Transapical endovascular implantation of neochordae using a suction and suture device

Francesco Maisano a,*, Iassen Micheva, Stanton Rowe c, Alessandro Addis b, Marino Campagnola a, Andrea Guidotti a, Antonio Colombo a, Ottavio Alfieri a

a San Raffaele Cardio-Thoracic and Vascular Department, Milano, Italy
b Veterinarian Medicine School, University of Milan, Italy
c Edwards Lifesciences LLC, Irvine CA, USA

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Abstract

Objective: Neochordae implantation is a standard method for treatment of mitral valve prolapse. We describe a transcatheter technology enabling transapical endovascular chordal implantation. Methods: Six adult pigs were anesthetized. Two 10F sheaths were introduced in the femoral vessels for monitoring and intracardiac echo. After midline sternotomy, the pericardium was opened, the apex was punctured inside two 2—0 polypropylene purse strings. A 0.035 in J tipped guidewire was introduced in the left ventricle and an ultra stiff 14F sheath (guide catheter) inserted through the apex. A suction-and-suture device was introduced in the left ventricle. The mitral valve was crossed under echo guidance. Using suction, either the anterior (two cases) or posterior (four cases) leaflet was captured and a loop of 4—0 polypropylene was thrown at the edge of the leaflet. The loop, with a pledget, was exteriorized through the introducer. The introducer was removed and the purse-string tied. Under echo guidance, the neochordae suture was pulled and tied over a pledget to evoke leaflet tethering. The animals were sacrificed and gross anatomy reviewed. Results: Leaflet capture was feasible in the intended location in all cases. Following suture tethering, variable degrees of MR were obtained. At gross anatomy, the neochordae were positioned at 1—4 mm from the leaflet free edge, and were firmly attached to the leaflets. Conclusions: Transcatheter endovascular neochordae implantation is feasible. A prolapse model is needed to further demonstrate feasibility under pathologic conditions. The apical approach allows easy and direct route to transcatheter beating heart minimally invasive mitral repair.

Keywords: Mitral valve regurgitation; Transcatheter valve repair; Valve repair; Beating heart; Minimally invasive surgery; Transapical approach

1. Introduction

Mitril repair is the standard treatment of chronic mitral regurgitation with more than 40 years of accumulated experience [1]. Current surgical results are excellent, with numerous techniques available to treat a large range of lesions. Early intervention is considered in most younger patients because of the potential of recovery of normal life expectancy and to avoid the risk of developing hemodynamic consequences of the chronic volume overload [2]. However according to Euro Heart survey [3], about 50% of symptomatic patients affected by severe mitral regurgitation are not undergoing surgery for a variety of reasons. Elderly patients have a higher surgical risk; therefore intervention is often denied or delayed until more severe symptoms develop. On the other hand, younger patients could be reluctant to undergo surgical repair due to the invasiveness of the procedure and the significant recovery time. Under these circumstances, endovascular approaches are being evaluated to offer a minimally invasive solution to make the treatment more acceptable to younger patients and to reduce the risk of the procedure in elderly individuals or in presence of comorbidities.

We describe a preclinical experience with a totally endovascular method of neochordae implantation using a suture based catheter, and an echo-guided approach.

2. Methods

Six domestic pigs were operated upon at the Veterinarian Lab of the University of Milano. All animals were treated in accordance with policies and principles of good laboratory practice for animal care and with the European Union guidelines (86/609/EEC) approved by the Italian Ministry of Health (Law 116/92). The study was reviewed and approved by the institutional ethics committee [4]. Animal weight was variable between 70 kg and 90 kg, aging about 6 months. All the animals were stabilized 7 days...
before the operation and monitored from the physical—
chemical viewpoint.

2.1. Anesthesia and monitoring

Prior to surgery, the animals were premedicated with midazolam (0.5 mg/kg), ketamine (10 mg/kg) and atropine 1 mg, intramuscular, followed by orotracheal intubation under general anesthesia with a mixture of oxygen and sevoflurane at 8%. Anesthesia was maintained for the whole duration of the operation with a mixture of oxygen and sevoflurane at 4%, plus fentanyl (40 mg/kg/h i.v.). Postoperative analgesia was provided with ketorolac (1 mg/kg IM). A peripheral venous access was obtained from the ear. The pig was placed on the operating table in supine position to gain inguinal access. The legs were pulled laterally and caudally to optimize groin exposure. Using percutaneous Seldinger technique, a 6F arterial sheath and a 10F venous sheath were introduced in the femoral vessels, and secured in place. Since the femoral vessels of the animal are relatively deep from the skin surface, long sheaths were used to avoid inadvertent loss of access. Heparin 5000UI were administered following introduction of the sheaths. An 8F intracardiac echocardiographic catheter (Acunav, Siemens Medical Solutions, Montain View, CA, USA) was then advanced in the right atrium under fluoroscopic guidance and connected to a Cypress echocardiograph (Siemens Medical Solutions, Montain View, CA, USA). The laboratory set-up is shown in Fig. 1.

Midline sternotomy was then performed and the pericardium was opened in an inverted T fashion and resuspended to the edges of the operative field to avoid heart luxation. Lidocaine 1 mg/kg was administered endoventously. Two concentric 2–0 prolene (Ethicon, Johnson & Johnson's, Somerville, NJ, USA) purse strings were performed at the apex. The left ventricle was then punctured and a 0.035 in. J tipped guidewire was introduced in the left ventricle. No fluoroscopy was used. An ultra stiff custom made, 20 mm, 14F sheath (guiding sheath) was inserted through the apex over the wire (Fig. 2). A 12F Mobius therapy catheter (Edwards Lifesciences LLC, Irvine CA, USA) was then introduced in the LV under intracardiac echo guidance [5].

The Mobius therapy catheter is an endovascular suture device designed to deliver a looped suture using suction to grab and stabilize the tissue while it is penetrated by two needles (Fig. 3). The tip of the catheter has a suction port, connected to high power suction line, which also incorporates a couple of needles and a catcher with an attached loop of 4–0 prolene with a Teflon pledget. The suction port is also connected to a pressure monitor to detect atrial, ventricular or intermediate pressure tracing and to guide the positioning of the device along the long axis of the heart. To grasp the leaflets, vacuum is activated while the suction port is facing the free edge of the target segment of the leaflet. Under echo guidance, the leaflet is grasped. Confirmation of tissue grasp is obtained by combination of leaflet movement restriction and by cessation of blood aspiration from the vacuum port, then the suture mechanism is actuated by pushing the needles through the tissue and into the catchers. The suture loop is then released from the catheter by pulling back the system.

Fig. 1. The set-up: The Echo Cypress machine is shown on top of the pressure monitor. On the side, the vacuum canister is placed in a visible spot to monitor blood flow during leaflet capture. Leaflet capture is confirmed by the restricted motion at echo and by cessation of blood flow into the canister.

Fig. 2. The apex is exposed through midline sternotomy. A 2–0 polypropylene purse string with pledges is used to seal the access. The stiff introducer guide is shown.
The capture and suture of the central portion of the posterior leaflet (P2) and of the anterior leaflet (A2) was attempted in four and two animals, respectively. The Mobius catheter was advanced into the left atrium, under echo guidance, avoiding entanglement into the subvalvar apparatus. The catheter was manipulated using the guiding sheath (Fig. 4). No guidewire was left in place. Mobius catheter suction port was oriented with the open window towards the target segment of the leaflet using echo guidance and pressure monitoring (Fig. 5). Once pressure tracing was showing an intermediate pressure pattern between the ventricular and the atrial tracing, vacuum was activated and leaflet grasped. The two needles were activated and penetrated the leaflet. Vacuum was then terminated and the device was pulled back to release the suture. The device was exteriorized to release the entire suture and the suture was tethered. Satisfactory suture placement was checked under echo guidance by demonstration of tethering of the captured segment and visualization of the pledget (Fig. 6). The 14F guiding sheath was then removed and the purse strings were tied. Under echo guidance, the looped suture was tethered to varying degrees to demonstrate a positive action of the neochordae on the leaflet motion and valve function (Fig. 7). The suture was then tied on the apex, at the maximum tethering and the animal survived for 1 h. Thereafter, the animal was sacrificed and the heart was inspected to check neochordae insertion and function.

Data are presented as mean ± standard deviation.

3. Results

Leaflet capture was feasible in the intended location in all cases. Blood loss relative to capture (collected in the suction canister) was 86 ± 98 ml. In all animals it was possible to demonstrate segmental restriction of movement and increasing degrees of mitral regurgitation jets at Doppler echocardiography, proportional to the degree of tethering. Neochordae
length titration was easily feasible, and echo guidance was a reliable method to guide the procedure. All animals survived at 1 h after the neochordae implant, but dobutamine infusion was needed in four animals to support the hemodynamics. At post-mortem examination, the neochordae were positioned at −4 mm from the leaflet free edge, and were firmly attached to the leaflets. The chordae were correctly positioned in A2 or P2 in all cases (Fig. 8). No signs of tears from the leaflets were visible.

4. Discussion

In this model we demonstrated a method to implant and to accurately size the length of the neochordae in a totally endovascular and beating heart fashion.

Neochordae implantation is gaining acceptance as a preferable method to correct mitral valve prolapse [6—8]. The advantages of chordal replacement are numerous. It can be used to correct anterior posterior and bileaflet disease. Chordal replacement respects the anatomy of the prolapsing valve, and retains the full mitro-ventricular continuity. It does not reduce the surface of the leaflets, as compared to leaflet resection, hence it allows larger surface of coaptation at the end of the procedure. As a matter of fact, neochordae implantation is also being used during minimally invasive and even robotic assisted procedures [9,10].

The main limitation of the surgical implantation of neochordae is related to the challenge of determining the length of the chordae under cardioplegic arrest. A number of different techniques have been developed to overcome this limitation, including preoperative echo measurements, and intraoperative adjustments [10—15].

Endovascular leaflet repair has been attempted with two devices. One is the suction and suture Mobius catheter. It has been used to create a double orifice repair by suturing the free edge of the opposing leaflets and securing the loop using a fastener clip. The procedure has been described in the animal [5], but the clinical experience has been limited to date.

The endovascular edge-to-edge repair is currently under clinical trial in the US, using the Evolve MitralClip™ device [16,17].

Approaches using the double orifice technique are limited by the acceptance of the technique in the surgical tradition. Creation of a double orifice conformation of the valve is considered not physiologic, and mitral valve competence can be restored at the expense of a reduction of mitral valve orifice area.

Endovascular chordal replacement, similar to the surgical counterpart, offers the potential of an anatomical repair, which could be a critical issue in early treatment. Ideally, as predicted by Carpentier 35 years ago, in the future, using similar devices, mitral valve with initial lesions may be treated even in the absence of severe mitral regurgitation to obviate the need for future degeneration or need for more complex interventions [1].
**References**


**Appendix A. Conference discussion**

Dr M. Jahangiri (London, United Kingdom): Dr Maisano and colleagues describe endovascular implantation of neochordae in a pig model with a normal mitral valve. This is a continuation of some of the previous work on beating heart percutaneous mitral valve repair based on the Alfieri technique.
in an animal model. There have been other minimally invasive attempts at implantation of chordae for repair of the mitral valve, including mini-thoracotomy and robotic assistance. However, with these techniques, cardiopulmonary bypass and arrest of the heart is needed. Measurement of the chordae and its assessment can be difficult in an arrested heart. Maisano and colleagues have overcome these difficulties in their model, making measurement of the chordae easier. I have two questions for you.

You have used midline sternotomy. Why did you use this as opposed to a mini-antero-lateral thoracotomy to reach the apex? My second question: is blood loss a problem in your model? I look forward to the demonstration of this technique under pathological conditions.

Dr Maisano: Midline sternotomy is needed in the pig model because of the rotation of the heart, and if you would transfer this procedure to the human setting, this would be done under regular transapical access in the fifth or sixth intercostal space in a left thoracotomy in the mid subclavian line.

Answering the question of the lack of a pathological model, I have been working on several of these devices, and obviously this would be very useful to prove not only the concept but also the feasibility of the procedure itself. Unfortunately, this model is not available, and it is very difficult to obtain on most occasions. You may obtain a chordal rupture model, but this is still not a viable model for mitral valve prolapse, because then you will have only the chordal rupture but not the degeneration of the tissue in the area of the chordal rupture. These are the obvious limitations of this model, but the aim of the study was to demonstrate the feasibility of a minimally invasive off-pump chordal implantation with real-time sizing on neochordae.

Blood loss was not an issue in this experience since leaflet capture was quite straightforward, keeping blood loss to a minimum.

Dr F. Casselman (Aalst, Belgium): All clinical studies on degenerative mitral valve repair show inferior results if no ring is placed. Now, I understand that this is a first phase, but do you think that in the future if this happens to be clinically available it should be complemented with some ring device or with some coronary sinus device in order to stabilize results in the longer term?

Dr Maisano: I think there is no doubt about this. Obviously mitral annular enlargement happens, although later in the course of the disease. So you may imagine that if you treat patients earlier, you may be able to avoid annuloplasty. But I don’t think there will be any problem in the future to approach these patients with a more broad spectrum of devices, and with associated procedures. Unfortunately there are some regulatory issues which will make this solution unavailable in the next few years, but in the long term, there will probably be a solution like this.

Dr G. Lutter (Kiel, Germany): You have told us about the difficulties, on the one hand visualization, and on the other hand, an available ischemic mitral regurgitation model. I believe the Gorman brothers’ work in Philadelphia could connect nicely to yours. A nice ischemic model with induced myocardial infarction and a resulting moderate-severe degree of mitral regurgitation to perform your experiments in this sheep model would be very interesting.

Dr Maisano: Unfortunately, I don’t think this chordal replacement is going to be directed to ischemic patients. So what is lacking is a degenerative mitral regurgitation model, which can be done but is not really reproducing what we see in the patients today we operate on. Obviously if you imagine the evolution of these technologies in the future and an earlier implant of these devices or an earlier application of these procedures, that might be a new disease to tackle. So we need to be prepared for many other experiments in the future. But thank you for your suggestion.

Dr Lutter: But this technology might at least be used in primary and secondary MR, to varying degrees, as you told us. Is this correct?

Dr Maisano: Sure.

[h1]: forgot to answer to this question, if the editor wants to include this...

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**Editorial comment**

This paper [1] on experimental transapical chordal implantation describes an innovative approach for future mitral valve repair for patients with mitral valve prolapse. The idea for this approach is quite unique and may have been influenced by recent clinical experiences in transapical aortic valve implantation. The straight access and short distance from the apex to the mitral valve seemed to be advantageous when applied to the Mobius catheter system. This same group of investigators has tried to use the same Mobius system for transfemoral ‘edge to edge MV repair’ without convincing clinical success. The current large animal experimental results are very encouraging for two reasons: first, the technical challenge seemed to be less than that encountered through a transfemoral approach and second, chordal replacement represents a standard and long lasting repair technique for mitral valve prolapse.

It should be pointed out, however, that the current Mobius system provides a Prolene suture instead of a PTFE suture, which is the current gold standard for surgical neo-chordae construction. The authors are aware of this drawback which requires a change before clinical application can be implemented.

The transmural PTFE chordal insertion has been previously proposed from investigators from the Mayo clinic. First clinical results for this device, however, are still pending. The current surgical technique for chordal replacement favors an anchoring of the neo-chords at both papillary muscles, which is a relative constant distance even when left ventricular dilatation occurs. The transapical chord insertion technique would allow for precise chordal length adjustment under echocardiographic control. Long-term studies will also need to be performed to determine if re-remodeling of the dilated left ventricle will result in transapical neo-chords that are too long, and subsequent recurrent mitral regurgitation.

**Reference**


Friedrich Wilhelm Mohr
Heart Center, Leipzig University, Struempfelstrasse 39, 04289 Leipzig, Germany
*Corresponding author. Tel.: +49 341 8651421; fax: +49 341 8651452

E-mail address: mohrf@medizin.uni-leipzig.de

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