Mitral Web - A New Concept for Mitral Valve Repair: Improved Engineering Design and In-Vitro Studies

Ersin Erek[1], Muralidhar Padala[3], Kerem Pekkan[2], Jorge Jimenez[3], Yusuf K. Yalçınbaş[1], Ece Salihoğlu[1], Tayyar Sarıoğlu[1], Ajit P. Yoganathan[3]

[1]Department of Cardiovascular Surgery, Acibadem Hospital, Istanbul, Turkey, [2]Department of Biomedical Engineering, Carnegie Mellon University, PA, USA, [3]School of Biomedical Engineering, Georgia Institute of Technology, GA, USA

Background and aim of the study: **A new mitral valve repair concept to treat mitral regurgitation (MR) due to valve prolapse was recently proposed. In this study, an improved design of this concept is presented, and the results of preliminary hemodynamic studies conducted in an in-vitro prolapse model are reported.**

Methods: **The new repair approach is based on using a web/net attached to a standard annuloplasty ring spanning the annulus of the mitral valve. Experiments were conducted in a left ventricular simulator, using native porcine mitral valves. Severe MR was created by transecting the marginal chordae to induce P2 prolapse, and also by displacing the papillary muscles basally to induce bileaflet prolapse.**

Results: **Implantation of the mitral web prevented leaflet prolapse and restored leaflet coaptation with trace mitral insufficiency, in both posterior and bileaflet prolapse. In posterior leaflet prolapse, implantation of the mitral web reduced the regurgitation volume from 10.43 ± 3.76 ml to 2.13 ± 1.83 ml per beat (p <0.05). No visual damage was observed on the mitral valve leaflets after 4 h of continuous operation.**

Conclusion: **Based on the study results, the mitral web may represent a feasible option to repair different types of mitral valve prolapse. The mitral web may also significantly simplify mitral valve repair for complex lesions**

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Myxomatous mitral valve disease is currently the most common cause of mitral regurgitation in western countries (1). Several clinical studies have reported that mitral valve repair is preferable to valve replacement, as it offers certain advantages that include relief from long-term anticoagulation therapy, decreased operative mortality and improved long-term outcome. Although the vast majority of patients with posterior leaflet prolapse are amenable to repair with fairly standardized techniques (2,3), prolapse of the anterior cusp and bileaflet prolapse requires a more complex type of repair.

The current repair techniques for mitral valve prolapse aim at restoring physiological mitral valve geometry by resecting the redundant leaflet tissue, chordal shortening, or by reconstructing the broken mitral valve chordae using a neochordoplasty. To date, only edge-to-edge repair is an exception as this constitutes a non-anatomic repair with a double-orifice mitral valve (4,5). Although, compared to the resective methods, the non-resective chordal techniques restore physiological valve function and aid long-term durability, they are technically more challenging. A novel and simplified concept of mitral valve repair, based on using a web/net attached to a standard annuloplasty ring spanning the annulus of the mitral valves, was recently proposed by the present authors' group (6). The details of an improved engineering design of this concept are presented here. Surprisingly - and almost simultaneously - Bernal et al. reported the details of an animal experiment in which the same concept (a 'valve racket') was adopted (7).

The study aim was to test the mitral web under pulsatile flow conditions in an in-vitro model of posterior and bileaflet prolapse developed in the authors' laboratory, and to demonstrate the efficacy of the web in correcting mitral regurgitation and restoring physiological leaflet coaptation.

Address for correspondence:
Ajit P. Yoganathan PhD, Wallace H. Coulter School of Biomedical Engineering, Georgia Institute of Technology, Room 2119 U. A. Whitaker Building, 313 Ferst Drive, Atlanta, GA 30332-0535, USA
e-mail: ajit.yoganathan@bme.gatech.edu

Materials and methods

Engineering design

The original prototypes of the mitral web featured an irregularly shaped network that was constructed manually in the operating room, using common surgical materials (nylon sutures manually mounted on a rigid, D-shaped annuloplasty ring; see Fig. 1) (6). These prototype designs were tested with pericardial flaps under static pressure conditions (Fig. 2) (6). In order to enhance their functional performance, the preliminary designs were critically evaluated and an improved version was developed for use in in-vitro studies. A flat 'D'-shaped annuloplasty ring frame was constructed from stainless steel, with an inter-trigonal length of 38 mm, a septal-lateral length of 30 mm, and a commissure-commissure length of 41 mm (vertical:horizontal diameter ratio, 0.75). The stainless steel ring was covered with a surgical-grade Dacron® sewing cuff, and the ring size validated with commercial annuloplasty ring sizers (Edwards Lifesciences, Irvine, CA, USA).

The results of preliminary studies conducted by the present authors have suggested that a network of horizontal and vertical sutures forming a '+'-shaped web disrupts the fluid dynamics and may lead to blood damage, similar to the stagnation points found ball-and-cage valve. To avoid this, in this new de only cambered bars running in the septal-lateral direction were used. Thus, nine 0.5 mm-diameter rods were welded equidistantly onto the annuloplasty ring frame. To maintain the native curvature of the leaflets during systolic valve closure, the rods were designed with a curvature with its deepest point closer to the posterior annulus and at 5 mm depth from the mitral annulus plane (Fig. 1). During peak systolic coaptation, due to its larger surface area, the anterior leaflet moves significantly more than the posterior leaflet before the leaflets coapt. This functional feature of the mitral valve was considered in the implant design, and the deepest point on the curved rods was approximately matched to the coaptation line of the leaflets. In addition, the gradual change in curvature from the anterior annulus to the deepest point, and then towards the posterior annulus, helps to maintain good leaflet curvature while preventing leaflet prolapse. Additionally, in the commissure-commissure direction, the bars had a gradually decreasing gradient in the depth:curvature ratio from the middle bar compared to those at the commissures (Fig. 1b,c).

In-vitro studies
Experimental set-up

Fresh porcine hearts of similar size and weight were obtained from the local abattoir and transported to the
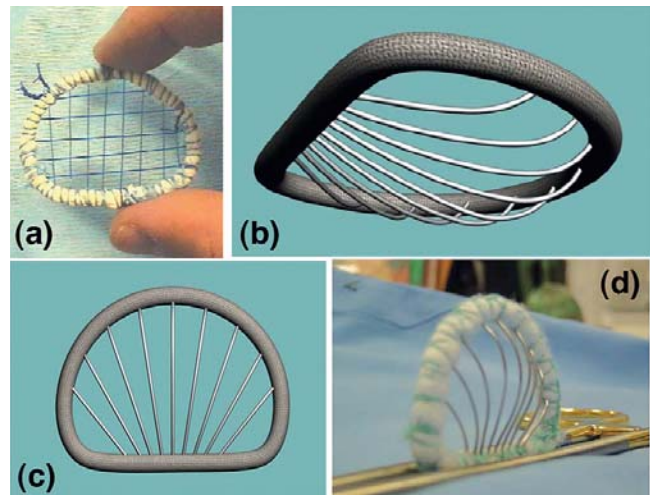

Figure 1: The evolution of mitral web designs. a) The original design with a flat, quadrilateral-shaped mesh network. b,c) An improved design to reduce blood damage due to flow and anatomical conformity in closure. d) The first prototype, constructed from stainless steel.

laboratory under ice-cold conditions. The mitral valve was dissected from each heart, keeping the annular and subvalvular apparatus intact. For the studies, the valve was mounted in the Georgia Tech left-heart simulator, which had been developed for mitral valve research (8-11).

The in-vitro simulator consisted of two acrylic chambers which simulated the left atrium and left ventricle. A silicone annulus was sutured onto an acrylic plate, positioned between the left atrium and left ventricle, and held tightly between both chambers. The excised mitral valve was sutured onto the silicone annulus and the papillary muscles were mounted onto two gear-adjustable papillary muscle holders that allowed displacement of the papillary muscles in all dimensions. A tilting-disc mechanical heart valve was used in the position of the aortic valve. A reservoir which maintained a constant head of 12 mmHg was connected to the left atrium in order to simulate pulmonary pressures, while a pulsatile bladder pump was connected to the left ventricle to generate pulsatile flow through the system. The pulsatile bladder pump was a compressed air-driven pump capable of generating various time-varying pressure waveforms by controlling the volume of compressed air that squeezed the bladder. In the present system, a circuit of solenoid valves was used which was connected to a microcontroller to achieve a physiological pressure waveform with a systolic duration of 220 ms from a total cycle time of 860 ms. The outflow through the aortic valve was drained into a reservoir connected to the left atrium through rubber pipes; hence, a closed loop was created. Several adjustable compliance chambers and mechanical
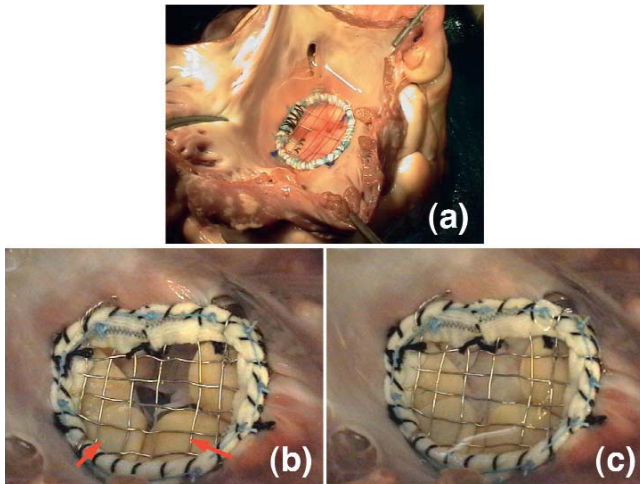
Figure 2: a) An earlier mitral web prototype implanted on a bovine heart. Static tests performed in the operating room using a mitral web with pericardial flaps during (b) diastole and (c) systole showed a perfect seal, with no papillary muscle attachment. In (b) the arrows indicate the pericardial flaps.

resistances were connected into the loop to obtain physiological pressure and flow curves. Physiological saline solution (0.9% NaCl) was used as the working medium. Pressures in the left atrium and left vent were monitored continuously and recorded using differential pressure transducer (DP9-40; Validyne Inc., USA); the mitral flow rate was measured using an electromagnetic flow probe (Carolina Medical Devices, NC, USA).

All data were recorded using a DAQ-card (DAQ-1200; PCMCIA, National Instruments, TX, USA) and displayed and written to the hard drive using an in-house code based on LABVIEW (National Instruments, TX, USA).

Experimental protocol

The experiments were conducted in three steps, as described below:

- *Normal conditions:* When the porcine mitral valve had been mounted into the in-vitro left heart simulator, the papillary muscles were orientated to their physiological positions; these positions were determined such that the tertiary commissural chordae were in a single plane and parallel to each other. The tips of the papillary muscles were also maintained in the plane of leaflet coaptation. The valves were then tested under physiological hemodynamic conditions of 120 mmHg peak transmitral pressure and a cardiac output of 5 l/min, at a heart rate of 70 beats per min. The mitral flow rate and regurgitation volume were recorded using the flow probe, and a high-speed video of the functioning

valve was obtained through the atrium. Under normal conditions, no mitral valve regurgitation or prolapse was observed.

- *Disease conditions:* Two types of leaflet prolapse were simulated in this study. First, to create bileaflet mitral valve prolapse, both papillary muscles were displaced by 10 mm basally towards the mitral annular plane, so as to induce slackness in the chordae tendineae. The valves were tested under identical hemodynamic conditions, as normal. Moderate to severe mitral regurgitation was evident from the flow data measured, and billowing of both mitral leaflets into the left atrium was clearly evident. The second type of prolapse to be simulated was the most common posterior leaflet prolapse due to chordal rupture. Here, the papillary muscles were restored to their normal positions, and the marginal chordae inserting into the free edge of the posterior leaflet were transected. Under pulsatile flow conditions, this chordal rupture resulted in severe posterior leaflet prolapse that led to eccentric jets which were captured using three-dimensional (3-D) echocardiography (iE 33; Philips Medical Systems, Andover, MA, USA). The mitral regurgitation volume was recorded over multiple cardiac cycles, and an average value calculated.

- *Repair conditions:* The mitral web was implanted onto the silicone annulus through the left atrial window, and the valve re-tested under the same hemodynamic conditions as described above. The mitral regurgitation volume after implanting the mitral web was measured for the posterior leaflet prolapse case, but not for the bileaflet prolapse. As the creation of bileaflet prolapse by displacing the papillary muscles basally is non-physiological, this case was used only to provide a qualitative assessment of ring efficacy. A high-speed video of the valve for the bileaflet prolapse case showed that the mitral web corrected leaflet prolapse very effectively, and provided good validation for the improved engineering design.

In all cases, the experiments were conducted for 4 h after implantation of the mitral web.

Results

Hemodynamic measurements

The mitral web reduced the regurgitation volume caused by posterior leaflet prolapse. In normal valves there was no regurgitation, whereas transecting the marginal chordae on the posterior leaflet resulted in severe P2 leaflet prolapse and a regurgitation volume of 10.43 ± 3.76 ml per beat. Insertion of the mitral web restricted the prolapse to a very large extent, the regur-
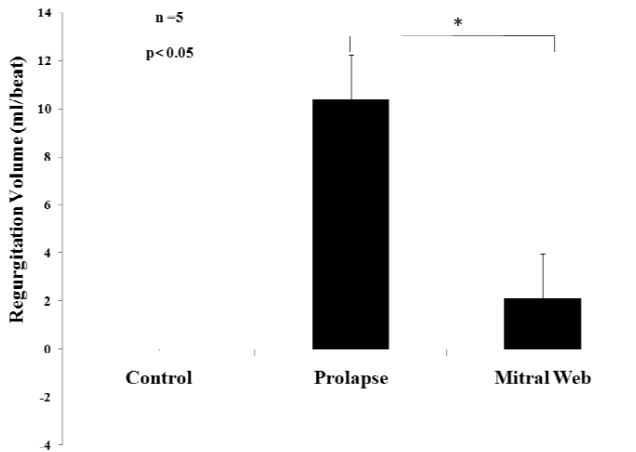
Figure 3: Regurgitation volumes for normal, posterior prolapse and mitral web implantation conditions. The mitral web caused a significant restriction in posterior leaflet prolapse and also a significant reduction in regurgitation.

gitation volume being reduced to 2.13 ± 1.83 ml per beat, and comparable to the normal valve (Fig. 3).

Videoscopic measurements

The two cases of videoscopic observation showed that correct coaptation of the mitral valve leaflets was achieved under dynamic conditions with displaced, partially free and free papillary muscles (see Movie 1; http://www.andrew.cmu.edu/user/kpekkan/Supplementary_Movie.mpg). Two expected causes of web failure were also tested by increasing local web spacing and suturing the valve to the annulus, with almost no localized anterior leaflet (Fig. 4a). The mitral web apparatus was effective in preventing mitral prolapse and insufficiency in all of the studied scenarios. However, unequal web spacing caused localized segmental prolapse of the leaflets (Fig. 4b); this localized prolapse slightly increased with time during the 4-h period of experimentation (Fig. 4c). Taken together, these results indicated a requirement for minor adjustments and controlled tolerances in web spacing for future versions of this design. No apparent damage or tearing of the leaflets was observed after 4 h of continuous operation.

Discussion

Mitral valve prolapse due to degenerative valve disease is the leading cause of mitral regurgitation, especially in developed countries (12). Prolapse of the posterior leaflet is more common than anterior leaflet prolapse (13). Very often, prolapse describes a normally functioning mitral valve with no regurgitation but with a morphologic particularity, namely billowing of

the mitral leaflets towards the left atrium. From a surgical point of view, however, the definition of valve prolapse is the failure of leaflet coaptation resulting in displacement of a part of the free edge of the leaflet towards the left atrium, with regurgitation of some blood (14). Although, in the past, several surgical techniques have been described to repair the posterior leaflet (with good long-term results), historically the repair of a prolapsing anterior leaflet has been more difficult and risky. Typically, surgical manipulation is limited because of the increased complexity associated with the anterior leaflet; this is due to the close proximity of the aortic root and fibrous trigones. The anterior leaflet is a well-defined structure compared to the posterior leaflet, and is fixed between both fibrous trigones. The anterior leaflet also has a higher degree of movement, with the strut chordae inserting into the central region of the leaflets on the ventricular side. These anatomic features restrict the use of posterior leaflet repair techniques on the anterior leaflet (15).

Previously, the conventional approach to repair anterior leaflet pathology has been either shortening of the elongated chordae, chordal transposition, or a limited triangular resection (15). Each of these techniques preserves the normal physiology and morphology of the valve. In theory, any abnormal reverse motion can be prevented in one of two ways. This situation can be likened to a trap door: in order to prevent the door from opening outwards a string can be placed inside the door, holding it in the closed position; alternatively, a blocker can be used to prevent the door from opening outwards. Until now, all repair techniques have employed the first principle, except for the edge-to-edge repair. However, in the present study, a simple blocker system - the mitral web - was used to prevent leaflet prolapse at the annular level.

Based on the success of the initial static experiments performed in the operating room (6), as well as blood trauma studies (7) and the present preliminary in-vitro experimental observations, it can be concluded that this concept deserves further study as a possible alternative to correcting mitral valve pathologies not amenable to repair with current techniques. Specifically, additional in-vitro experiments with improved designs (based on insights from the present study) are required to understand the valve mechanics with this new type of arrangement. Clearly, the results of the present study encourage for future animal studies and a continuation with in-vitro tests. In-vitro tests aimed at acquiring quantitative data, using a greater number of valves and improved web designs, are currently under way. The intention is that the web design improvements will focus on valve size-dependent wire separation and the incorporation of a non-thrombogenic material. Moreover, chordal force measurements
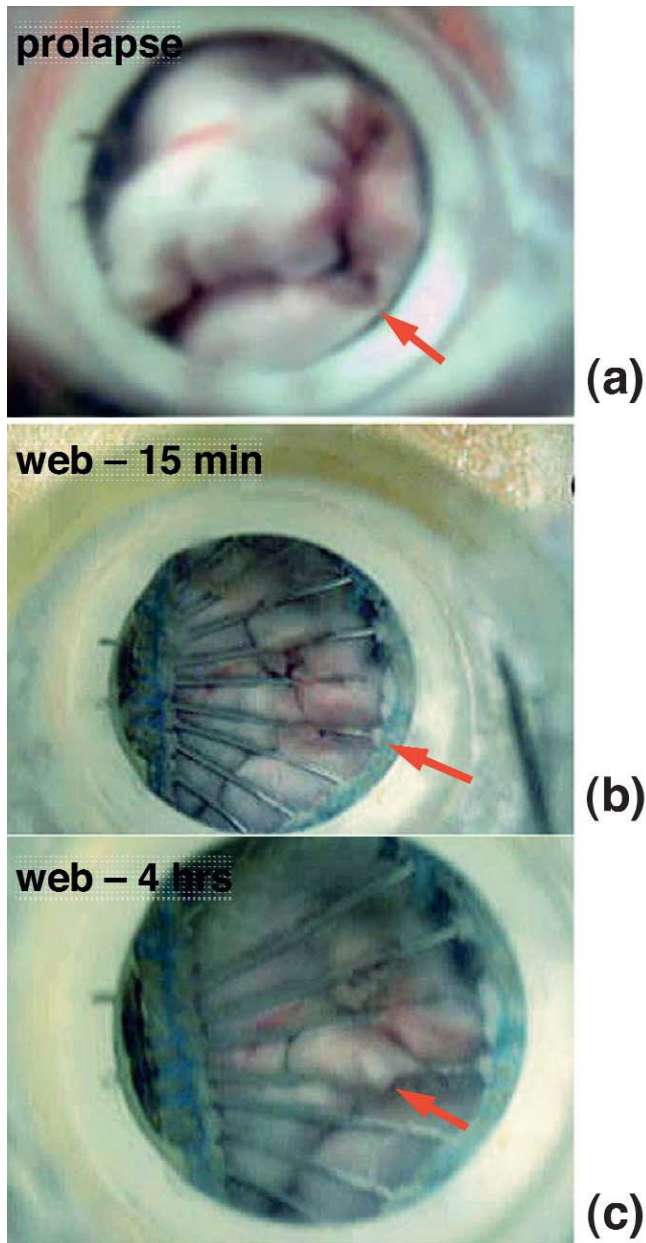
Figure 4: High-speed video snapshots from the 5 l/min experiment during valve closure. a) Severe prolapse created in the in-vitro flow chamber with no force on the chordae tendinea; the papillary muscles are left free. b) Mitral web facilitating improved coaptation. c) Mitral web during closure after 4 h of continuous operation. In (b) and (c) the arrows indicate the anterior leaflet, with almost no leaflet area. In (c) the arrow indicates a posterior leaflet locally prolapsing due to the larger wire spacing. All images were captured using a CCD camera during pulsatile operation. All experiments were performed in a flexible-walled, left-heart simulator. The reader is referred to Movie 1 (http://www.andrew.cmu.edu/user/kpekkan/Supplementary _Movie.mpg) for correct functioning of the mitral web.

should also be made in order to understand the effect of this system on the subvalvular apparatus.

The possibility of causing chronic damage to the mitral valve leaflet surfaces represents a critical limitation that requires further animal experiments to be conducted. A simple static force analysis estimates the maximum local compressive (bearing) pressure acting on the valve leaflets by the mitral web wires to be approximately 37 kPa during valve closure. (This is calculated using the area in contact with the leaflets, and a transmitral pressure of 120 mmHg.) The normal physiological compressive loading on valve leaflets due to peak transmitral pressure (120 mmHg acting over the 38 mm annular area) is 13.6 kPa, which suggests that either a thicker wire or a greater number of wires might be used in future designs. Recent satisfactory reports on blood damage performance (7) and the presented low-profile design (nine 0.5 mm-diameter mitral-web wires caused an 11% reduction in the effective orifice area - considerably less than the typical flow constriction of 17% created by a typical edge-to-edge repair procedure) (4) will allow these improvements for reduced compressive stresses (up to five more wires can be added for a 17% flow restriction that decreases compressive stress to ~24 kPa). These calculations assumed a zero papillary muscle force, which was also the case for the preliminary experiments where prolapse was eliminated even when all of the papillary muscles were left free. In more realistic cases there would still be some force on the chords, and this would be beneficial not only to reduce the compressive stress but also to augment the correct coaptation of the valve.

For further comparison, the compressive stress generated by the mitral web was one order of magnitude less than the average chordal tension (16), and two-orders lower than the estimated biaxial stress values of a normal mitral valve (17). Likewise, for a typical Alfieri-stitch repair, the local stress acting on the leaflets is estimated at 300 kPa (through four sutures) (18), for this edge-to-edge repair procedure stitch stress acts over a longer period (more than two-fold) with systolic and diastolic peaks (4). These loading values indicate that compressive stresses acting on the leaflet are likely to be tolerated by the leaflet tissue.

Another important issue worthy of mention is the risk of thrombosis. However, in a series of animal studies performed using this device, Bernal et al. (7) did not observe any indications of thrombosis in healthy valves. These findings provided the additional confidence required for the clinical application of the proposed repair alternative. When revisiting the history of mechanical vascular prostheses - including some contemporary devices such as mechanical heart valves and vena cava traps - it is possible to identify those

that can be successfully implanted in patients but which generate exceedingly complex fluid dynamic flow patterns compared to the mitral web. The mitral web device, with its reduced number of thin circular wires and absence of '+' intersections, produces less-complex flow structures, and a blood-damage potential which compares well with that of existing vascular prostheses. For example, in contemporary aortic mechanical heart valve leakage, flow through the hinge regions can generate jet flows with Reynolds (Re) numbers of about 800. For a jet flow the Re number range is essentially turbulent, and may lead to the generation of considerable fluid flow-induced blood trauma. In contrast, the mitral-web flow regime resembles a laminar 'flow over a thin cylinder', with a typical peak Re number of only 150-200 (the average Re is ~35) (19). In comparative terms, the flow over the mitral web wires is essentially laminar, with two recirculation vortices in steady flow (in pulsatile and 3-D flow these vortices would periodically be washed out). Therefore, based on the authors' experience with other mechanical prostheses - and pending detailed quantitative calculations - this latter flow regime would be considered comparatively less severe in terms of blood damage. The exposed artificial material surface area is also significantly less than the typical values observed for mechanical heart valves.

Conventional mitral valve repair is heavily surgeon-dependent and necessitates extensive surgical experience; in contrast, the mitral web implantation is simple and surgeon-independent. Most repair cases require the implementation of a mitral ring, in addition to the actual significant repair effort. The mitral web device reduces the repair time considerably, as only mitral ring implantation is required. Compared to those conventional repair techniques that fail at the subvalvular level, the mitral web concept - by using a simplified approach - introduces fewer changes to the valve, fewer suture lines, and also lessens the need for chordal translocation or replacement; hence, it is likely to improve repair durability. In fact, the technique may also serve a prophylactic purpose for pathologies not present at the time of mitral repair. It would appear that, once a practical deployment strategy has been designed, the mitral web may have the potential for use in minimally invasive procedures as it would provide simple, easy and fast repairs.

Study limitations

The primary limitation of the study was that the normal porcine mitral valves used differed from the targeted diseased human mitral valve, which has a myxomatous pathology. In addition, the posterior prolapse model does not duplicate clinical degenerative disease with posterior scallop or flail. The reason why

the clinical condition differs from the model is that, by the time a clinical case comes to surgery, the affected segment of the posterior leaflet is often significantly distorted. The initial experience with the mitral web device indicates that the more redundant and thicker valve tissues associated with this condition might make the mitral web more effective. Indeed, it is possible that this might also be true for diseased human valves.

In conclusion, the results of preliminary in-vitro experiments have shown that the mitral web may represent a simple means of repairing mitral valve prolapse with complex pathologies. However, further studies are required to translate this technology to the clinical setting.

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