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In Vitro System for Measuring Chordal Force Changes Following Mitral Valve Patch Repair

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Abstract

Background—Attention towards optimization of mitral valve repair methods is increasing. Patch augmentation is one strategy utilized to correct functional mitral regurgitation or systolic anterior motion in complex mitral valve repairs. This article describes a system for investigating the redistribution of chordae tendineae tension as a reflection of altered stress distribution of the valve leaflet following patch augmentation.

Methods and materials—An in vitro test setup was constructed to hold native porcine mitral valves containing an annulus and papillary muscle positioning system. The alterations caused by patch augmentation should be visual from both the atrial and ventricular views. Ventricular pressure was regulated stepwise in a range of 0–150 mmHg. To test the system, the anterior mitral leaflet was extended by a pericardial patch sutured to the mid/basal part of the leaflet, and the chordae tendineae force was measured as the ventricular pressure was applied.

Results—The system demonstrated the capacity to hold native porcine mitral valves and introducing patch repairs according to clinical practice. The porcine mitral valve test setup indicated strong correlation between the forces in the mitral valve secondary chordae tendineae and the applied transvalvular pressure ($R^2 = 0.95$).

Conclusion—This test setup proved the ability to obtain normal mid-systolic mitral valve function, secondary chordae force measurements, and important preservation of the visual access: Hence, obtaining the pressure-force relationship as well as identifying any shift of the secondary chordae insertion point on the anterior leaflet relative to the coaptation zone was made possible.

Keywords

Mitral valve; In vitro; left ventricle; force; biomechanics

Background

The mitral valve (MV) is positioned between the left atrium and the left ventricle, and ensures unidirectional blood flow through the left side of the heart. The MV comprises an anterior and posterior leaflet. Both are attached to the annulus and tethered to the papillary muscles (PM) through the chordae tendineae (CT) in the subvalvular apparatus [1], [2]. Mitral valve repair is generally preferred over valve replacement for the treatment of patients with mitral regurgitation, and is associated with a lower risk of thrombo-embolic complications [3]. Attention towards optimization of repair methods in terms of minimizing adverse loading of the valve tissue is currently heightened [4]. Restoration of the leaflet functionality with patch augmentation to extend leaflet area is increasing in popularity [5]-[6]. While altering the leaflet geometry, it is inevitable that the force balance of the left ventricle changes. Whether this change in force balance is preferable in terms of valve repair durability is unknown. Hence, it is important to describe these alterations caused by an augmented leaflet.

The purpose of this study was to investigate the feasibility of identifying the force balance changes following patch repair of the anterior leaflet of the MV, with particular attention to the secondary chordae tendineae. Therefore the aim of this study was to build and test an in vitro setup capable of visualizing and measuring the geometrical alterations of the MV, as well as forces acting on the CT.

Materials and Methods

The in vitro left heart chamber was made of transparent acrylic and was sized for optimal visualization. The chamber comprised a height adjustable annular plane and a three-dimensional PM positioning system. The chamber was designed for static experiments. Pressure in the ventricular chamber was established through a manual water inlet (see Figure 1). Air was present on the atrial side of the valve.

Since the geometry of MVs with CTs and the PMs vary from heart to heart, the need for individual adjustment of the position of the PM holder was essential. The PM positioning system was composed of two guided rods, two PM rods and two PM holders (see Figure 2). The guided rods were placed 20 mm apart and were able to slide through two adjustable guide fittings in the chamber wall. The guide fittings are capable of locking the rods in position. The apical PM displacement was accomplished by mechanical adjustment. The accuracy of the PM holder position is ± 1 mm in the x - direction, ± 1 mm in the y - direction, and ± 1 mm in the z - direction (see Figure 2).

The PMs were attached to the PM-holders allowing the system to obtain the optimal position for proper valve functionality (see Figure 2), as well as having the possibility for positioning the PMs in a pathological state, as it is seen in functional ischemic mitral regurgitation [7]. A competent MV in an in vitro setup is defined as having complete coaptation with no prolapsing leaflet tissue extending beyond the annular plane in the atrial direction.

Pressure in the left ventricular chamber was acquired with a Microtip pressure catheter transducer (Model: SPC-350; Millar Instruments, Houston, TX) and connected to a

controlling unit (PCU-2000; Millar Instruments, Houston, TX) for real-time pressure measurements. Force measurements were performed using dedicated and calibrated CT tension transducers [8]. The pressure and force transducers were connected to a data acquisition module rack (NI cDAQ 9172; National Instruments, Austin, TX) with two input modules (NI 9215 and NI 9237; National Instruments). Pressure and force recordings were performed on a computer using an in house build data-acquisition software program (LabVIEW Version 8.6; National Instruments). The size and anatomy of the adult human heart is similar to that of an 80 kg pig, which allows the usage of these porcine valves [9]. Hence, extracted porcine mitral valves with CT and PMs from 80 kg pigs were implanted in the setup. The distance from commissure to commissure was 5 cm and anterior-posterior distance was 4 cm. The system was designed to test valves at their healthy stage and subsequently with simulated augmented leaflets. The valve function before patch augmentation was first evaluated by observation, then adjusted and approved when no regurgitation occurred at 100 mmHg water pressure applied to the ventricular chamber (see Figure 3), 150 mmHg was chosen to simulate peak systolic ventricular pressure. The leaflet augmentation was performed with a glutaraldehyde-treated porcine pericardial patch sutured to the mid/basal part of the anterior mitral leaflet (see Figure 3).

Test setup for explanted porcine mitral valves

For the pilot test experiment, one MV was extracted from fresh porcine hearts and treated with a 37% formaldehyde solution for two hours and kept in pH buffered 0.9 % saline at 4°C until used. The valve was sutured to a custom made flange made from rapid prototyping in ABS plastic material and sized to match the explanted MVs.

To verify system functionality, left ventricular chamber pressure and anterior leaflet secondary CTs forces were recorded without patch, and subsequently recorded on the same MVs with a patch implanted in the anterior leaflet between the annulus and secondary CT insertion point (according to clinical practice [10], [11]), using the exact same anatomical geometry settings of the in vitro setup before and after patch implantation (see Figure 3). The patch was ellipsoidal shaped having a short axis length of 20 mm and a long axis length of 30 mm.

Results

As pressure was applied to the chamber, a force response immediately occurred in the CT (see example on Figure 4). As the pressure was increased continuously to 150 mmHg, the valve closed fully, and the functionality responded in a satisfying fashion, as described in Materials and Method, and with reference to established in vitro models described in literature [12]. The correlation between left ventricular chamber pressure and CT force was strong: Figure 4 displays the force recorded as a response to pressure changes from 0-150 mmHg for the anterior and posterior PM before and after patch implantation. The correlation between the applied pressure and the resulting force is verified with a linear regression r^2 values of above 0.95 (see Figure 5). It was observed that the secondary CTs attachment point on the anterior leaflet moved apically and posteriorly, towards the coaptation zone following patch implantation (see Figure 3).

Discussion

A new in vitro model to investigate the effect of patch repair with respect to the forces in secondary CTs has been developed and tested. The left ventricular chamber allowed physiological mid-systolic behavior of the valve while identifying isolated aspects of the mechanical loading of the CTs before and after patch augmentation. Establishing visual access to the MV makes it possible to compare measured forces to geometrical changes, providing better insight into the mechanical implications of the valve repair.

Although suturing the MV to the annular plane flange could lead to folding or stretching of tissue around the annular perimeter, care was taken to alleviate that problem. In case of leaking fluid around the sutured annular circumference, silicone was used for sealing. This problem is secondary in importance since the focus of this model is to compare the CT force in the valves before and after patch insertion as a response to applied pressure. Hence, any individual differences in valves as well as their insertion in the model will be controlled for in a repeated measures analysis or analyzed as a covariate of future research projects with this system.

The fixture of the PM is crucial for obtaining correct valvular function, as stated in the Material and Methods section. Fixating the PMs in a non-physiologic position would lead to a redistribution of the CT forces, leading to a malfunctioning valve. Allowing the PMs to obtain angular rotation in all directions solved this issue.

Valve alterations caused by patch augmentation in this in vitro model were made visual from both the atrial and ventricular views. This enables further investigation of the background for any possible change in forces in the chordae tendineae following repair. Figure 4 and the pressure-force correlation data from this system displayed in Figure 5, indicates a similar trend as has been published previously in a model of MV prolapse [13]. In this ex-vivo and in-vivo study, the prolapse (confirmed with 2D ultrasound) was obtained by implanting a pericardial patch in the same position and fashion as it was implanted in this in vitro model. Following patch implantation, a reduction of the forces in the secondary CT was found to be reduced by $34\% \pm 13.0\%$, $p < .001$ [13]. This reduction could partly be caused by the displacement of the insertion point of the secondary CT in the direction towards the coaptation zone, as was visually indicated in this new in vitro setup (see Figure 3). This CT displacement would cause the posterior leaflet to push on the insertion points CTs on the anterior leaflet, which is positioned in or closer to the coaptation zone following patch augmentation. This concept is illustrated in Figure 6. Indeed, these initial data illustrate a healthy valve and a valve with a patch augmented anterior leaflet. In the setting of a pathologic papillary muscle displacement, the valve geometry will differ and may change the outcome as well as its similarity to the results reported within this study. In addition, relocating the insertion points of the secondary CT with a posterior shift reshapes the geometry by means of a change of angle formed between: The secondary CT, the primary CT and the leaflet, thereby the triangular force balance as described in literature [14] is changed.

The concepts described above are part of the focus for future usage of the in vitro patch augmentation model. In addition, it may be possible to define an alternative use for the new patch augmentation in vitro model: To investigate the biomechanics of pathological conditions of the MV, such as prolapse, myxomatous or Barlow's disease. These conditions are caused by excess leaflet tissue and are diagnosed by a billowing of a part of the leaflets towards the left atrium during systole (≥ 2 mm above a line connecting the annular hinge points on an echocardiographic parasternal long-axis view) [15]. Valvular excess connective tissue and myxomatous degeneration causes increased total leaflet area and leaflet thickness, while the chordae tendineae CT are often elongated. Because of the decreased tissue tensile strength and redistribution of the chordal forces associated to histologic changes, CT rupture is often observed [16,17]. If these conditions can be replicated in vitro, it may be possible to simulate the geometrical conditions of mitral valve prolapse in the in vitro setup.

However, the current focus of this model is to establish a platform to investigate the effects of MV repair. Force equilibrium must be maintained in the MV apparatus, since the anchoring points (papillary muscles and the annulus) do not move. Any change in secondary chordal force must result in a reduced or additional force to the remaining CTs or the MV annulus. It is thereby given that the stress pattern of the leaflet is also altered compared to the healthy case. If high local stresses occur, the risk of adverse strain distribution in the valvular tissue and attaching components is increased. Therefore, further investigation of the stress mapping of MV repair is important. Such investigations may be carried out in an advanced finite element model as described in literature [18]. These finite element models can be modified to simulate patch repair of a MV in a left ventricle with ischemia and following patch repair. A comparison between the finite element analysis and a series of in vitro experiments conducted with the model described in this paper could significantly substantiate the results from these in vitro measurements as well as better explain the consequences of prolapse force changes as identified by Granier and colleagues [13].

Establishment of a model that can mimic disease conditions of functional ischemic mitral regurgitation with PM displacement and following patch repair has been obtained: In this model, functional ischemic mitral regurgitation is simulated by only displacing the posterior papillary muscle (Carpentier type IIIB) hereby isolating this effect from the confounding annular dilatation and flattening as seen in FIMR. In summary, this new in vitro system can identify any likely reflection of a redistribution of leaflet forces from the original load-bearing area of the MV leaflets towards the patch augmented region and the mitral annulus. This valvular stress redistribution may adversely affect repair durability, and identifying possible precautions necessary during repair will make the use of these models extremely valuable. In a large perspective, stress studies initiated from knowing the geometry of the MV and force in the CT, could provide essential information to the surgeon on the best possible location of the patch repair on the leaflet. As a future perspective, a series of experiments using the equipment and methods described in this paper, will be conducted.

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Figure 1.

CAD drawing of the in vitro model. The height adjustable flange in the middle of the chamber acts as an annular plane, and is sealed and waterproof. Below the annular plane is the ventricular chamber, and above the plane is the atrial chamber. The annular plane can be raised or lowered from the outside of the chamber. The middle part of this flange can be replaced by other valve-fixating parts. The water-inlet is connected to a water supply, and through this, fluid pressure is built in the ventricular chamber.

Figure 2.

Illustrations of the papillary muscle positioning system and the degrees of freedom of the PM holders. The PM position can be adjusted in three dimensions x, y and z. Top left is shown how the PMs are secured to the PM holders. The accuracy of the PM position is $\pm 1\text{mm}$.

Figure 3.

View from atrial side showing the porcine mitral valves sutured to the annular plane- Left: Healthy mitral valve with dark markers on anterior leaflet to identify the insertion points of secondary chordae tendineae. Right: The same mitral valve is remodeled with excess leaflet tissue simulated by suturing a pericardium patch to the anterior leaflet. The insertion points of the secondary chordae tendineae are indicated with arrows. The coaptation zone is shown with a dashed line.

Figure 4.

Descriptive example of test results of in vitro force measurements as a response to applied ventricular chamber pressure. Forces measured on healthy (left) and simulated repaired porcine mitral valve (right). Forces are measured on the secondary chordae tendineae on the anterior leaflet attached to the posterior and anterior papillary muscles. Pressure was continuously increased from 0 to 150 mmHg over a duration of ten seconds.

Figure 5.

Pressure – force correlation of the mitral valve chordae tendineae force measurements. A linear correlation between applied pressure and forces measured in the secondary chordae tendineae is illustrated.

Figure 6.

Illustration of alternated geometries when excess tissue is applied to the anterior leaflet.

Left: Healthy mitral valve. Right: Mitral valve with excess tissue implanted in the anterior leaflet. 1) Secondary chordae tendineae in which the force is measured; 2) Healthy anterior leaflet; 2*) Anterior leaflet with patch inserted; 3) Posterior leaflet; 4) Change of angle (Φ) on secondary chordae tendineae due to excess leaflet tissue; 5) Inserted patch. Insertion point of secondary chordae tendineae moves towards the coaptation zone of the leaflet. Arrows illustrate that leaflet tension may be reduced due to excess tissue.