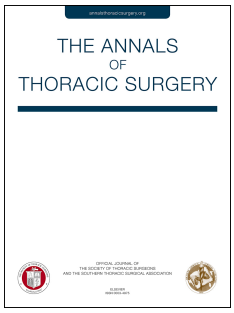

Automated Implantation of Artificial Mitral Chords: Preliminary Results from the Feasibility Trial

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PII: S0003-4975(19)31425-0

DOI: https://doi.org/10.1016/j.athoracsur.2019.08.037

Reference: ATS 33059

To appear in: *The Annals of Thoracic Surgery*

Received Date: 24 February 2019

Revised Date: 12 July 2019

Accepted Date: 8 August 2019

Please cite this article as: Weber A, Rucinskas K, Janusauskas V, Zakarkaite D, Zuber M, Vogel R, Carrel T, Automated Implantation of Artificial Mitral Chords: Preliminary Results from the Feasibility Trial *The Annals of Thoracic Surgery* (2019), doi: https://doi.org/10.1016/j.athoracsur.2019.08.037.

Automated Implantation of Artificial Mitral Chords:

Preliminary Results from the Feasibility Trial

Running head: Automated mitral chords implantation

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Word count: 2500

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Abstract

Purpose. A novel chordal system enables automated implantation of artificial mitral chords to treat mitral regurgitation (MR). This paper summarizes the “first-in-man” initial clinical results.

Description*.* The CHAGALL trial is a single arm, multi-center, prospective study to test the feasibility of this system for mitral repair. The interim clinical and echocardiographic results of the first 5 patients with a 12 months follow-up are presented.

Evaluation. Five patients (mean age 64 years) with severe MR received implantation of neochords with this device under cardiopulmonary bypass. Technical success was obtained in all patients. TEE showed either no or trace residual MR (<1+/4+) following repair. Survival at 30 days was 100% and no device-related complication occurred. Reduction of mitral regurgitation was sustained up to 12 months.

Conclusions. This novel chordal system is promising because it greatly facilitates the deployment of neochords to repair the mitral valve. Results at 12 months are encouraging. The device is currently under development for transcatheter approach.

Technology

Surgical repair of the mitral valve (MV) represents an established treatment of severe degenerative mitral regurgitation, with superior outcomes over valve replacement (1,2). However, the rates of MV repair are highly variable, with less successful repair rates in low-volume centres (3). Different techniques allow excellent results in term of efficacy and durability, but largely depend on valve anatomy and surgeon preference. Among them, the implantation of e-PTFE neochords has been associated with excellent long-term outcome (4-7). Nevertheless, a simple and standardized technology allowing a significant increase of valve repair especially in low-volume centres and for high-risk patients is welcome. The ChordArt® system (CoreMedic, Radolfzell, Germany) has been designed for quick and reliable implantation of artificial mitral chords to treat degenerative MR through a standard sternotomy, a less-invasive surgical or even a transcatheter approach. Feasibility, safety and efficacy of the ChordArt System are under clinical investigation in the First-in-Man prospective CHAGALL (CHordArt system study for the treatment of mitral ReGurgitAtion due to leaflet proLapse or fLail) trial (NCT03581656).

Technique

The ChordArt is a single-use, hand-held device designed for placing artificial neochords in an antegrade way to restore optimal coaptation of a prolabing mitral leaflet. The delivery system is designed to deploy the pre-loaded implant in a stepwise mode, advancing the 1.5 mm needle tip through the leaflet into the papillary muscle.

ChordArt® consists of the delivery system (Figure 1) and the Implant (Figure 2). The Implant is pre-loaded in the system and consists of 3 components: the proximal anchor (for leaflet anchoring), the cord (ePTFE suture) and the distal implant (papillary muscle anchor). The distal anchor is a two-pieces assembly consisting of the crown pressed on the collet. The anchors are made of nickel-titanium alloys connected with a prefabricated cv5 ePTFE chord (size ranging from 10 to 30 mm length in 2 mm steps) that is commonly used as cardiovascular implant.

The appropriate size is identified using 3D-echocardiography and confirmed by intraoperative measurement (Figure 3).

Additional informations on the device/implant and operative technique are described in the Supplementary file. The target prolapsing segment is identified and grasped with the ChordArt® device. After confirmation of stable leaflet grasping, puncture of the leaflet is performed with the needle tip of the system. Thereafter, the target papillary muscle is localized and the tip of the Chordart® guided towards it. The papillary muscle is punctured at his fibrotic tip and the distal anchor delivered (Figure 4). If multiple chordae are required, the steps are repeated. Valve repair is completed with annuloplasty or further leaflet repair. Figure 4 shows implantation and Figure 5 depicts pre- and postoperative echocardiography.

Clinical Experience

This is an interim analysis of the first 5 patients with protocol-specified clinical and echocardiographic follow-up conducted at 30-days and 3, 6 and 12 months to support European market conformity (CE). The protocol was approved by the national authorities and the ethics committee. All patients provided written informed consent.

Primary safety endpoints are freedom from death and major adverse events (MAE) at 30 days. Primary efficacy endpoints are technical success (absence of MAE, successful deployment and retrieval of the device, no need for re-intervention until end of the procedure) and device success (MR Reduction > 1 grade from baseline assessed at 30 days). The study is conducted according to the guidelines of the Mitral Valve Academic Research Consortium (MVARC) as well as International Standards Organization (8).

Serious adverse events (SAEs) were reported and adjudicated by a data safety and monitoring committee of independent physicians. Monitoring, collection of data and initial data analysis were performed by the sponsor.

Patients underwent protocol-directed pre-operative trans-oesophageal 2D and 3D echocardiography. MR severity was quantified using semi-quantitative and quantitative assessment by an independent Core-Lab that also assessed postoperative echocardiography. Anatomical feasibility was determined by an independent steering committee. Main exclusion

criteria were: commissural lesion, anterior or bileaflet prolapse, functional MR, severe calcification, concomitant aortic or tricuspid disease requiring treatment and myocardial revascularisation.

Five consecutive male patients (range from 47 to 76 years) with severe degenerative MR (STS score 0.67% (range 0.31-1.22%) underwent MV repair and received neochords implantation with this device. Characteristics are summarized in Table 1.

Four patients received 2 ChordArt® Implants, while one patient received 1 implant. In one case, initial implants were removed and replaced with two longer implants without any complications. Single ChordArt® implantation ranged from 1 to 5 min. In all cases the device was successfully deployed and the delivery system retrieved as intended to use.

No intraoperative adverse event was observed. After weaning from CPB, TOE showed no or trace residual MR (<1+/4+) in all patients (Figure 5). Discharge echocardiography confirmed these results in all patients (Table 2).

Survival was 100% until 12 months and no patients experienced any MAE. Primary safety endpoints were achieved in 5/5 patients (100%). Four adverse events were observed during the hospitalisation; atrial fibrillation (n=2), respiratory infection (n=1) and convulsion after extubation (n=1).

At the time of the present report, all patients have reached 1 year follow-up. Echocardiography confirmed stable results of the MV repair, with all patients showing no or trace MR (<1+/4+). CT scan was performed at 1 month after the procedure and showed proper position of the implant (Figure 6).

Comment

This study demonstrates early feasibility of an automated ePTFE neochords implant system. Recently, MV repair using neochords has received more attention because of a shift from resection to more conservative approach of prolapsing leaflets ("respect instead of resect" strategy) (9). Our data show that implantation of ePTFE neochords with the ChordArt® System achieves very satisfactory early results comparable to those obtained with neochord loops that we have used since many years. In all cases, the lesion was repaired as planned, with no significant residual MR. In contrary to other devices (Mitra-Clip, Cardioband) the "foot-print" left by ChordArt® on cardiac structures is minimal and allows uncomplicated further repair or replacement.

The choice of the proper length of a neochord is critical and needs careful assessment of the papillary muscle to annulus distance. Pre-operative sizing of the optimal chordal length using transesophageal echocardiography has improved the standardization of the techniques even in less experienced hands.

Two different devices have been used so far. The NeoChord is a beating-heart system that uses adjustable PTFE sutures through a transapical approach. It enables support of the free edge of the leaflets with real-time adjustment of the chordal length. The device obtained CE mark in 2012 and has been used in over 600 patients (5-6). The efficacy in reducing MR clearly depends on the complexity of the lesion. One-year freedom from composite endpoints was 94% in simple anatomy but lower in more complex cases.

The Harpoon device (Edwards Lifescience, Irvine, USA) has been investigated in an early feasibility trial in posterior prolapse (7). It is a 14 Fr device that allows transventricular implantation of multiple PTFE chord with subsequent echo-based adjustment of the length. It differs from the NeoChord since leaflet anchoring occurs with a preformed knot instead of free-edge leaflet fixation. Among 30 patients reported in the initial feasibility trial, three required conversion to mitral surgery. At one month, MR was mild or less in 89% (24/27) and moderate in 11% (3/27). At six months, MR was mild or less in 85% (22/26), moderate in 8% (2/26), and severe in 8% (2/26).

The major difference between ChordArt and these two technologies is the access (left atrium versus left ventricle) and the fact that ChordArt is anchored anatomically and not close to the left-ventricular apex.

MRI simulations in healthy volunteers have shown that ChordArt neochords anchored into the papillary muscles mimick the real anatomy. This approach should be preferred to the left ventricular apex, since it is associated with a reduced risk of leaflet tears, residual prolapse and incidence of systolic anterior motion (10).

MV repair with the ChordArt® System is safe, simple and allows effective reduction of MR in the short-term. The safety and effectiveness of the ChordArt therapy needs further validation on a larger patient population. A fully transcatheter system represent the natural evolution of the technique and will be available soon.

Disclosures and Freedom of Investigation

The authors received no funds for the conduct of this study. The material used for the patients was generously donated by Coremedic company to the users.

All authors had complete freedom of investigation as well as full control of the design of the study, methods used, outcome parameters, analysis of data, and production of the present written report.

Disclaimer: The Society of Thoracic Surgeons, The Southern Thoracic Surgical Association, and The Annals of Thoracic Surgery neither endorse nor discourage the use of the new technology described in this article.

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Figure Legends

Figure 1. The ChordArt device consists of four major components, the handle, the trigger, the shaft and the needle tip. The delivery system is used to advance the needle tip through the valve leaflet at the site of the planned leaflet anchoring, down to the papillary muscle.

Figure 2. The ChordArt implant (A) consists of three major components: the proximal implant (nitinol pledget for leaflet securement), the chord (ePTFE suture) and the distal implant (papillary muscle anchor). The distal implant is a two-piece assembly consisting of the crown pressed on the collet. Panel B shows the final aspect of the neo-implanted chord, fixed proximally to the leaflet and distally to the papillary muscle.

Figure 3. TEE images showing a pre-procedural mitral valve 3D surgical view highlighting posterior leaflet flail (A), a 3D calculation of the expected implant length between posterior leaflet and the head of the papillary muscles (B), a post-procedural mitral valve 3D surgical view highlighting the leaflet coaptation restoration.

Figure 4. Intraoperative view during implantation of a mitral chord. Proper localization of the site on the leaflet (A), punction of the posterior leaflet 3-4 mm from the free edge with the delivery device (B) and inspection of the leaflet following retrieving of the delivery device (C) with the proximal implant deployed on the leaflet.

Figure 5. Echocardiographic assessment before (A) and after mitral repair using the ChordArt system: before discharge (B), at one month (C) and 6 months (D) follow-up.

Figure 6. Computerized Tomography at 1 month follow-up of two implanted ChordArt® systems in a reconstructed 2-chamber view showing minimal footprint and proper positioning of the implants (A), including the proximal implant anchors (B) and the distal implant anchors (C).

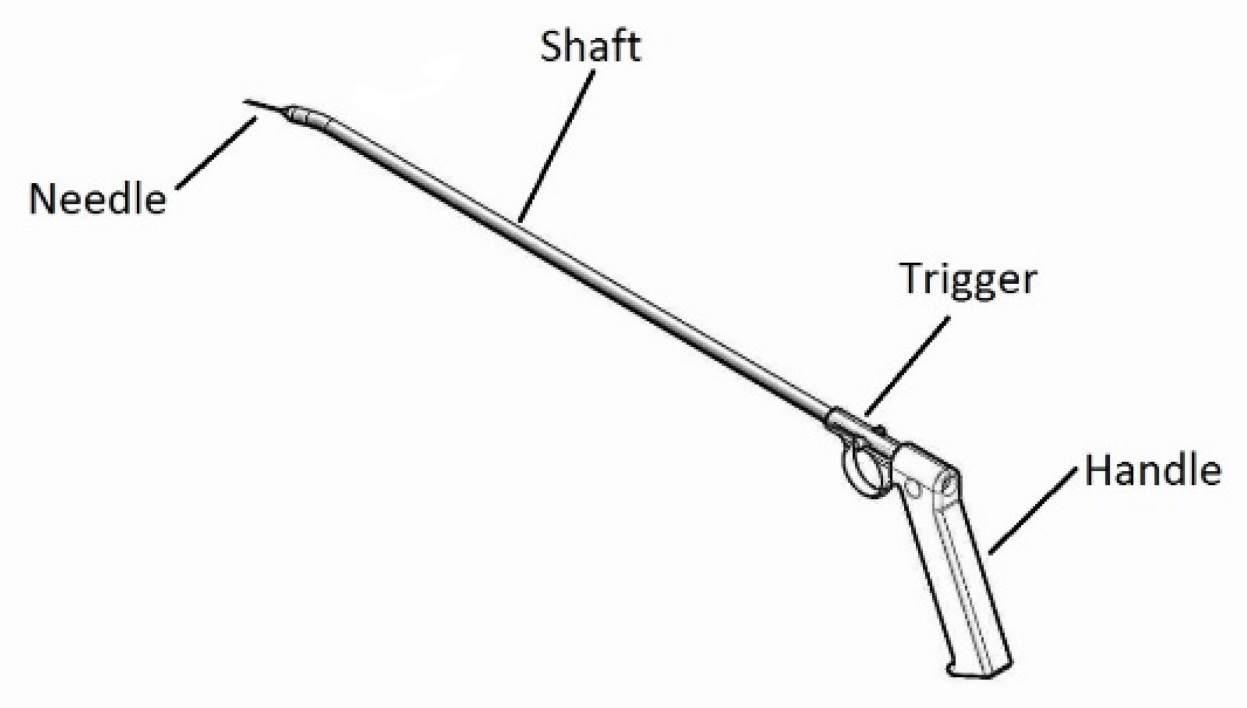
Table 1. Pre-operative characteristics of the 5 patients

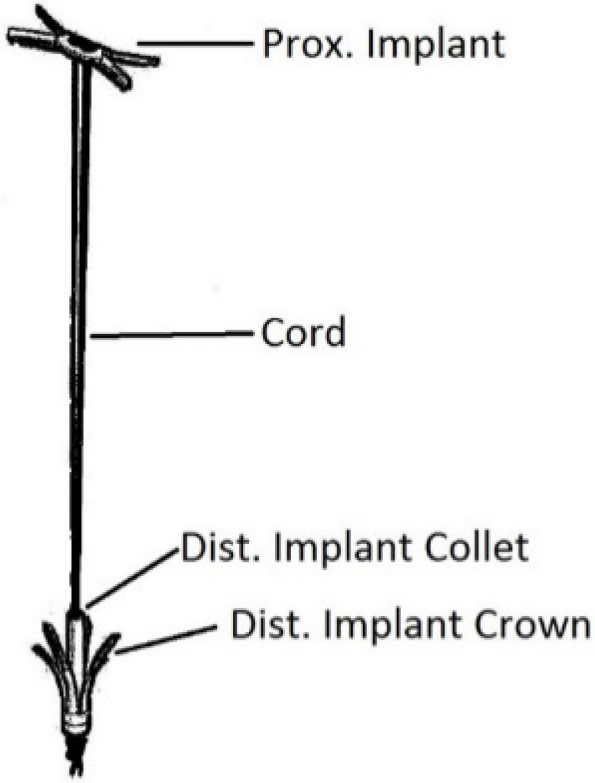
Pt ID	Age	STS score (%)	LVEF (%)	sPAP	LV internal diameter in end systole (LVIDs - cavity size) (mm)	LV internal diameter in end diastole (LVIDd - cavity size) (mm)	Additional pathologies	NYHA class
1	59	0.315	55	40,67*	45	65	Paroxysmal AF	II
2	64	0.477	61	41	38	57	Paroxysmal AF Hypertension	II
3	76	1.223	65	49	41	64	Hypertension Mildly dilated aorta (4.4cm)	II
4	47	NA	62	40,7*	41	60	-	III
5	68	0.654	55	32	40	61	History of PCI LAD stented in 2016, RCA stented in 2018) Hypertension	II

* Estimated value by average imputation
NA= Not Available

Table 2. Intra-operative data

Pt ID	# of chords used	Residual MR	Overall procedure time (min)	Time of Atrial Access (min)	Time of device retrieval (min) from atrium (min)	Time of atrium closure (min)	Chordae Implant time (min)			
							1st	2nd	3rd	4th
1	2	None	142	60	35	47	2	3	-	-
2	2	Trace	141	24	60	57	1	5	-	-
3	2	Trace	74	25	27	22	1	2	-	-
4	1 (1 chord, too short, removed)	None	135	40	70	25	2	-	-	-
5	2 (2 chords implanted and removed,replaced with 2 chords of another size)	Trace	200	70	88	42	3	1	1	3




Prox. Implant
Cord
Dist. Implant Collet
Dist. Implant Crown