Repair of posterior mitral valve prolapse with a novel leaflet plication clip in an animal model

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Objective: Recently, there has been increased interest in minimally invasive mitral valve prolapse repair techniques; however, these techniques have limitations. A new technique was developed for treating mitral valve prolapse that uses a novel leaflet plication clip to selectively plicate the prolapsed leaflet segment. The clip's efficacy was tested in an animal model.

Methods: Yorkshire pigs (n = 7) were placed on cardiopulmonary bypass (CPB), and mitral valve prolapse was created by cutting chordae supporting the P2 segment of the posterior leaflet. Animals were weaned off CPB and mitral regurgitation (MR) was assessed echocardiographically. CPB was reinitiated and the plication clip was applied under direct vision to the P2 segment to eliminate the prolapse. The animals survived for 2 hours. Epicardial echocardiography was obtained before and after prolapse creation and 2 hours after clip placement to quantify MR grade and vena contracta area. Posterior leaflet mobility and coaptation height were analyzed before and after clip placement.

Results: There were no cases of clip embolization. Median MR grade increased from trivial (0-1.5) to moderate-severe after MR creation (2.5-4+) ($P < .05$), and decreased to mild after clip placement (0-3+) ($P < .05$). Vena contracta area tended to increase after cutting the chordae and decrease after clip placement: 0.08 ± 0.10 cm^2 versus 0.21 ± 0.15 cm^2 versus 0.16 ± 0.16 cm^2 ($P = .21$). The plication clip did not impair leaflet mobility. Coaptation height was restored to baseline: 0.51 ± 0.07 cm versus 0.44 ± 0.18 cm ($P = 1.0$).

Conclusions: The leaflet plication clip can treat mitral valve prolapse in an animal model, restoring coaptation height without affecting leaflet mobility. This approach is a simple technique that may improve the effectiveness of beating-heart and minimally invasive valve surgery. (J Thorac Cardiovasc Surg 2014;147:783-91)

Video clip is available online.

Mitral regurgitation (MR) is one of the leading valve-related indications for cardiac surgery, with degenerative mitral valve disease being the predominant pathology.[1]

Prolapse of the middle scallop of the posterior leaflet (P2) caused by chordal elongation or rupture is the most common lesion seen in degenerative mitral valve disease.[2] The conventional surgical technique for repair of mitral valve prolapse (MVP) involves resection of the prolapsed posterior leaflet segment along with a mitral annuloplasty, as described by Carpentier.[3] In addition, folding valvuloplasty techniques have recently been revisited and are viewed by some as a preferred method of MVP repair, particularly in the setting of minimally invasive mitral valve surgery.[4-7] Surgical repair of MVP is effective, durable, and safe: 10-year freedom from reoperation exceeds 90% and perioperative mortality approximates 0.5%.[8,9] However, there are patients who are not candidates for conventional heart surgery and cardiopulmonary bypass (CPB).[10-13] For this cohort, minimally invasive and beating-heart mitral valve repair techniques and devices have an important role, offering the opportunity for valve repair while avoiding the potential risks associated with heart surgery and CPB. Emerging devices address the components of the mitral apparatus, including the leaflets, annulus, and chordae tendineae.[14] Most notable is the MitraClip (Abbott Vascular, Inc, Menlo Park, Calif), a transcatheter device that treats MR by mimicking a surgical edge-to-edge repair. Although the MitraClip has been one of the most

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Abbreviations and Acronyms

ANOVA = analysis of variance
CH = coaptation height
CPB = cardiopulmonary bypass
IACUC = Institutional Animal Care and Use Committee
ICC = intraclass correlation coefficients
LPC = leaflet plication clip
MVP = mitral valve prolapse
VCA = vena contract area

extensively tested and used devices, this technology has been used predominantly in patients with ischemic MR. Therefore, there remains a need for alternative mitral valve repair devices to address myxomatous mitral valve disease and expand the versatility and effectiveness of minimally invasive and beating-heart mitral valve surgery.

In an effort to answer this unmet need, a new technique of leaflet plication was developed that uses a novel leaflet plication clip (LPC) to treat MVP. The LPC folds (or plicates) the prolapsed leaflet segment without involving the neighboring leaflet segments or the anterior leaflet. Although the ultimate goal is to implant the LPC in minimally invasive procedures, including image-guided beating-heart techniques, the aim of the present study was to test the clip's performance and short-term efficacy for treating MVP using open surgery in an animal model.

MATERIALS AND METHODS

Device Overview

The LPC is composed of a folded nickel-titanium alloy (nitinol) wire that is 0.45 mm in diameter. The device has a central loop and 2 sharpened ends distally (Figure 1, *A*). It has a closed resting state and can be opened to expose the sharpened tips and incorporate the entire prolapsed leaflet segment during implantation (Figure 1, *B* and *C*). For the current study, the clip measuring 11 mm in length and 3 mm in width in its resting state was used in all cases, except 1 where a larger clip was used. In its open state, the clip tips are approximately 6 mm apart, which defines the amount of leaflet tissue that is plicated. Clips can be manufactured in a range of sizes to plicate varying amounts of tissue. A specialized, hand-held deployment device was developed that engages the LPC and can open/close the device for implantation (Figure 1, *D*).

Device implantation involves the following steps (Figure 2, Video 1):

1. Open the LPC, which is mounted on the tip of the deployment device (Figure 1, *D*, *arrow*).
2. Direct the distal clip arms toward the belly of the prolapsed leaflet segment with the device oriented perpendicular to the leaflet hinge point.
3. Puncture the prolapsed segment midway between the leaflet hinge point and the free edge.
4. Advance the LPC until the proximal elbow abuts the leaflet tissue.
5. Close the LPC, which folds/plicates the involved leaflet tissue into the device.
6. Disengage the LPC from the deployment device. The clip remains in its closed state due to the shape memory of the nitinol material.

The clip that was used in this study does not involve the annular tissue. It solely plicates the leaflet tissue between the midbelly and the free edge of the leaflet. This positioning allows for leaflet plication without affecting annular geometry. Notably, the LPC can be removed and reinserted without causing significant leaflet trauma, thus allowing for repositioning in cases of suboptimal clip implantation.

Investigational Protocol

The experimental protocol was approved by the Boston Children's Hospital Institutional Animal Care and Use Committee (IACUC). All animals received humane care in accordance with the 1996 *Guide for the Care and Use of Laboratory Animals* recommended by the US National Institutes of Health.

Yorkshire female pigs (60-73 kg, n = 7) were anesthetized using intramuscular injection of telazol (4.4 mg/kg), xylazine (2.2 mg/kg), and atropine (0.04 mg/kg), and then intubated with a cuffed endotracheal tube and ventilated with a volume-control ventilator (Fabius Tiro; Draeger Medical, Andover, Mass). Anesthesia was maintained with inhaled desflurane (4%-9%). A transurethral urinary catheter was inserted for monitoring of urine output. Arterial and central venous lines were placed percutaneously in the left femoral artery and vein for arterial and central venous pressure monitoring, respectively. Electrocardiography and temperature monitoring were accomplished via esophageal and rectal probes, respectively. A right groin incision was made and the right femoral artery was exposed for arterial cannulation. After administration of intravenous cisatrocurium (0.1 mg/kg), a left posterolateral thoracotomy was performed through the fourth intercostal space. Stay sutures were placed in the pericardium to optimize access to the left atrial appendage, and a baseline two-dimensional (2D) and three-dimensional (3D) epicardial echocardiogram was performed. After intravenous heparin administration (300 U/kg) to achieve an activated clotting time of >350 seconds, arterial cannulation was performed via the right femoral artery using an 18F cannula. Venous cannulation was achieved via the right atrial appendage with a 34F straight, single-stage cannula. CPB was initiated using an oxygenator (FX25; Terumo Medical Corporation, Somerset, NJ). Fentanyl (50-200 μ/kg) and midazolam (0.2 mg/kg) were administered for anesthesia during CPB. The animals were cooled to 32°C, at which point the ascending aorta was crossclamped and cold cardioplegia solution (del Nido cardioplegia solution) was delivered in an anterograde fashion via the aortic root.[15] After cardiac arrest, the left atrial appendage was opened and suspended upward with stay sutures to expose the mitral valve. Valve competence was assessed by cold saline injection. Then primary marginal and secondary chordae tendineae supporting the P2 segment of the posterior mitral leaflet were cut, mimicking chordal rupture and MVP/flail. MVP was confirmed with repeat cold saline injection, after which the left atrial appendage was closed. The animals were rewarmed, the heart was deaired, and the aortic crossclamp was removed. After weaning off CPB, repeat 2D/3D epicardial echocardiography was performed to document valve function. The animals were then placed back on CPB and cooled to 32°C. The ascending aorta was again crossclamped and the heart was arrested in the same manner as before. The left atrial appendage was reopened, and after examining the prolapsed P2 segment, the LPC was applied under direct vision to repair the prolapse. Repeat cold saline injection was administered to assess device position and valve competence. The left atriotomy was then closed and the animals were rewarmed. After deairing, the aortic crossclamp was removed, the animals were weaned off CPB, and the cannulae were removed. 2D/3D epicardial echocardiography was repeated 2 hours after discontinuing CPB. The animals were then euthanized by intravenous injection of overdosed pentobarbital sodium (Fatal-Plus; Vortech Pharmaceuticals, Dearborn, Mich; 86 mg/kg). The heart was then excised and opened for direct inspection.

Echocardiographic Measurement and Analysis

Epicardial 2D and 3D echocardiograms were obtained at 3 time points: (1) before MVP creation, (2) after MVP creation, and (3) 2 hours after clip