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ORIGINAL RESEARCH

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Device-based Therapy for Mitral Regurgitation and Ventricular Reshaping

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ABSTRACT

Background: A clinically effective treatment for functional mitral regurgitation (fMR) due to left ventricular (LV) remodeling may need to address both annular and LV dilation to improve symptoms of heart failure (HF). Here we describe the effects of a device intended to reduce mitral annular dimensions and also reduce the radius of curvature of the LV to improve function.

Methods: Patient 202–051 is a 79-year-old man with ischemic cardiomyopathy and 3-to-4+ fMR treated with guideline recommended HF therapies. Echocardiography showed an effective regurgitant orifice (ERO) of 0.36 cm^2, a regurgitant stroke volume of 69 ml, an LVEF of 14% and an LV diastolic diameter of 6.2 cm. The patient underwent percutaneous implantation of the Ancora Heart device which consists of a series of intramyocardial anchors connected via a cinching cable implanted into the LV free wall below the mitral annulus and behind the papillary muscles. Tension applied to the cable resulted in an acute ~15% decrease of the circumferential distance between the first and last anchors. Cinching was maintained with a locking mechanism placed at the end of the cable.

Results: Echocardiographic follow up performed over the course of 1 year showed that ERO decreased to 0.12 cm^2, regurgitant stroke volume to 23 ml, LV dimension to 5.6 cm and EF improved to 34%. ntPro-BNP decreased from 3440 to 1450 pg/ml.

Conclusion: These findings provide proof-of-concept that a percutaneously deployable, sub-valvular intramyocardial implant that cinches the myocardial wall below the mitral annulus has the potential to reduce the severity of fMR and improve LV function.

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KEYWORDS Heart failure; medical devices; mitral value; remodeling

Introduction

A common of consequence ventricular remodeling in chronic heart failure (CHF) is functional mitral regurgitation (fMR). This is because as the failing ventricle dilates, there is apical and lateral papillary muscle displacement that pulls the leaflets downward and apart in a manner that prohibits proper coaptation.[1,2] However, although fMR results from a pathology of the ventricle, the common surgical and currently available percutaneous device-based approaches attempt treatment by reducing the size of the mitral annulus or by pulling the leaflet tips together.[3]

Alternatively, an approach that addresses the fundamental problem of ventricular remodeling may have dual benefits. First, by reducing ventricular size, myocardial wall stress can be decreased and in principle chamber contractility may be improved. Second, by bringing the bases of the papillary muscles closer together, leaflet coaptation may be improved. Ancora Heart (Santa Clara, CA) has developed a sub-mitral plane ventricular implant that consists of a cable passing through the eyelets of a series of intramyocardial anchors that, when cinched, reduces chamber circumference. In this report we describe the impact of the Ancora implant on LV size, LV function and mitral regurgitation. The clinical case described in this report illustrates proof-of-concept of the synergy between the two mechanisms by which this approach can treat both fMR and heart failure.

Materials and methods

Patient 202–051 is a 79-year-old man with ischemic and hypertensive cardiomyopathy, severe mitral regurgitation and NYHA functional class III symptoms. His history was otherwise significant for a prior inferior myocardial infarction but there was no active ischemia or indication for revascularization. He was recently hospitalized for a heart failure exacerbation treated with intravenous diuretics and inotropes. His medications included furosemide (40 mg/day), enalapril (5 mg/day), spironolactone (25 mg/day), lovastatin (20 mg/day), carvedilol (6.25 mg/day) and aspirin (100 mg/day). He had mild renal insufficiency (eGFR 50 mL/min/1.73 m^2) and elevated ntPro-BNP (3440 pg/ml); hepatic function and hematologic evaluations were otherwise normal. The patient was considered for inclusion into a study of the Ancora device according to a protocol approved by the Ethics Committee of Clinica Cardio VID, Medellin, Colombia (where the implant was performed), and by the local governmental authority (INVIMA). The patient provided informed consent prior to baseline testing.

Baseline echocardiography (interpreted by a core laboratory) revealed moderate-to-severe (3+ to 4+) mitral regurgitation with a large central jet and restricted anterior and posterior leaflet motion. The effective regurgitant orifice (ERO) was 0.36 cm^2, the regurgitant volume was 69 ml

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(estimated from the ERO and the time velocity integral of the regurgitant jet) and a forward stroke volume was 45 ml (estimated from the LV outflow track area and time velocity integral). He had an LVEF of 14% and an LV chamber internal diameter of 6.2 cm.

After meeting the study's clinical inclusion criteria and completing baseline testing, the patient underwent implantation of the Ancora device (Figure 1). In brief, the device consists of a series of guidewires and catheters that allow for implantation of up to 14 anchors into the myocardial wall behind the mitral apparatus. The anchors are connected to each other with a cable coursing through the eyelets of each anchor. After preparing the patient and inducing anesthesia and achieving femoral artery access with a 16 French sheath, the AccuCinch Guide catheter is placed retrograde across the aortic valve into the LV subvalvular space and tangent to the LV wall, adjacent to and apical of the P1 leaflet of the mitral valve (MV) (Figure 1A). Next, under fluoroscopic and transesophageal echocardiographic guidance, a specially designed "Navigator" catheter loaded with a floppy tip guidewire is advanced out of the guide catheter the entire way around the circumference of the heart in the subannular space behind the valve (Figure 1B). The Navigator catheter is then removed, leaving the guidewire in place. The next catheter, the "TracCath," is introduced over the wire and is parked distally with its tip at the junction between the interventricular septum and the free wall under P3 and the guidewire is withdrawn. The TracCath is comprised of two concentric and slidable lumens with multiple windows along the distal portion of the outer lumen and a single end-lumen on the inner shaft. An "Anchor Delivery Catheter" (ADC) is advanced through the TracCath which opens the windows and allows the ADC to exit, enter the myocardial tissue and deploy an electropolished Nitinol Anchor (Figure 1C). The anchors are placed into the LV wall one at a time, starting under P3 and extending around the perimeter of the ventricular free wall to under P1. Force distribution members (FDMs) introduced between adjacent pairs of anchors distribute the end-anchor load among several anchors at the two ends of the cable, providing a firm attachment to otherwise what might be friable myocardium (Figure 1C and D). In this patient, 13 anchors with seven force distribution members were deployed (Figure 2). The TracCath is then removed and a "Cinch & Lock" catheter is introduced over the cable; tension is applied to the cable which reduces its length, cinching the LV free wall. In this patient, the implant length was cinched approximately 15%. After cinching, a locking element is deployed to maintain the cinch and the Cinch & Lock Catheter is removed. A "Cut Catheter" is introduced and used to cut excess cable. The catheter is then removed, leaving the implant in the LV. Hemostasis following catheter removal is generally obtained with two Perclose (or similar) devices.

Results

Per protocol, the patient was followed for a total of 12 months. Clopidogrel (75 mg/day) was prescribed for 1 month following the procedure. Upon hospital discharge, the enalapril dose was increased to 20 mg/day and carvedilol was discontinued until being reintroduced (6.25 mg qd) again at 6 months. Doses of other medications remained constant. Results of echocardiographic evaluations revealed reduction of the degree of MR to 1+. Quantitative analysis showed reductions in ERO and LV end-diastolic dimension and increases in forward cardiac output (Figure 3). All parameters improved significantly by 30 days, continued to improve through 90 days and then were stable through the 12-month follow-up evaluation (Figure 3). In particular, ERO decreased to 0.12 cm^2, LV end-diastolic dimension decreased to 5.6 cm and forward stroke volume increased to 61 ml. In addition, annular anterior-posterior and commissure-to-commissure diameters decreased from 3.7 to 2.9 cm and 3.1 to 2.4 cm, respectively. The height of mitral tenting decreased from 1.30 to 0.67 cm and tenting area decreased from 2.30 to 1.0 cm^2. Concomitantly, estimated regurgitant volume decreased to 23 ml and ejection fraction increased to 34%. There was no change in systolic blood pressure at the times the echocardiograms were performed (122 mmHg at baseline and 121 mmHg at 12 months). ntPro-BNP decreased to 1450 pg/ml. There was an improvement in NYHA from functional class III to functional class I.

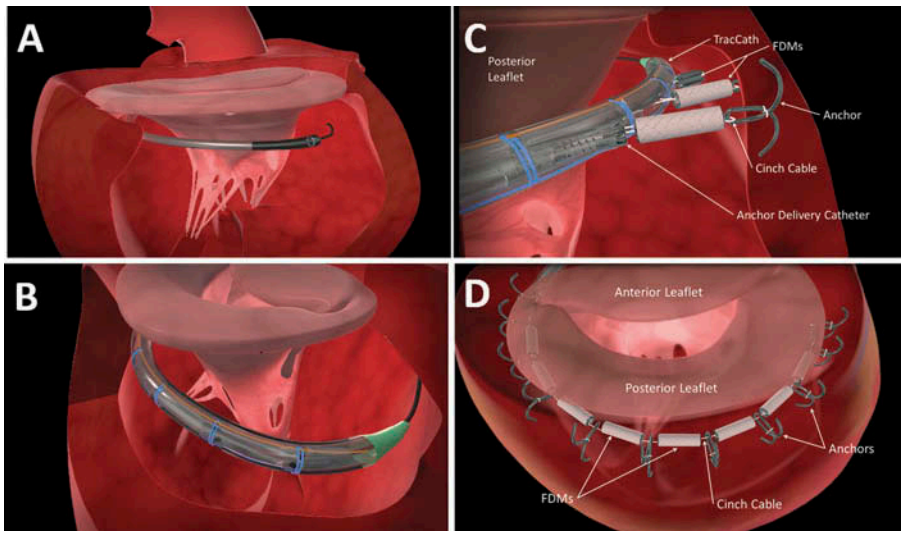

Figure 1. The various catheters and steps of the Ancora device and procedure are illustrated in panels A through D. See text for details.

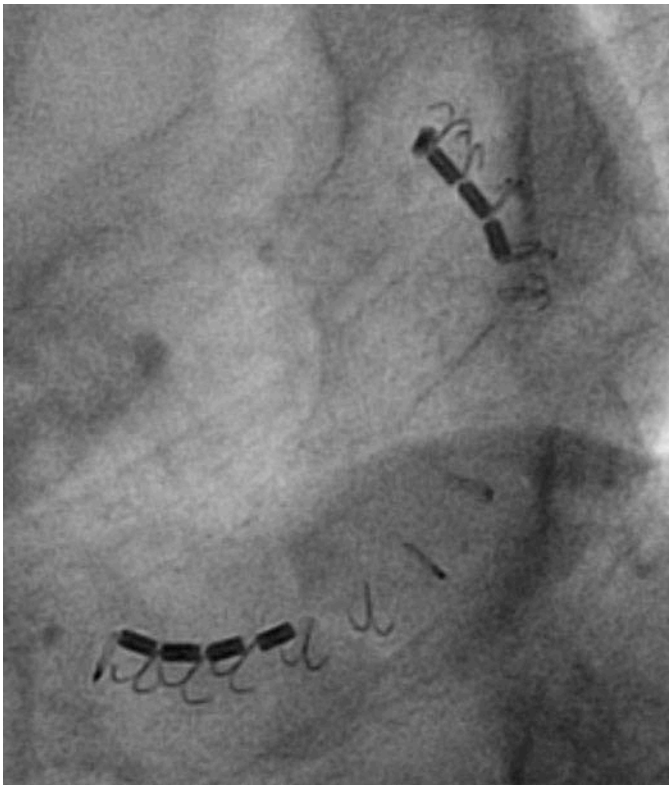

Figure 2. Left anterior caudal fluoroscopic image of the Ancora implant in this patient showing the anchors distributed around the circumference of the ventricular free wall. Radioopaque force distribution members are seen between distal and proximal sets of anchors.

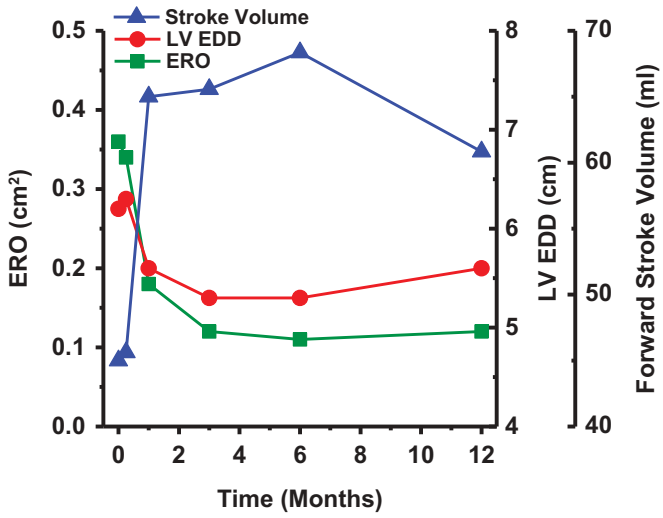

Figure 3. Time course of change of forward stroke volume, left ventricular end-diastolic dimension (LV EDD) and effective regurgitant orifice from baseline (at time = 0). See text for details.

Discussion

The Ancora sub-mitral annular, myocardial implant cinches the LV free wall with theoretical effects of bringing in the bases of the papillary muscles, reducing the size of the mitral annulus and reducing the radius of curvature of the LV. Working in concert, these effects are intended to reduce the degree of mitral regurgitation, decrease myocardial wall stress and induce reverse ventricular remodeling. In the current case, echocardiographic evaluations showed reductions in MR followed by progressive improvements in ventricular size and function that plateaued at ~90 days and remained stable during the 1-year follow-up. This timing is consistent with the time course of structural reverse remodeling reported for other heart failure therapies such as cardiac resynchronization therapy[4] and left ventricular assist devices.[5] The degree of reverse remodeling observed in the current patient is generally larger than reported for other forms of percutaneous mitral repair[6] as well as surgical mitral repair and replacement.[7] This suggests a significant contribution of the implant to the overall observed effect.

Interestingly, prior attempts to induce reverse remodeling by surgically excising a portion of the LV wall to reduce the radius of curvature and reduce wall stress (e.g. the Batista operation[8]) have been unsuccessful. We postulate that the main difference between surgical and Ancora approaches is that the surgical approach removes contracting (though weakened) myocardium; it has been shown that such a surgical approach induces leftward shifts of the end-diastolic pressure-volume relationship that are greater than those induced to the end-systolic pressure-volume relationship resulting in iatrogenic diastolic dysfunction.[9] Reducing radius without losing viable muscle offers the possibility to achieve reduced wall stresses without compromising net LV function. This was shown to be the case in a finite element analysis (FEA) of a different technology,[10] the Coapsys device. That device applied tension to a cable that was passed through the middle of the LV chamber; from the lateral wall to septum. The results of a clinical study of that device, which was also intended to reduce mitral regurgitation and wall stress, showed improved survival and reduced cardiovascular events.[11]

As with other devices being developed to address functional mitral regurgitation, the Ancora Heart device and implantation procedure have been in development for a number of years. While early pre-clinical data were promising, the transition to the clinical environment proved challenging, with changes required in the delivery system, the implant, and procedural endpoints. The present case represents the first patient with a 12-month follow-up in which all those changes were achieved. While additional refinements are anticipated, this case nonetheless provides a proof-of-concept of the potential for such a device. Additional procedures with long-term follow-up will be needed to more fully understand the magnitude and reproducibility of clinical results.

Conclusion

In conclusion, the Ancora Heart device reduced the degree of mitral regurgitation and was associated with reverse LV remodeling with improved LV function. These effects are all interrelated: reduced mitral regurgitation can contribute to reverse remodeling and reverse remodeling can reduce mitral regurgitation. And so, the vicious cycle of LV enlargement and increased MR might be interrupted. The degree to which these separate effects contributed to the overall clinical response cannot be unraveled. The current case report provides proof-of-concept that a ventricular reshaping device that does

not rely on excision of myocardial tissue and reduces the degree of fMR has potential as a treatment for heart failure.

Disclosure statement

Daniel Burkhoff is a consultant to HeartWare division of Medtronic, Sensible Medical, Cardiac Implants, BackBeat Medical, and Corvia Medical. Patrick Perier and Franz Kleber are consultants to Ancora Heart. None of the other authors have anything to declare.

References

1. Enriquez-Sarano M, Akins CW, Vahanian A. Mitral regurgitation. *Lancet*. 2009;373:1382–1394. doi:10.1016/S0140-6736(09)60692-9.
2. Asgar AW, Mack MJ, Stone GW. Secondary mitral regurgitation in heart failure: pathophysiology, prognosis, and therapeutic considerations. *J Am Coll Cardiol*. 2015;65:1231–1248. doi:10.1016/j.jacc.2015.02.009.
3. Maisano F, Alfieri O, Banai S, et al. The future of transcatheter mitral valve interventions: competitive or complementary role of repair vs. replacement? *Eur Heart J*. 2015;36:1651–1659. doi:10.1093/eurheartj/ehv123.
4. St John SM, Plappert T, Abraham WT, et al. Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure. *Circulation*. 2003;107:1985–1990. doi:10.1161/01.CIR.0000065226.24159.E9.
5. Madigan JD, Barbone A, Choudhri AF, et al. Time course of reverse remodeling of the left ventricle during support with a left ventricular assist device. *J Thorac Cardiovasc Surg*. 2001;121:902–908. doi:10.1067/mtc.2001.112632.
6. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364:1395–1406. doi:10.1056/NEJMoa1009355.
7. Acker MA, Parides MK, Perrault LP, et al. Mitral-valve repair versus replacement for severe ischemic mitral regurgitation. *N Engl J Med*. 2014;370:23–32. doi:10.1056/NEJMoa1312808.
8. Artrip JH, Oz M, Burkhoff D. Left ventricular volume reduction surgery for heart failure: a physiologic perspective. *J Thoracic Cardiovasc Surgery*. 2001;122:775–782. doi:10.1067/mtc.2001.116208.
9. Burkhoff D, Wechsler AS. Surgical ventricular remodeling: a balancing act on systolic and diastolic properties. *J Thorac Cardiovasc Surg*. 2006;132:459–463. doi:10.1016/j.jtcvs.2006.04.045.
10. Carrick R, Ge L, Lee LC, et al. Patient-specific finite element-based analysis of ventricular myofiber stress after Coapsys: importance of residual stress. *Ann Thorac Surg*. 2012;93:1964–1971. doi:10.1016/j.athoracsur.2012.03.001.
11. Grossi EA, Patel N, Woo YJ, et al. Outcomes of the RESTOR-MV trial (randomized evaluation of a surgical treatment for off-pump repair of the mitral valve). *J Am Coll Cardiol*. 2010;56:1984–1993. doi:10.1016/j.jacc.2010.06.051.