

Transcatheter Chordal Repair for Degenerative Mitral Regurgitation

Current and future directions of therapeutic options for patients with degenerative MR.

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Surgical mitral valve repair (MVR) is the gold standard for treating patients affected by severe degenerative mitral regurgitation (DMR). In patients with functional mitral regurgitation (FMR), poor left ventricular (LV) function and comorbidities make the ideal treatment still a matter of debate. Transcatheter MVR (TMVR) technologies have emerged as an alternative to the conventional surgical approach and were first intended to treat high-risk patients. Nowadays, these technologies are growing and their potential allows them to be adopted as a valuable alternative to surgery in low- and medium-risk patients.¹

According to the targeted MV apparatus component, MVR devices for DMR can be classified as leaflet repair, direct/indirect annuloplasty, and chordal repair. This classification includes some overlap.²

Transcatheter chordal implantation using expanded polytetrafluoroethylene (ePTFE) sutures is an appealing technique that is supported by its success in conventional open heart surgery, conforming with the “respect rather than resect” principle in MVR.³ The transcatheter chordal repair panorama includes various technologies. Currently, the NeoChord system (NeoChord, Inc.) is leading the count with approximately 1,000 cases performed at the time of this writing, followed by the Harpoon system (Edwards Lifesciences) with 62 patients treated. Additional new technologies are currently under development, including Mitralis (Mitralix, Ltd.), V-Chordal (Edwards Lifesciences), ChordArt

(CoreMedic), Polares (Polares Medical), and MitraPatch (Chawla Heart Technologies, LLC). These technologies are further discussed in the following sections.

NEOCHORD SYSTEM

Transapical off-pump MVR with NeoChord implantation is performed with the NeoChord DS1000 system using two-dimensional (2D) and three-dimensional (3D) transesophageal echocardiographic (TEE) guidance for prolapse and/or flail treatment of the anterior and/or posterior mitral leaflets (Figure 1A).⁴⁻⁶



Figure 1. The NeoChord DS1000 system (A) and its application on mitral posterior leaflet through transventricular access (B). The Harpoon device (C).

A left lateral minithoracotomy is performed and the LV access site is identified 2 to 4 cm posterolateral from the apex to be aligned with the middle of the virtual line passing between the papillary muscles (more posterolaterally than in transapical transcatheter aortic valve repair to maintain physiologic behavior of the implanted chords and to avoid anterior leaflet apparatus damage). After ventriculotomy, the NeoChord DS1000 device is inserted in the left ventricle, and TEE imaging is used to guide the device to the affected leaflet and implant the neochordae (Figure 1B). The neochordae are then tensioned under direct TEE control and secured to the LV epicardium using Teflon pledgets.⁷

The NeoChord system has been shown to be safe in terms of intraoperative adverse events, with low morbidity and mortality rates.^{4,5} In addition to the nearly 1,000 patients treated with the NeoChord system, an ongoing investigational device exemption pivotal trial is currently enrolling subjects to compare the NeoChord system with conventional MVR in a randomized controlled trial design. A recent European multicenter study with the largest cohort analyzed ($n = 213$) confirmed high procedural success (96.7% patients with mild or less residual MR after successful placement of ≥ 2 neochordae), with a 1-year follow-up overall survival of $98\% \pm 1\%$ and freedom from composite endpoints (major adverse cardiac events) of $84\% \pm 2.5\%$ (reduction in MR severity and improvement in New York Heart Association functional class).⁸ An additional study has been performed that specifically evaluates procedural reproducibility and learning curve requirements.⁹ The actual incidence of 1-year patient failure was 11% (12 of 112 cases), with a cluster of failures within the first 20 cases. The CUSUM analysis demonstrated an initial learning curve; however, the upper boundary (alarm line) was never crossed. The reassurance line was first crossed after 40 procedures and performance remained stable after 49 procedures, demonstrating that the procedure reached the point of being technically standardized and reproducible.

Currently, there is open debate regarding the selection of feasible and ideal patients for the NeoChord procedure. This procedure has been proven as a viable alternative to conventional surgery for a subset of patients with MR in an early phase when the disease is limited to the leaflets and does not extend to the annulus and/or left ventricle.¹⁰ NeoChord repair positively influences MV geometry immediately and at short-term follow-up in patients with isolated posterior leaflet disease (LV volume and annulus diameter) and demonstrates subsequent significant MR reduction.¹¹

TABLE 1. MITRAL VALVE MORPHOLOGY ACCORDING TO DISEASE CLASSIFICATION

Type A	Isolated central posterior leaflet prolapse/flail
Type B	Posterior multisegment prolapse/flail
Type C	Anterior, bileaflet, or paracommissural disease with or without leaflet and annular calcifications

The leaflet-to-annulus index (LAI) is a standardized index that identifies the quantity of overriding leaflet that is predictive of the final coaptation length after the procedure. It significantly correlates with a residual MR of less than mild at 1-year follow-up when the LAI is > 1.2 .^{12,13} As recently reported, patients with a lower LAI (1.1–1.2) presenting with isolated central/P2 segment disease, might also undergo a successful NeoChord repair when a more anterior ventricular access is used.¹⁴ This access modifies the working angle of the posterior leaflet, stretching it below the anterior leaflet and thereby increasing the potential leaflet coaptation.¹⁴ In patients with multisegment, posterior leaflet disease, special consideration must be given to the LV access site because of the potential for a problematic chordal interference of the implanted chords with the native chords of the anterior subvalvular apparatus.

MV morphology according to disease classification (Table 1) is another parameter that affects residual MR.^{4–8} Early results show significantly better overall outcomes in type A and B patients when compared to type C,⁸ as well as results observed in conventional MVR surgery. As patient selection criteria for the NeoChord procedure are becoming more well established, we estimate that approximately 25% of patients presenting with DMR can be safely and effectively treated with an isolated NeoChord procedure. This percentage will likely increase significantly in the future when the new American College of Cardiology/American Heart Association/European Society of Cardiology guidelines are strictly followed, ensuring an early stage MVR before the occurrence of secondary annular dilatation. In addition to a second-generation transapical system that will incorporate a dedicated ventricular sheath, development of a transseptal access system is in progress.

HARPOON SYSTEM

The Harpoon TSD-5 device is a 10-F external diameter transcatheter system proposed for the implantation of artificial neochordae under 2D/3D TEE guidance

(Figure 1C). It uses a minimally invasive transapical technique similar to the NeoChord DS100, but unlike the NeoChord procedure, its use is currently under investigation and limited to use in posterior leaflet disease. Compared to NeoChord, Harpoon is inserted through a more anterior ventricular access site. After identification of the target site on the prolapsing leaflet, the device is stabilized and then activated. A specially designed 21-gauge needle wrapped with 50 ePTFE coils in a preformed knot configuration perforates the leaflet. A double-helix ePTFE knot is formed on the atrial side of the leaflet, securing the associated pair of artificial ePTFE chords to the leaflet. The device is then removed from the ventricle, and the chordae are exteriorized outside the apex. The desired MV coaptation is achieved by tensioning of all the chordae at the same time under TEE guidance. The chordae are secured on the epicardial side of the ventricular access site in a similar fashion as in the NeoChord procedure.¹⁵

The clinical experience consists of a prospective multicenter study involving 30 consecutive patients. Successful implantation of chords with MR reduction to moderate or less was met in 27 of 30 (90%) patients at 1 month. Three patients required conversion to open repair. There were no intraoperative deaths.

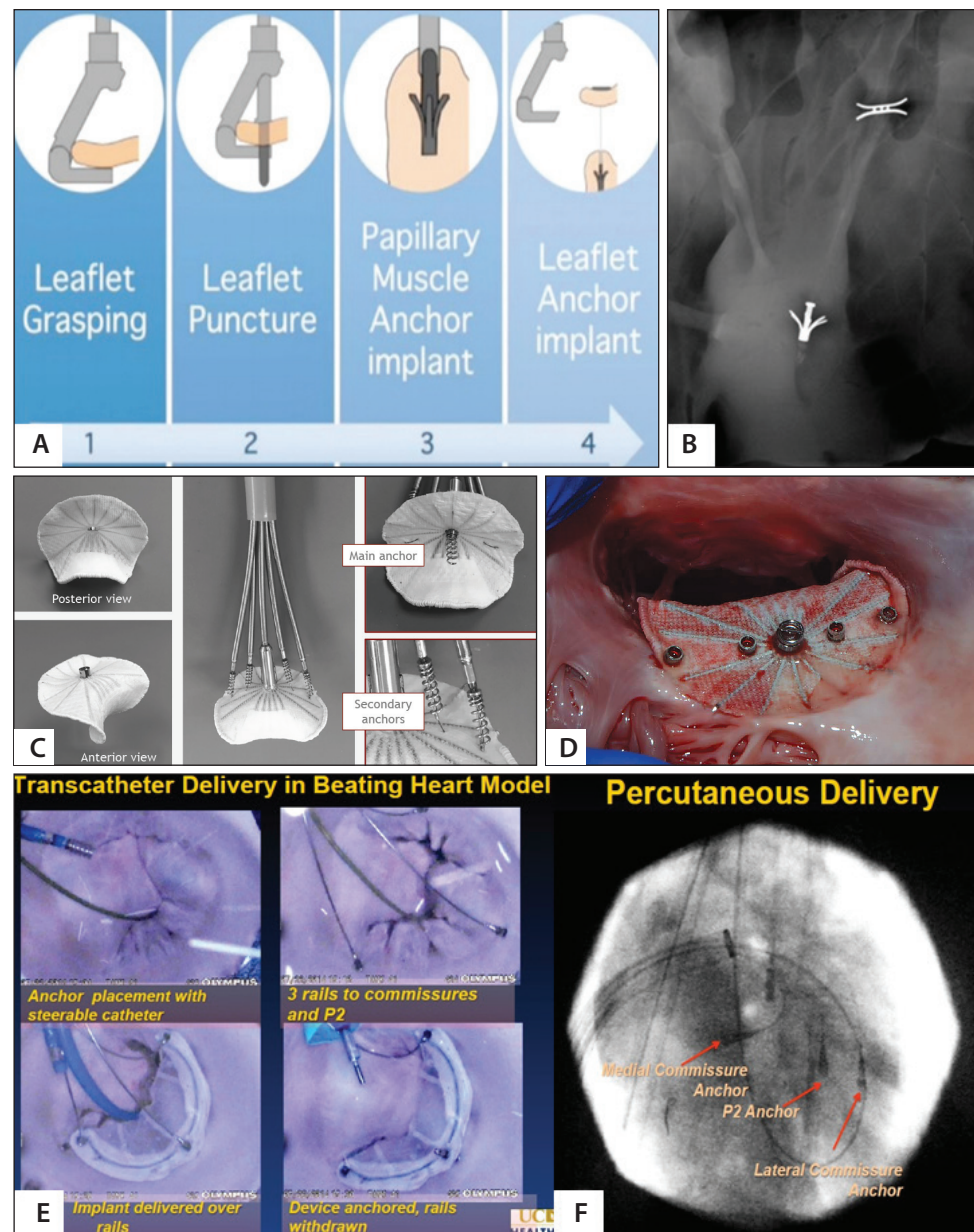


Figure 2. The ChordArt device and steps of its use (A). Cardiac fluoroscopy showing ChordArt final implantation (B). The Polares device (C) and ex vivo mitral positioning (D). Steps of Polares transcatheter delivery (E) and fluoroscopic final result of Polares implantation (F).

At 6 months, MR was mild or less in 85%, moderate in 8%, and severe in 8%. There was also a significant reduction of LV diameter and annular dimensions.¹⁶ The total clinical experience includes 62 total cases, but recently, the company temporarily paused the program indicating a need to refine the device design and procedure workflow based on a higher than expected rate of failure at 1-year follow-up. This technology should be available again by 2019.

MITRALIS DEVICE

Mitralis is a concept-stage device that utilizes an annuloplasty anchoring device and extensions anchored on the LV wall. A tissue matrix is then positioned between the annular member and the LV anchor, draping over the native leaflet of the MV. This system overlaps two of the classifications and is both an annuloplasty and chordal repair device.² No published reports are available at this time.

V-CHORDAL ADJUSTABLE ARTIFICIAL CHORDAE SYSTEM

V-Chordal is an open surgery device and is anticipated to be adapted for a transfemoral procedure, but is still in the concept phase. It allows accurate and reliable on-pump chordal implantation and off-pump length adjustment through transatrial access. The device is inserted through a left atrial root incision, crosses the MV, and reaches the papillary muscle where the chordal loop is anchored. Gore-Tex neo-chordae (Gore & Associates) are then sutured onto the prolapsing leaflet scallop, and the heart is restarted and weaned from extracorporeal circulation, leaving the device implanted. This system allows the surgeon to adjust the chordal length and fine tune the leaflet coaptation on a beating heart. Surgical feasibility has been demonstrated in six patients in a European study, and four of them completed 1-year follow-up. A clip-attaching mechanism is under development to allow transfemoral access instead of a minithoracotomy left atriotomy approach.

CHORDART SYSTEM

ChordArt is a transcatheter mitral repair system with a sutureless neochordal device that has been designed from its inception to enable transseptal delivery. The preclinical in vivo validation has been completed, with an animal study in five adult swine and five adult sheep. Direct atrial access is used on the beating heart to achieve mitral leaflet grasping and puncturing. The distal anchoring mechanism is then delivered into the posterior papillary muscle under echocardiographic and fluoroscopic guidance. The leaflet anchor is deployed, restoring normal valve coaptation (Figure 2A and 2B).

At necropsy, the location of the valvular implant was within a few millimeters of the leaflet-free boundary without any leaflet lesion or side effects observed. In the long-term survivors (180 days), no inflammatory response or chordal dehiscence was detected.¹⁷ The first-in-human prospective multicenter European trial was initiated in 2018 to validate the safety and

effectiveness of the ChordArt therapy. The low-profile transfemoral platform is designed for reduced implantation complexity and improved safety, and it is under validation.

POLARES DEVICE

Polares is a combination device that serves several functions, including annuloplasty, leaflet repair, and chordal support, with the implantation of a posterior neoleaflet to restore leaflet coaptation in either FMR or DMR. A dual layer of ePTFE is directly implanted over the existing posterior leaflet through a Dacron annular ring, and PTFE felt is used for ventricular attachment (Figure 2C–F). Surgical implantation has been performed in animals, and the transcatheter treatment is under development.² The first-in-human procedure is expected to be performed in 2019.

MITRAPATCH DEVICE

The MitraPatch device consists of a multichordal apparatus cut from a single sheet of ePTFE. Each patch has a papillary muscle section (neomuscle), four chordae that extend from this single muscle section, with each chord having an expanded leaflet section (neoleaflet). The hemodynamic efficacy of repairing mitral prolapse and regurgitation was assessed in a porcine animal model at 30-day echocardiographic follow-up, showing minimal to mild MR.¹⁸ Each neochord can support either the anterior or posterior leaflet and has an expanded neoleaflet section to support the site of insertion in order to reduce the risk of stress concentration imposed by individual neochordal loops.¹⁹ Transcatheter technology is currently under investigation.

CONCLUSION

Development of TMVR procedures to treat DMR is unstoppable and represents an extremely appealing therapeutic option to target low- and high-risk patients based on the proven safety profile of the most commonly used commercial device. Currently, limits to this technology are due to the lack of long-term clinical data in a large number of patients and by a higher rate of asymptomatic moderate recurrent MR when compared to conventional surgical treatment.²⁰ To improve the acceptance of the current technologies and platforms, it is necessary to continue to investigate the processes of patient selection and approximate current surgical standard approaches through the development of combined procedures with chordal/leaflet repair plus annuloplasty repair to increase the pool of treatable patients. Moreover,

it would be appropriate and necessary to standardize the MR assessments to improve comparisons between surgical and transcatheter solutions. It would also be important to understand the true impact of residual moderate MR on asymptomatic patients in the early stage of the disease. A final practical consideration is the economic feasibility of the use of multiple devices to perform a surgical-like, TMVR within current reimbursement schedules. ■

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