [3]. MitraClip (MC) is an edge-to-edge intervention initially developed to treat mitral regurgitation [8,9], with reported safety and efficacy when applied to treat TR [3,10]. This device is implanted by a percutaneous procedure that limits the TR by edge-to-edge clipping of the MV leaflets [11].

Procedural failure has been reported as an important factor in the outcomes of MC intervention [12]. The contributing factors to procedural failure include anatomical aspects of the leaflets (such as flail leaflet), location of the regurgitation jet, size of orifice area and difficulty in grasping the leaflets [13,14]. To the best of our knowledge, the effects of MC location on the efficacy of MC intervention have not been investigated using a quantitative approach.

We hypothesize that the site of MC implantation affects the clip failure (inadequate reduction of TR after MC implantation) [14]. To test this hypothesis, we investigated the effects of MC location on TV regurgitation (TR). We used Smoothed Particle Hydrodynamics (SPH) [15] to simulate the effects of MC location on TV closure and regurgitation. Although there are a few numerical studies that focused on the TV [16–18], this is the first study that simulated the effects of MC on TR using an FSI model. Once validated [19], the results of this study would have potential clinical implications for optimal MC treatment for TR.

2. Methods

Abaqus software Version 614.3 (Simulia, Johnston, RI, USA) was used to examine the effects of MC placement on TR, computational solid mechanics (CSM) of the TV, and blood flow through the valve.

2.1. Computational Set Up

The geometry of the model includes the TV and the chordae tendineae surrounded by an irregular tube-like structure (Fig. 1). The geometry of the valve was used based on the three-dimensional computer-aided model from Zygotte [20]. We modified the valve and chordae geometry to ensure: (1) proper closure between leaflets, and (2) coaptation between leaflets agrees with morphological descriptions related to the dimension of anterior, posterior and septal leaflets, as well as chordae insertion locations [16,21]. The leaflets were assumed as an anisotropic hyperelastic material with the following constitutive equation [22–24]:

$$\Psi_{\text{dev}} = \frac{a}{2b} e^{b(I_1 - 3)} + \sum_{i=f,t} \frac{a_i}{2b_i} \{ e^{b_i(I_{4i} - 1)} - 1 \} + \frac{a_{ft}}{2b_{ft}} \{ e^{b_{ft}(I_{8ft})} - 1 \}$$

$$\Psi_{\text{vol}} = \frac{1}{D} \left(\frac{J^2 - 1}{2} - \ln(J) \right)$$

where a and b are isotropic stiffness material parameters of the leaflet tissue. The parameters with subscripts f , t , and ft refer to material parameters associated with additional stiffness in the fiber direction, in plane trans-fiber direction, and the connection between fibers and transfiber matrix, respectively. The invariants I_1 , I_{4i} and I_{8ft} are:

$$I_1 = \text{tr}(\mathbf{C})$$

$$I_{4i} = \mathbf{C}:(\mathbf{f}_0 \otimes \mathbf{f}_0)$$

$$I_{8ft} = \mathbf{C}:\text{sym}(\mathbf{f}_0 \otimes \mathbf{t}_0)$$

In these equations, $\mathbf{C}$, $\mathbf{f}_0$ and $\mathbf{t}_0$ are the right Cauchy-Green tensor, and vectors for the local fiber and in plane trans-fiber directions, respectively. J is the determinant of the deformation gradient, and $D = 2/K$ where K is the Bulk modulus. The direction of fibers were based on data from literature [25].

The surrounding structure was modeled as an elastic shell tube. The chordae tendineae were considered as Marlow hyperelastic materials [26]. The blood flow was modeled using the SPH methodology [26].

To model MC intervention, the MC body was not considered, but the effect of clipping was implemented in the model. The MC intervention was modeled using a connector between two nodes that represented the regions clipped by MC. These nodes were coupled to nearby nodes (in the same leaflet) using a kinematic coupling method [26] (Figs. 2 and 3).

To model blood regurgitation, a pressure load was applied to the ventricle side of leaflets to close the valve. The blood flow through the valve was then simulated using FSI analysis to implement the interaction between leaflets and blood flow. The blood flow was enforced by the displacement of a plate located at the ventricle side of the blood domain. TR was quantified as a percent of blood particles at the atrial side to the particle at the ventricle side of the tube. The TR was calculated at the time point when the plate approximately reached the leaflets (Fig. 1 and Supplementary Animation 2).

2.2. Scenarios for MC Intervention

First, the valve with normal condition was simulated. Then, one group of chordae was removed from the model to simulate the diseased valve. Next, the MC intervention was simulated. To examine the effects of MC position, several valve-clipping scenarios were considered (Figs. 2 and 3), which we outline in more detail below.

In the first scenario, it was assumed that one MC is placed near the annulus (Figs. 2 and 3c). In the next scenario, the MC position was changed to approximately midway between the annulus and the leaflet tip (Figs. 2 and 3d). In the third scenario, the MC was placed near the leaflet tip (Figs. 2 and 3e). To examine the effects of implementing two clips, another scenario was considered whereby one MC was placed near the midway point and another MC was placed near the leaflet tip (Figs. 2 and 3f).

The simulation of each MC scenario has three stages (Supplementary Animations 1 and 2). In the first stage, the MC implementation is simulated. In the second stage, the leaflets are closed by a pressure load. Neither stage is an FSI analysis. In the third stage, the flow through the closed valve is modeled. This stage is a FSI analysis in which the blood particle movements and the leaflet deformations affect each other.

3. Results

The TV leaflet deflections were altered by MC positions (Fig. 3). Noticeably, the TR was higher in the diseased valve, but decreased after the MC was placed (Fig. 4c-f and Table 1). The approximate TR for the normal condition was 2.5%, for the diseased condition it was 7.5%, and for repaired valve it was minimized up to 1.9% (when one MC was placed near the midpoint between the annulus and leaflet tip. Fig. 4d).

The location of the MC changed the TR (Figs. 4c-e). The clip positioned approximately midway between the annulus and leaflet tip produced the lowest TR (1.9%), and the clip placed close to the leaflet tip had the least effect on TR (7.3%). An intermediate amount of regurgitation was observed when the clip was placed close to the annulus (3.2%) (Table 1).

Not only the site of clipping but also the number of MCs affected TR. When two clips were used, the regurgitation was lower than for one clip close to the annulus or one clip close to

the leaflet tip (Table 1). However, the regurgitation for two clips was higher than the lowest regurgitation with one clip approximately at the midpoint between the annulus and leaflet tip (approximately 2.3% versus 1.9%, respectively) (Table 1).

The maximum leaflet stress was altered by MC location. The leaflet tissue near the clipping region typically experienced high stresses (Fig. 5). When the MC was located near the leaflet tip, the stresses were higher than when the MC was close to the annulus or approximately midway between the annulus and leaflet tip. When two MCs were used, stresses further increased near the clipping regions (Fig. 5). In other words, when two clips were used, the maximum stress was higher than when one clip was used (Fig. 5).

4. Discussion

To the best of our knowledge, this is the first study that quantifies the effects of MC placement on the TV using an FSI analysis. Our results show that TR could be reduced up to 75.2% with one clip, and it was reduced by 68.7% with two clips (Table 1 and Fig. 4), returning total TR to normal conditions. However, the clipping of the leaflets typically increased stresses in the leaflets, particularly if the clip was placed near the leaflet tip, and the use of two clips led to higher stresses than the scenario with one clip (Fig. 5). The effects of MCs on the leaflets followed the position and number of MCs (Fig. 3). Our results quantified the effects of MC on TR, and confirmed previous clinical findings on the efficacy of MC for TR [3,10].

Our results demonstrate the profound role of MC positions on TR and leaflet stresses. Because MC implantation is a percutaneous procedure (rather than an open-heart surgery), the surgeon's control over MC placement could be limited, which may reduce the ability to position the MC in the optimal location. Quantifying the alteration in TR and leaflet stress with MC position makes it possible to find the optimal location for the clip. Also, such quantification could help to explain the importance of deviations from the optimal clip position.

When one MC is used, its position is a key factor in reducing TR (Table 1 and Fig. 4). Obviously, the MC is expected to take over some of the role of the missing chordae to reduce TR. Our results show that the clipping procedure may not produce optimal outcomes in terms of the reduction of TR when the MC is placed relatively close to the annulus or the leaflet tip (Table 1 and Fig. 4). While the use of two clips reduced TR substantially, it was not as effective as a single clip in the optimal position (1.9% for a single clip approximately at the midpoint between the annulus and the leaflet tip, versus 2.3% for two clips; Table 1).

We suspect that the location of missing chordae also plays a critical role in MC repair for TR. Therefore, an optimal MC placement in terms of reducing TR may depend on at least two factors: 1) position of the missing chordae, and 2) position of the MC. Further investigations are needed to ascertain if our findings are applicable to other scenarios for TR, or if they are specific to the particular scenarios we considered. Nevertheless, the methodology presented here is applicable to a more comprehensive study of effects of MC on different scenarios for TR.

If the stresses are too high, the risk of leaflet tear will increase [27,28]. Thus, an MC position that leads to the lowest TR might not be the optimal position if it leads to relatively too high stresses. In the conditions with one MC, the MC located near the midway point between the annulus and leaflet tip caused a better TR than the clips located near the annulus or the leaflet tip (Table 1 and Fig. 4); however, the MC near the midway point also caused higher stresses than the MC close to the annulus (Fig. 5). Therefore, a range of MC positions should be considered to determine the clipping position that optimizes both TR and leaflet stresses.

More than one clip may be needed for an effective MC intervention [3]. Our results showed that with two MCs, the TR may be lower than with one MC (depending on the position of the single MC), but stresses in the leaflets may be higher (Fig. 5). This implies that although using two clips may reduce TR more than only one clip, using two clips may not always be optimal. A simulation of MC implantation can provide key information about MC intervention that will otherwise unexpectedly impact the outcomes of surgery.

This study has some limitations. We used a simple tube-like structure for the RV geometry, which is not realistic. Inclusion of the ventricle and atrium provides a more realistic chamber geometry. Also, if the geometry of the ventricle and atrium is included, more realistic boundary conditions for the blood flow can be implemented. We did not include the geometry of the MCs, but did model the effect of clipping. Moreover, we used data from a single subject. The results will be more reliable if a statistically meaningful number of TR cases are simulated using these modeling techniques. Our study also excludes the effects on cardiac output that changes in TR would have. A future direction for this research would be to study these effects using the Living Heart Model, as we have done in other studies [29,30]. Moreover, the material properties could be improved based on data for material characterization tests for TV [31].

In this study, we assumed that TR occurred as a result of TV chord rupture. Although chord rupture is a less common cause of TR [32], our methodology can be applied when TR occurs as a result of other, more common, factors.

The values of TR in this study were relatively low. For the untreated disease scenario, the TR was 7.5%, which is below the ranges for severe TR [33]. More severe grades of TR can be created by removing more or different chordae from the normal condition. However, this limitation does not change the conclusion of this study, which was that the MC effectively reduces TR.

In reality, the leaflets close because of their interactions with blood flow. Although we did not consider an FSI between blood flow and leaflets when the valve opens and closes, we did consider an FSI between leaflets and blood flow when the leaflets were closed (we did not model the full cardiac cycle; see Supplementary Animation 2). Because the focus of this study was on TR, we first closed the valve using a pressure load, and then the blood particles moved through the closed valve with deformable leaflets. As such, the model presented here does not simulate some TV characteristics such as leaflets opening and closing and the blood pressure drop across the valve. Both of these characteristics are important parameters

for TV mechanics. A more comprehensive analysis may consider a full cardiac cycle, including the valve opening and closing, and a two-way coupled FSI.

5. Conclusion

In this study, we simulated blood flow through the TV with and without the MC intervention to examine its impact on TR. To the best of our knowledge, this is the first simulation that quantifies TR with MC interventions using an FSI approach. Our results confirmed the efficacy of MC for TR using a quantitative approach. Moreover, this study illustrated that the effects of clip placement may not be fully determined without the assistance of computational modeling. FE modeling could provide stresses, which are critical to device failure, and can uncover counterintuitive effects. For instance, our optimal treatment protocol was a single clip placed midway between the annulus and the leaflet tip. When an additional clip was added to the leaflet tip, TR was not further improved. The results of this study could lead to the design of more efficient MC interventions for TR.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights:

- Tricuspid valve regurgitation decreases after MitraClip intervention as suggested by fluid-structure interaction models
- The effects of MitraClip position and number can be simulated by computational models
- Tricuspid valve leaflets may experience high stresses after MitraClip intervention
- Computational modeling should lead to optimal strategies for MitraClip interventions

Fig. 1:
The in-silico set up to examine the regurgitation of TV. The TV, blood particles and surrounding tube were used to model the domains of FSI. First, the valve was closed by a pressure load and then the plate was used to make the blood flow through the closed valve.

Fig. 2.

The positions considered for MCs: near the annulus (Annulus MC), approximately midway between the annulus and leaflet tip (Middle MC), and near the leaflet tip (Tip MC). PL: posterior leaflet, SL: septal leaflet, AL: anterior leaflet.

Fig. 3.

Different scenarios for the MC were considered: (a) the healthy valve, (b) the valve with missing chordae, (c) the treated valve with the MC near the annulus, (d) the treated valve with the MC near the midway point between the annulus and the leaflet tip, (e) the treated valve with the MC near the leaflet tip, and (f) the treated valve with two MCs, one between the leaflet tip and annulus, and one near the leaflet tip.

Fig. 4.

TR for different scenarios: (a) the healthy valve, (b) the valve with missing chordae, (c) the treated valve with the MC near the annulus, (d) the treated valve with the MC near the midway point between the annulus and leaflet tip, (e) the treated valve with the MC near the leaflet tip, and (f) the treated valve with two MCs, one between the leaflet tip and annulus, and one near the leaflet tip.

Fig. 5.

The von Mises stress distribution for different scenarios: (a) the treated valve with the MC near the annulus, (b) the treated valve with the MC near the midway point between annulus and leaflet tip, (c) the treated valve with the MC near the leaflet tip, and (d) the treated valve with two MCs, one approximately between the leaflet tip and annulus, and one near the leaflet tip.

Table 1:

The TR for healthy valve, the diseased valve, and four scenarios for MC intervention.

Scenario	TR (%)
Normal	2.5
Diseased	7.5
MitraClip Annulus	3.2
MitraClip Middle	1.9
MitraClip Tip	7.3
MitraClip Middle and Tip	2.3