Transcatheter Left Ventricular Restoration in Patients With Heart Failure

NADIRA HAMID, MD,[1,2] ULRICH P. JORDE, MD,[3,4] MARK REISMAN, MD,[5] AZEEM LATIB, MD,[3,4] D. SCOTT LIM, MD,[6] SUSAN M. JOSEPH, MD,[7] ALENA KURLIANSKAYA, MD, PhD,[8] OLEG POLONETSKY, MD, PhD,[8] PETR NEUZIL, MD, PhD,[9] VIVEK REDDY, MD,[10] JASON FOERST, MD,[11] HEMAL GADA, MD, MBA,[12] KENDRA J. GRUBB, MD, MHA,[13] GUILHERME SILVA, MD,[14] DEAN KEREIAKES, MD,[15] SATYA SHREENIVAS, MD,[15] SEAN PINNEY, MD,[16] GIEDRIUS DAVIDAVICIUS, MD, PhD,[17] PAUL SORAJJA, MD,[18] JOHN P. BOEHMER, MD,[19] FRANZ X. KLEBER, MD, PhD,[20] PATRICK PERIER, MD,[21] NICOLAS M. VAN MIEGHEM, MD, PhD,[22] NICOLAS DUMONTEIL, MD,[23] MARTIN B. LEON, MD,[1,2] AND DANIEL BURKHOFF, MD, PhD[2]

New York, New York; Bronx, New York; Virginia; Baltimore, Maryland; Minsk, Belarus; Prague, Czech Republic; Roanoke, Virginia; Harrisburg, Pennsylvania; Atlanta, Georgia; Texas; Cincinnati, Ohio; Chicago, Illinois; Vilnius, Lithuania; Minneapolis, Minnesota; Hershey, Pennsylvania; PGS Wittenberg, Germany; Bad Neustadt/Saale, Germany; Rotterdam, the Netherlands and Toulouse, France

ABSTRACT

Background: Left ventricular (LV) volume reshaping reduces myocardial wall stress and may induce reverse remodeling in patients with heart failure with reduced ejection fraction. The AccuCinch Transcatheter Left Ventricular Restoration system consists of a series of anchors connected by a cable implanted along the LV base that is cinched to the basal free wall radius. We evaluated the echocardiographic and clinical outcomes following transcatheter left ventricular restoration.

Methods and Results: We analyzed 51 heart failure patients with a left ventricular ejection fraction between 20% and 40%, with no more than 2+ mitral regurgitation treated with optimal medical therapy, who subsequently underwent transcatheter left ventricular restoration. Serial echocardiograms, Kansas City Cardiomyopathy Questionnaire scores, and 6-minute walk test distances were measured at baseline through 12 months. Primary analysis end point was change in end-diastolic volume at 12 months compared with baseline. Patients ($n = 51$) were predominantly male (86%) with a mean age of 56.3 $\pm$ 13.1 years. Fluoroscopy showed LV free wall radius decreased by a median of 9.2 mm amounting to a 29.6% decrease in the free wall arc length. At 12 months, the LV end-diastolic volume decreased by 33.6 $\pm$ 34.8 mL ($P < .01$), with comparable decreases in the LV end-systolic volume. These decreases were associated with significant improvements in the overall Kansas City Cardiomyopathy Questionnaire score (16.4 $\pm$ 18.7 points; $P < .01$) and 6-minute hall walk test distance (45.9 $\pm$ 83.9 m; $P < .01$). There were no periprocedural deaths; through the 1-year follow-up, 1 patient died (day 280) and 1 patient received a left ventricular assist device (day 13).

Conclusions: In patients with heart failure with reduced ejection fraction without significant mitral regurgitation receiving optimal medical therapy, the AccuCinch System resulted in decreases of LV volume, as well as improved quality of life and exercise endurance. A randomized trial is ongoing (NCT04331769). (*J Cardiac Fail 2023;29:1046−1055*)

Key Words: Transcatheter, heart failure, left ventricle.

From the [1]Columbia University Medical Center/ NY Presbyterian Hospital, New York, New York; [2]Cardiovascular Research Foundation, New York, New York; [3]Montefiore Medical Center, New York, New York; [4]Albert Einstein College of Medicine, Bronx, New York; [5]Weill Cornell Medicine, New York, New York; [6]University of Virginia, Charlottesville, Virginia; [7]University of Maryland Medical Center, Baltimore, Maryland; [8]Republican Scientific and Practical Center Cardiology, Minsk, Belarus; [9]Na Homolce Hospital, Prague, Czech Republic; [10]Icahn School of Medicine Mount Sinai, New York, New York; [11]Carilion Roanoke Memorial Hospital, Roanoke, Virginia; [12]UPMC Heart and Vascular Institute, Pinnacle Health, Harrisburg, Pennsylvania; [13]Emory University School of Medicine, Atlanta, Georgia; [14]Baylor College of Medicine Houston Texas; [15]The Christ Hospital, Cincinnati, Ohio; [16]University of Chicago, Division of Cardiology, Chicago, Illinois; [17]Clinic of Cardiac and Vascular Diseases, Faculty of Medicine, and Cardiology and Angiology Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania; [18]Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital, Minneapolis, Minnesota; [19]Penn State Health, Hershey, Pennsylvania; [20]Martin Luther Universität Halle-Wittenberg, PGS Wittenberg, Germany; [21]Campus Bad Neustadt, Herzchirurgie, Bad Neustadt/Saale, Germany; [22]Department of Interventional Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam, the Netherlands and [23]Groupe CardioVasculaire Interventionnel, Clinique Pasteur, Toulouse, France.

Manuscript received February 28, 2023; revised manuscript received March 13, 2023; revised manuscript accepted March 13, 2023.

Reprint requests: Daniel Burkhoff, Cardiovascular Research Foundation, 1700 Broadway, New York, NY 10019. Phone: 201-294-6081. E-mail: dburkhoff@crf.org

1071-9164/$ - see front matter

Heart failure (HF) is a major world-wide public health issue.[1,2] Recent advances and developments in drug therapy,[3] implantable cardioverter-defibrillators, cardiac resynchronization therapy, transcatheter edge-to-edge repair for mitral regurgitation, pulmonary artery pressure monitoring, left ventricular (LV) assist devices, and heart transplantation have greatly improved prognosis and outcomes of patients with HF with reduced ejection fraction (HFrEF).[4–8] Both pharmacological and nonpharmacological treatments can induce ventricular reverse remodeling, characterized by reduced LV end-diastolic and end-systolic volumes. Such reverse remodeling, which is believed to occur in response to decreased wall stress, has been associated with improvements of myocardial properties, symptoms and survival.[9–11]

Surgical approaches have long been used to reshape the failing, dilated ventricle to restore more normal LV chamber architecture and function.[12–14] However, owing to the invasiveness of the surgical intervention and mixed results among studies, these procedures are not performed with significant frequency. As with other approaches for treating structural heart diseases, transition of therapies from surgical to less invasive percutaneous catheter-based procedures facilitate their investigation in clinical trials and increase their adoption into clinical practice.

The AccuCinch Transcatheter Left Ventricular Restoration (TLVR) system is a completely percutaneous, transcatheter, device-based therapy that consists of a series of anchors deployed into the myocardium and connected by a cinching cable that decreases the length of the arc along the free wall, thus decreasing the radius of curvature of the LV. In principle, this decreases myocardial wall stress and may initiate the process of reverse ventricular remodeling that could be beneficial to patients with HFrEF. Accordingly, the purpose of this retrospective analysis was to evaluate the echocardiographic and clinical outcomes following TLVR implantation in patients with HFrEF.

Methods

Study Design

Clinical investigation of the AccuCinch TLVR system was initiated in Europe and the United States in a series of open-label, nonrandomized studies starting in 2016. Overall, 94 patients were enrolled in 4 separate studies between August 2016 and March 2021 with the same follow-up and testing schedules and overlapping entry criteria, which included patients with ischemic or nonischemic cardiomyopathy (LV ejection fraction [LVEF] of $\leq$40%) with mitral regurgitation (MR) ranging from 0 to 4+ (further details in Supplemental Table 1; clinicaltrials.gov registration numbers also included in this table). Early study results revealed that, while treating MR, device use was associated with significant decreases in LV size and improved quality of life and functional status, irrespective of decreases in MR (unpublished data); the focus then shifted to investigation of this device as a treatment for HF in patients with at most 2+ MR. Therefore, the purpose of this retrospective analysis was to evaluate the efficacy and safety of the AccuCinch TLVR system for LV volume reduction and restoration in all patients enrolled in prior studies with at most 2+ MR and an LVEF of less than 40%. Each individual study protocol was approved by applicable governmental regulatory agencies and the ethics committee of each participating institution. All patients provided written informed consent. The study was conducted according to the principles of the Declaration of Helsinki.

Patients

To be eligible for inclusion in this retrospective pooled analysis, patients were required to: (1) be 18 years old or older; (2) have symptomatic HF with New York Heart Association (NYHA) functional class II or greater disease despite maximally tolerated guideline-directed medical therapy for at least 3 months with stable doses for 1 month before enrollment (with "stable" defined as no more than a 100% increase or 50% decrease of the total daily doses); (3) have an LV end-diastolic dimension of 55 mm or greater, an LVEF of between 20% 40%; (4) have no more than 2+ MR by echocardiography; (5) have a cardiac resynchronization device for at least 3 months before enrollment if they had left bundle branch block and QRS duration of 150 ms or longer; and (6) have an implantable cardioverter-defibrillator in place for at least 1 month before enrollment, if indicated. Patients with severe tricuspid regurgitation or other significant valvular pathologies, severe right ventricular (RV) dysfunction or untreated clinically significant coronary artery disease requiring revascularization were excluded. Other exclusion criteria included patients with myocardial infarction, percutaneous cardiac intervention, or cardiovascular surgery within 3 months.

Patient eligibility was confirmed by a committee consisting of interventional cardiologists, a HF cardiologist, and a cardiac surgeon (committee members provided in the Acknowledgments). In addition to reviewing the basic study inclusion criteria, the committee focused special attention on the appropriateness of baseline HF medical therapies and specific ilio-femoral and cardiac anatomic considerations determined by computed tomography scans. The iliofemoral artery was assessed to ensure adequacy

for device implantation, with the diameter, tortuosity, and presence of calcification as key considerations. The main cardiac criterion was a LV free wall thickness of 6 mm or greater throughout the perimeter to ensure the device anchors (described elsewhere in this article) would not perforate.

Device Description and Procedure

The AccuCinch TLVR system consists of a series of Nitinol anchors, coupled with an ultra-high-molecular-weight polyethylene cable, with each pair of anchors separated by polyester-covered Nitinol cylindrical sliders, which serve to evenly distribute force amongst the anchors (Fig. 1A). During the procedure, which is performed through a 20F femoral introducer sheath, a specially designed catheter is passed retrograde across the aortic valve and the anchors and sliders are implanted in series along the LV basal myocardium, extending from the posterior junction of the septum and LV free wall to the aortic outflow tract (Fig. 1B). At the end of the procedure, the cable is cinched so that the arc length of the LV free wall is decreased, also decreasing the radius of curvature (Fig. 1C). This is performed with a cinch and lock catheter, which is also used to deploy a Nitinol lock that secures the implant in its cinched configuration by attaching to the cable. During this final step, the cinch and lock catheter automatically feeds a prespecified amount of slack back into the implant to provide flexibility during systole. After implantation, tissue ingrowth occurs via endothelization of the implant components embedded into the myocardium, as well as direct cellular penetration of the multifilament cable (Fig. 1D) (also detailed further in the Supplemental Material and Supplemental Figs. 1–4). Antiplatelet therapy is recommended for 3 months after the procedure, which should continue if the patient has a clinical indication.

Testing Schedule and End Points

Patients were evaluated at baseline and 1, 3, 6, and 12 months after TLVR implant. Evaluations included transthoracic echocardiograms, 6-minute hall walk test distance (6MWD), and Kansas City Cardiomyopathy Questionnaire (KCCQ). Echocardiograms were evaluated in a core laboratory by 2 experienced readers (a research sonographer and a board-certified echocardiographer) who were blinded to the timing of individual studies and results of other studies from any given patient; all measurements were performed

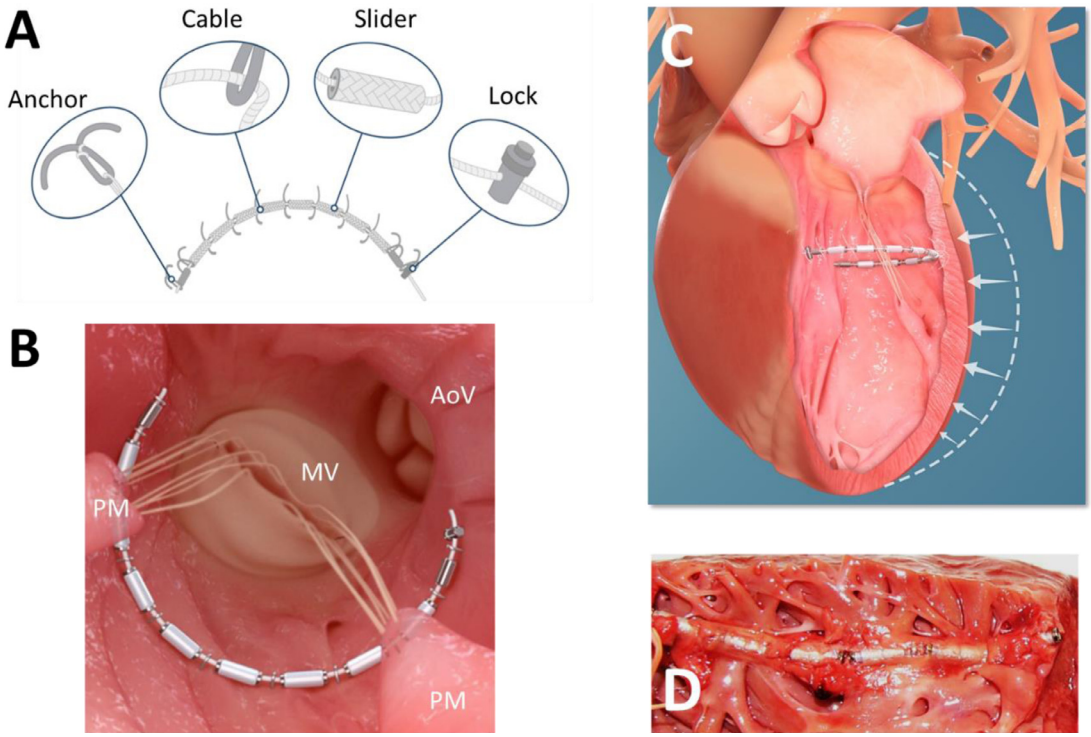

Fig. 1. AccuCinch Transcatheter Left Ventricular Restoration (TLVR) system. (**A**) The implant consists of the intramyocardial anchor, the cinching cable, sliders placed between the anchors, and a locking component that maintains the cinch after the implant. (**B**) An animation of an apical view showing the implant positioned behind the valve leaflets and chordae tendineae. (**C**) After the cinching and locking, the left ventricular free wall is drawn in, decreasing the arc length of the free wall and reducing its radius of curvature. (**D**) Autopsy specimen from an end-stage heart failure patient who received the implant (not part of this study) who died 10 days after the procedure showing the endothelialization of the device and its incorporation into the wall of the myocardium. AoV, aortic valve; MV, mitral valve leaflet; PM, papillary muscle.

according to American Society of Echocardiography guidelines. Echocardiographic evaluations included LV end-diastolic and end-systolic volumes and dimensions, LVEF, end-diastolic RV mid-chamber and basal dimensions, stroke volume, and tricuspid annular plane systolic excursion.

The primary efficacy end point of this study was the change of LVEDV compared with baseline through 12 months follow-up. Other secondary end points included changes in the 6MWD, KCCQ, NYHA functional class, and other echocardiographic metrics of LV size and function from baseline through 12-months of follow-up. Serious adverse events were tracked by the investigators and were reviewed by an independent clinical events committee, which adjudicated whether the events were device and/or procedure related.

Statistical Analysis

Baseline characteristics are presented as mean ± standard deviation [range] or median [range] as appropriate for continuous measurements and proportions for categorical variables. Changes in continuous echocardiographic parameters over time were calculated as the difference of values from baseline to each follow-up time point. Statistical comparisons of values at follow-up were compared with baseline values using paired *t* tests. For all tests, a *P* value of less than .05 was considered statistically significant. All testing was exploratory and hypothesis generating. Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Inc).

Results

Baseline Characteristics

Among the 4 studies, 94 patients received an AccuCinch TLVR system implant between August 2016 and March 2021 (Supplemental Table 1). After removing patients from the FMR study ($n = 35$), we had a cohort of 59 patients. Of those 59, 7 did not meet the criteria for the subset analysis (5 had MR grade 3 or 4 and 2 did not have an EF of 20%−40%). One patient had an implant attempted but owing to LV scaring, the procedure was terminated after the deployment of 4 anchors. The patient was followed to 3 months per protocol and did not experience any adverse events during their time in the study. This patient is not included in the current analysis. The investigators and sites contributing to this study are listed in Supplemental Table 2.

The baseline characteristics of the 51 included patients are summarized in Table 1. The patients were predominantly male (86.3%) with a mean age of 56.3 ± 13.1 years and a mean LVEF of 29.2 ± 4.8%. All patients were in NYHA functional class II to IV, 26% had ischemic cardiomyopathy, 65% had hypertension, 24% had diabetes, and 20% had a cardiac resynchronization device in place before the TLVR implant. Patients were well-medicated with guideline-directed medical therapies including diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists (with or without neprilysin inhibitors), and mineralocorticoid inhibitors (Table 1).

Table 1. Baseline Characteristics ($n = 51$)

Variable	Summary Statistics ($N = 51$)
Age, years	56.3 ± 13.1 (51) [33.0−87.0]
Male sex	44 (86.3%)
Ischemic CMP	13 (25.5%)
Atrial fibrillation	9 (17.6%)
Hypertension	33 (64.7%)
Hyperlipidemia	32 (62.7%)
Diabetes	12 (23.5%)
Prior CABG	8 (15.7%)
Prior PCI	9 (17.6%)
CRDM device Implanted pre procedure	
None	27 (52.9%)
ICD	14 (27.5%)
CRT	10 (19.6%)
NYHA functional class	$n = 50$
II	27 (54.0%)
III	22 (44.0%)
IV	1 (2.0%)
Prior cerebrovascular disease	3 (5.9%)
Prior stroke	5 (9.8%)
Heart failure (GDMT) medications	
Beta-blockers	47 (92.2%)
ACE-I/ARB	13 (25.5%)
ARNI	33 (64.7%)
Mineralocorticoid antagonist	44 (86.3%)
Diuretic	36 (70.6%)
SGLT2 (new in 2022)	6 (11.8%)

ACE-I/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CABG, coronary artery bypass grafting; CMP, ; CRDM, ; CRT, cardiac resynchronization therapy; GDMT, guideline-directed medical therapy; ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; SGLT2, sodium-glucose transport protein 2.

Procedural Details

For the 51 patients in whom the AccuCinch was successfully implanted (98.1%), the median procedural time was 2.2 hours (range 1.4−4.0 hours). A median of 13 anchors (range 12−16 anchors) were implanted. At implant, fluoroscopy showed that LV free wall radius decreased by a median of 9.3 mm (range 3.0−13.0 mm), amounting to a median decrease of 29.5% (range 10.0%−37.6%). Concomitantly, the LV free wall arc-length decreased by a median of 37.4 mm (range 8.8−54.0 mm) amounting to a median decrease of 29.7% (range 8.0%−34.3%). Fluoroscopic images of the implant before and after

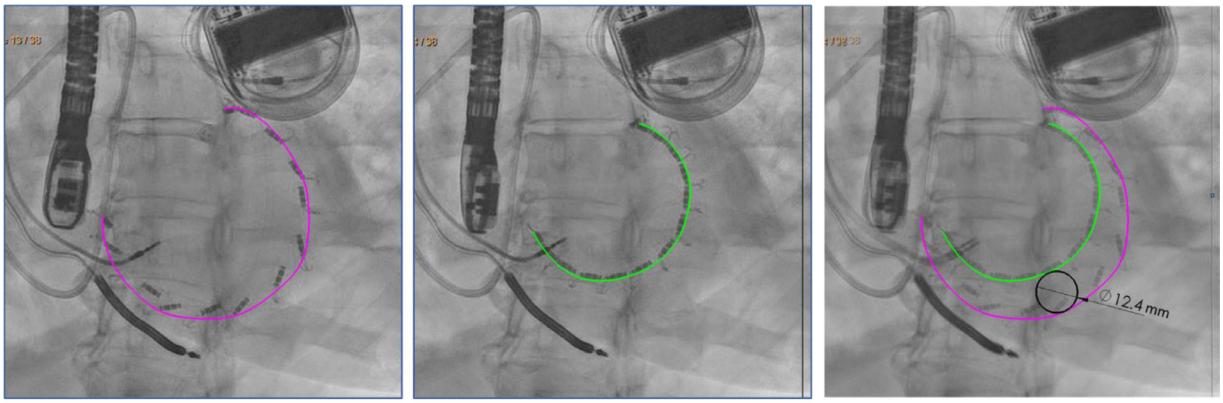

Fig. 2. Apical fluoroscopic images of the implant showing the anchor and sliders before cinch (left) and after cinch (middle). (Right) Pre- and postcinch images superimposed to reveal, in this case, a 12.4-mm decrease in the LV free wall radius of curvature.

cinching are shown in Fig. 2, respectively (solid lines tracing the cable). The right-most panel of Fig. 2 shows the pre- and post-cinch images superimposed to reveal, in this case, a 12.4-mm decrease in the LV free wall radius of curvature. Additional parameters characterizing the procedure are summarized in Supplemental Table 3.

Patient Accountability and Echocardiographic and Clinical Outcomes

After accounting for missed visits or testing owing to the COVID-19 pandemic ($n = 5$), poor quality images ($n = 3$), 1 patient who received an LVAD on day 13 who exited the study, and 1 patient who died at home on day 280 after implant, LVEDV paired data were available from 41 patients at 12 months. Compared with baseline, LVEDV decreased by 11.2 ± 18.7 mL (95% confidence interval (CI) −56.6 to −22.9; $P < .001$), 22.3 ± 32.5 mL (95% CI −32.3 to −12.3; $P < .001$), 28.2 ± 26.2 mL (95% CI −36.5 to −19.9; $P < .001$) and 33.6 ± 34.8 mL (95% CI −44.6 to −22.6; $P < .001$) at 1, 3, 6, and 12 months, respectively (Fig. 3A; all paired data, number of pairs indicated in the figure and table). Other echocardiographic parameters from paired samples from baseline to 12 months are summarized in Table 2. The other parameters showing statistically significant reductions included LV end-systolic volume, end-diastolic diameter, and end-systolic diameter, while there was a statistically significant increase of LVEF. With regard to RV changes, only the tricuspid annular plane systolic excursion decreased by 0.2 cm and there were no significant changes with the RV linear dimensions. Similar results were obtained at 6 months (Supplemental Table 4).

These echocardiographic changes in LV size were associated with significant and sustained improvements in the overall KCCQ score 18.0 ± 18.0 points (95% CI 12.8−23.1; $P < .001$) at 3 months, 20.1 ± 20.2 points (95% CI 14.2−26.0; $P < .001$) at 6 months and 16.4 ± 18.7 points (95% CI 10.9−22.0; $P < .001$) at 12 months, and 6MWD 53.8 ± 71.2 m (95% CI 31.8−75.7; $P < .001$) at 3 months, 51.4 ± 66.3 m (95% CI 30.7−72.1; $P < .001$) at 6 months and 45.9 ± 83.9 m (95% CI 20.4−71.4; $P < .001$) at 12 months (Fig. 3B and 3C).

There were also improvements in NYHA functional class at 6 and 12 months of follow-up (Fig. 4) ($P < .001$ for 6 months and 12 months vs baseline, both by Wilcoxon signed-rank test). Only 1 patient had a worsened NYHA classification comparing baseline with 6 months (class II to III), with 67% experiencing at least a 1-class improvement and 30% remaining in the same class. Similarly, at 12 months, compared with baseline, 65% improved by at least 1 class and 29% remained in the same class.

These clinical effects were observed without significant changes to background medical therapy. Comparing baseline with 12 months of follow-up, there were only minor changes in the number of patients receiving loop diuretic (discontinued in 1 patient), beta-blockers (discontinued in 1 patient), angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (no changes), angiotensin receptor-neprilysin inhibitor (no changes), or mineralocorticoid antagonist (discontinued in 2 patients).

Cable Discontinuities

Fluoroscopic images were obtained per protocol to assess the implant at 1, 3, and 12 months after device implant. Such images were available from 49 patients at 1 and 3 months and 43 of the patients at 12 months. Discontinuities, representing breaks of

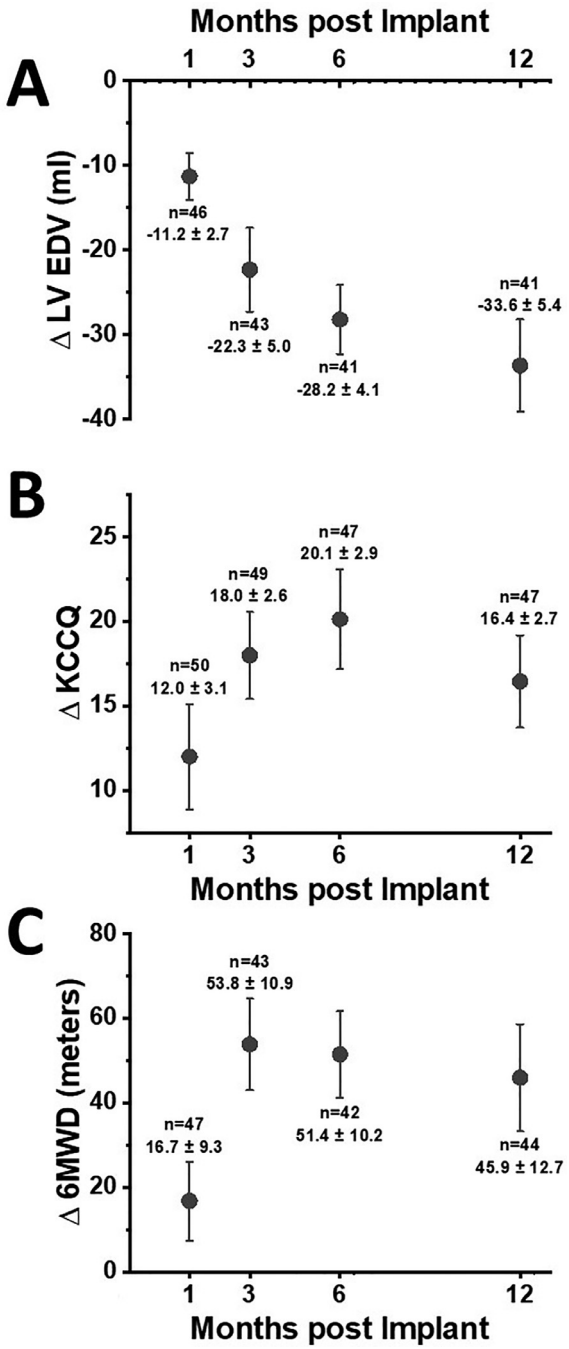

Fig. 3. Data plots illustrating the changes of left ventricular end diastolic volume (LVEDV) (**A**), Kansas City Cardiomyopathy Questionnaire (KCCQ) (**B**), and 6-minute walk test (6MWT) (**C**) from baseline. Values are means ± standard errors.

the cinching cable, were identified in 2 patients (4%) at 1 month, an additional 4 patients (8%) at 3 months, and 19 additional patients (39%) at 12 months, so that 25 of the 43 patients with available images up to 12 months were noted to have experienced a cable discontinuity (58%). The majority of cable discontinuities (23 of 25 [92%]) were detected after 30 days, a time point when integration of the implant into the endocardial wall is expected (see Fig. 1D and Supplemental Figs. 1–4), including endothelization of implant components and fibrous ingrowth into the porous cinching cable. Further details are described and illustrated in the Supplemental Material. Importantly, the individual implant components are likely well-integrated into the endocardial wall; thus, the physical and clinical effects were not diminished in patients in whom the cable discontinuities were identified. Specifically related to the 51 patients in the present HF cohort, the changes in LVEDV, KCCQ, and 6MWD did not differ significantly in patients with or without cable discontinuities (Supplement Fig. 5).

Safety

During the first year of follow-up, 1 patient died at home (day 280, no autopsy performed) and 1 patient received an LVAD (at day 13). Both events were adjudicated as not being related to the AccuCinch device or the implantation procedure. Fourteen of the 51 patients (27%) experienced a total of 20 device or procedure-related serious adverse events (Supplemental Table 5). Eleven events were adjudicated as definitely or possibly related to the device and 9 events were adjudicated as definitely or possibly related to the procedure, but not related to the device. These events were related to vascular access site complications, Dressler's syndrome or pericarditis, pericardial effusion requiring drainage, complete heart block, ventricular arrhythmias, and a stroke. Other possible device- or procedure-related adverse events include development of atrial fibrillation on day 1 after the procedure, cardiogenic shock on day 6, and atrial flutter on day 10. There were no long-term sequelae of any of these events, except that the patient with complete heart block underwent upgrade of a VVI implantable cardioverter-defibrillator to a cardiac resynchronization therapy defibrillator device. Related to the stroke, the patient had a history of atrial fibrillation and was admitted with subtherapeutic international normalized ratio; the neurologic deficit resolved.

Discussion

LV restoration and LV reconstruction are terms used to describe methods to physically decrease LV volumes and restructure the LV toward a more normal geometry. Ventricular restoration has been performed both surgically[15] and via hybrid surgical and percutaneous approaches.[16] In the present study, we assessed the echocardiographic and clinical outcomes after TLVR, a completely percutaneous, transcatheter procedure, in patients with HFrEF without significant MR. In these patients, TLVR was associated with significant and progressive decreases in LV volumes and increases in LVEF beyond what was

Table 2. Echocardiographic Parameters at Baseline and 12 months

Variable	Timepoint			
	Baseline	12 Months	Change from baseline to 12 months	95% CI
LVESV (mL)	146.4 ± 45.8 (41) [63.3 to 292.8]	117.9 ± 42.2 (41) [37.3 to 231.8]	−28.5 ± 28.2 (41) [−89.4 to 62.6]	−37.4 to −19.6 *
LVEDV (mL)	206.0 ± 55.8 (41) [96.5 to 372.3]	172.4 ± 52.8 (41) [78.7 to 315.6]	−33.6 ± 34.8 (41) [−107 to 67.6]	−44.6 to −22.6 *
LVESD (cm)	5.6 ± 0.8 (44) [3.7 to 7.1]	5.3 ± 0.8 (44) [3.7 to 6.9]	−0.3 ± 0.7 (44) [−1.8 to 1.9]	−0.5 to −0.04 *
LVEDD (cm)	6.6 ± 0.6 (45) [5.5 to 7.9]	6.2 ± 0.7 (45) [5.0 to 7.5]	−0.4 ± 0.6 (45) [−1.8 to 1.3]	−0.6 to −0.2 *
LVEF (%)	29.7 ± 4.9 (42) [20.7 to 39.4]	32.8 ± 7.3 (42) [20.7 to 52.7]	3.1 ± 6.9 (42) [−7.0 to 22.5]	1.0 to 5.3 *
Stroke volume (mL)	63.2 ± 13.9 (44) [43.9 to 105.0]	57.6 ± 12.9 (44) [35.3 to 97.3]	−5.6 ± 15.9 (44) [−43.0 to 42.1]	−10.5 to −0.8 *
Left atrial volume (mL)	94.2 ± 47.8 (46) [30.9 to 323.8]	102.1 ± 61.4 (46) [43.3 to 434.6]	7.9 ± 36.5 (46) [−70.3 to 110.8]	−2.9 to 18.8
RV end-diastolic mid− ventricular diameter (cm)	2.9 ± 0.7 (45) [1.9 to 4.9]	3.1 ± 0.7 (45) [1.8 to 5.1]	0.2 ± 0.7 (45) [−1.9 to 2.1]	−0.01 to 0.4
RV end-diastolic basal ventricular diameter (cm)	4.3 ± 0.8 (45) [3.1 to 6.6]	4.4 ± 0.8 (45) [3.4 to 6.7]	0.2 ± 0.6 (45) [−1.1 to 1.9]	−0.03 to 0.3
TAPSE (cm)	1.9 ± 0.3 (39) [1.4 to 2.6]	1.7 ± 0.4 (39) [1.1 to 2.5]	−0.2 ± 0.3 (39) [−1.3 to 0.4]	−0.3 to −0.07 *
KCCQ	61.3 ± 21.6 (47) [14.6 to 96.4]	77.7 ± 19.0 (47) [24.3 to 100.0]	16.4 ± 18.7 (47) [−30.7 to 53.6]	10.9 to 21.9 *
6MWT	344.1 ± 79.7 (44) [64.8 to 474.6]	390.0 ± 106.6 (44) [64.2 to 521.4]	45.9 ± 83.9 (44) [−185 to 240.0]	20.4 to 71.4 *

6MWT, 6-miute walk test; CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEDD, left ventricular end-diastolic diameter; LVEDV left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD. left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; TAPSE, tricuspid annular plane systolic excursion.

Values are mean ± SD (*n*), [range].

*$P < .05$.

achieved by the initial device implant. These patients also experienced improvements in quality of life (overall KCCQ score) and 6MWD.

As noted, the reverse remodeling observed with the TLVR system seems to occur over 2 phases. First is the initial effects of the implant on LV size and shape. This initial physical reverse remodeling is mainly characterized by a decrease in the radius of curvature of the LV basal free wall. This, in principle, has the theoretical effect of reducing wall stress, which may induce a secondary phase of biological reverse remodeling that, over time, builds on the initial physical effects of the permanent implant. The data show that this biological response continues over a period of time since LV volume continues to decrease, at least through 12 months after device implantation. Of the total decrease in the LVEDV noted at 12 months (34 mL), approximately 11 mL (33%) is attributed to phase 1, physical reverse remodeling, and the remaining approximately 23 mL (67%) is attributed to the secondary, phase 2 biological reverse remodeling and the scar formation around the implant. The mechanisms of the biological changes with TLVR require further study, but, as with other therapies associated with reverse remodeling, may reflect the combined effects of the decreased wall stress, improved LV function, and subsequent improvements in the neurohormonal milieu.[17] A deeper understanding of the mechanisms may help to optimize the therapy and identify characteristics of patients most likely to benefit from this form of therapy.

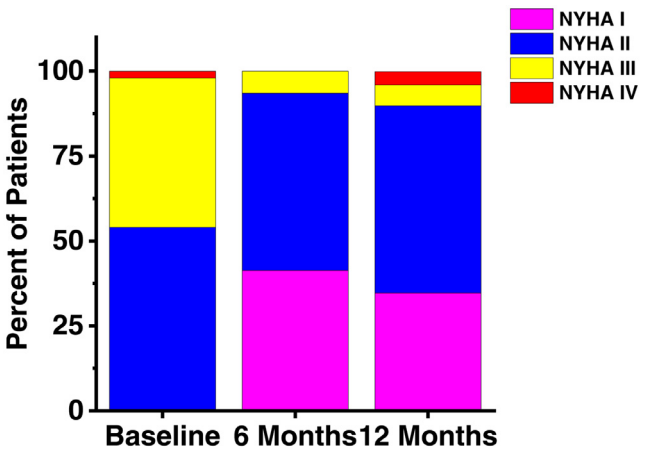

Fig. 4. Distribution of New York Heart Association functional classes at baseline and 6 and 12 months of follow-up. $P < 0.001$ for 6 months vs baseline, and $P < 0.001$ for 12 months vs baseline, both by Wilcoxon signed− rank test.

Treatment with the AccuCinch TLVR system was associated with improvements of quality of life (indexed by the KCCQ) and exercise tolerance

(indexed by the 6MWD). These parameters have been shown to reflect clinically important changes in health status in cohorts of patients with HF.[18,19] However, these results need to be put into the context that they were obtained in an unblinded study, because both parameters are subject to the placebo effect and improvements may also be related to better adherence to medical therapies and lifestyle recommendations while enrolled in the study (i.e., the Hawthorne effect). It was for this reason that the primary end point was chosen to be an objective end point, assessed by a reader blinded to patient data and timepoints (N.H.), that is considered to be a surrogate for clinical outcomes.[20,21]

Regarding safety, the majority of adverse events were related to vascular access. This likely relates to catheter profile and duration of the procedure, factors that could be improved with further device modifications and operator experience.

Limitations

The major limitations of this study include its small sample size; nonrandomized, noncontrolled, unblinded nature; significant amount of missing data owing to the COVID-19 pandemic; and poor echocardiographic image quality in several of the tests. Regarding imaging technique, use of a 3-dimensional method (eg, 3-dimensional echocardiography, magnetic resonance imaging or computed tomography scanning) may result in more accurate assessment of LV size and function over time. Regarding missing data, all analyses of changes of echocardiographic and clinical parameters are derived from paired analysis. Thus, to the degree that the data are missing at random (and not due to a specific cause such as worsening HF or death), the findings can be considered representative of the treatment effects. A fully powered randomized study is currently underway to address the need for a larger study with a control group (clinicaltrials.gov NCT04331769).

Conclusions

As summarized in the Fig. 5, when implanted in patients with HF and dilated hearts, the AccuCinch TLVR system immediately decreased the LV radius, resulted in progressive LV volume decreases in the following year and was associated with improvements of quality of life and exercise tolerance. Overall, the results demonstrate feasibility of this approach. Most important, these results justify the conduct of further study to more definitively assess the clinical benefits (both safety and efficacy) of the TLVR system. Accordingly, a randomized controlled study of the AccuCinch TLVR system has been initiated (The CORCINCH-HF study; clinicaltrials.gov NCT04331769).

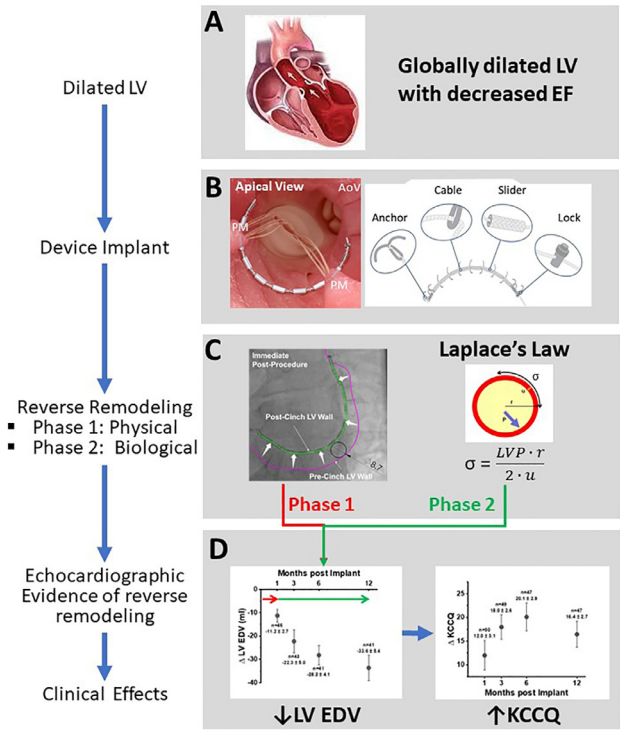

Fig. 5. The AccuCinch Transcatheter Left Ventricular Restoration system is designed for patients with heart failure and dilated left ventricle (**A**). The device creates an initial decrease in the radius of curvature of the free wall base (**B**), which, in principle, decreases wall stress according to Laplace's law (**C**). After an initial phase of volume reduction, we observed a second phase of progressive decreases in the left ventricular (LV) end-diastolic volume, documented through at least 12 months of follow-up (**D**). Transcatheter left ventricular restoration therapy was also associated with improvements of quality of life as quantified by Kansas City Cardiomyopathy Questionnaire (KCCQ) (**D**). EF, ejection fraction.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE

HFrEF is characterized by an enlarged LV resulting from the progressive process of ventricular remodeling. The increased LV radius increases wall stress which contributes to the progressive nature of remodeling.

COMPETENCY IN PATIENT CARE AND PROCEDURAL OUTCOMES

In patients with HFrEF and with no significant mitral regurgitation, the AccuCinch TLVR system decreases the LV volumes progressively over a 1-year period. This change is associated with improvements in quality of life and exercise tolerance.

TRANSLATIONAL OUTLOOK

Additional studies are needed to understand the mechanism by which the AccuCinch TLVR induces the structural improvements of the left ventricle and better characterize the long-term clinical benefits of the TLVR system in patients with HFrEF with no significant mitral regurgitation. A randomized controlled study of the AccuCinch TLVR system has been initiated (The CorCinch-HF study; clinicaltrials.gov NCT04331769).

Conflicts of Interest

Nadira Hamid reports Institutional grant support. Ulrich Jorde reports travel support from Ancora Heart. Mark Reisman reports travel support from Ancora Heart. Azeem Latib has nothing to declare. D. Scott Lim has nothing to declare. Susan Joseph has nothing to declare. Alena Kurlianskaya has nothing to declare. Oleg Polonetsky, MD, reports consultancy fees from Ancora Heart, and consultancy or proctoring fees from Edwards Lifesciences and Medtronic. Petr Neuzil has nothing to declare. Vivek Reddy has nothing to declare. Jason Foerst has nothing to declare. Hemal Gada has nothing to declare. Kendra J. Grubb reports advisory board and consulting fees for Medtronic, Boston Scientific, Abbott, Ancora, 4C Medical, and honorarium for Edwards Lifesciences. Guilherme Silva has nothing to declare. Dean Kereiakes has nothing to declare. Satya Shreenivas has nothing to declare. Sean Pinney reports consulting fees from Abbott, CareDx, Medtronic, Procyrion, and Transmedics. Giedrius Davidavicius is a consultant to Ancora Heart. Paul Sorajja has nothing to declare. John Boehmer has nothing to declare. Franz X. Kleber is a consultant to Ancora Heart. Patrick Perier has nothing to declare. Nicolas M. Van Mieghem reports research grant support from Abbott, Boston Scientific, Edwards Lifesciences, Medtronic, PulseCath BV, Abiomed, Siemens, and Daiichi Sankyo. Nicolas Dumonteil reports consultancy fees from Ancora Heart, is the co-PI of the CorCinch European study; and reports consultancy and proctoring fees from Abbott Vascular, Boston Scientific, Edwards Lifesciences, and Medtronic. Martin B. Leon reports institutional clinical research grants from Abbott, Abiomed, Ancora, Boston Scientific, Edwards, and Medtronic. Daniel Burkhoff reports institutional grant support from Ancora Heart to the Cardiovascular Research Foundation.

Acknowledgments

This study was sponsored by Ancora Heart, Inc.

The study patient review committee (PRC) consisted of Dr. Susan Joseph (heart failure), Dr. Franz X. Kleber (interventional cardiologist), and Dr. Patrick Perier (cardiac surgeon).

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2023.03.003.

References

1. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. Nat Rev Cardiol 2011;8:30–41.
2. Hollenberg SM, Warner Stevenson L, Ahmad T, et al. 2019 ACC Expert Consensus Decision Pathway on Risk Assessment, Management, and Clinical Trajectory of Patients Hospitalized With Heart Failure: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2019;74:1966–2011.
3. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med 2022;387:1089–98.
4. Teuteberg JJ, Cleveland JC, Cowger J, et al. The Society of Thoracic Surgeons INTERMACS 2019 annual report: the changing landscape of devices and indications. Ann Thorac Surg 2020;109:649–60.
5. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019;381:1995–2008.
6. Packer M, Butler J, Filippatos GS, et al. Evaluation of the effect of sodium-glucose co-transporter 2 inhibition with empagliflozin on morbidity and mortality of patients with chronic heart failure and a reduced ejection fraction: rationale for and design of the EMPEROR-Reduced trial. Eur J Heart Fail 2019;21:1270–8.
7. Lindenfeld J, Abraham WT, Grayburn PA, et al. Association of effective regurgitation orifice area to left ventricular end-diastolic volume ratio with transcatheter mitral valve repair outcomes: a secondary analysis of the COAPT trial. JAMA Cardiol 2021;6:427–36.
8. Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. Lancet 2021;398:991–1001.
9. White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. Circulation 1987;76:44–51.
10. Isomura T, Hoshino J, Fukada Y, et al. Volume reduction rate by surgical ventricular restoration determines late outcome in ischaemic cardiomyopathy. Eur J Heart Fail 2011;13:423–31.

11. Konstam MA. Reliability of ventricular remodeling as a surrogate for use in conjunction with clinical outcomes in heart failure. Am J Cardiol 2005;96:867–71.
12. Buckberg G, Athanasuleas C, Conte J. Surgical ventricular restoration for the treatment of heart failure. Nat Rev Cardiol 2012;9:703–16.
13. Athanasuleas CL, Buckberg GD, Stanley AW, et al. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol 2004;44:1439–45.
14. Athanasuleas CL, Buckberg GD, Stanley AW, et al. Surgical ventricular restoration: the RESTORE Group experience. Heart Fail Rev 2004;9:287–97.
15. Jones RH, Velazquez EJ, Michler RE, et al. Coronary bypass surgery with or without surgical ventricular reconstruction. N Engl J Med 2009;360:1705–17.
16. Klein P, Anker SD, Wechsler A, et al. Less invasive ventricular reconstruction for ischaemic heart failure. Eur J Heart Fail 2019;21:1638–50.
17. Kim GH, Uriel N, Burkhoff D. Reverse remodelling and myocardial recovery in heart failure. Nat Rev Cardiol 2018;15:83–96.
18. O'Keeffe ST, Lye M, Donnellan C, Carmichael DN. Reproducibility and responsiveness of quality of life assessment and six minute walk test in elderly heart failure patients. Heart 1998;80:377–82.
19. Shoemaker MJ, Curtis AB, Vangsnes E, Dickinson MG. Triangulating clinically meaningful change in the six-minute walk test in individuals with chronic heart failure: a systematic review. Cardiopulm Phys Ther J 2012;23:5–15.
20. Konstam MA, Kramer DG, Patel AR, Maron MS, Udelson JE. Left ventricular remodeling in heart failure: current concepts in clinical significance and assessment. JACC Cardiovasc Imaging 2011;4:98–108.
21. Konstam MA, Udelson JE, Anand IS, Cohn JN. Ventricular remodeling in heart failure: a credible surrogate endpoint. J Card Fail 2003;9:350–3.