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Transcatheter Mitral Annuloplasty in Chronic Functional Mitral Regurgitation

6-Month Results With the Cardioband Percutaneous Mitral Repair System

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ABSTRACT

OBJECTIVES This study sought to show safety and efficacy of the Cardioband system during 6 months after treatment.

BACKGROUND Current surgical and medical treatment options for functional mitral regurgitation (FMR) are limited. The Cardioband system (Valtech Cardio, OrYehuda, Israel) is a novel transvenous, transseptal direct annuloplasty device.

METHODS Thirty-one patients (71.8 ± 6.9 years of age; 83.9% male; EuroSCORE II: 8.6 ± 5.9) with moderate to severe FMR, symptomatic heart failure, and depressed left ventricular function (left ventricular ejection fraction 34 ± 11%) were prospectively enrolled.

RESULTS Procedural success rate, defined as delivery of the entire device, was 100%. There were no periprocedural deaths (0%), and mortality rate at 1 month or prior to hospital discharge and at 7 months was 5% and 9.7% respectively. Cinching of the implanted Cardioband reduced the annular septolateral dimension by >30% from 3.7 ± 0.5 cm at baseline to 2.5 ± 0.4 cm after 1 month and to 2.4 ± 0.4 cm after 6 months, respectively ($p < 0.001$). Percentage of patients with FMR ≥3 was reduced from 77.4% to 10.7% 1 month after the procedure ($p < 0.001$) and 13.6% ($p < 0.001$) at 7 months. Percentage of patients with New York Heart Association functional class III/IV decreased from 95.5% to 18.2% after 7 months ($p < 0.001$); exercise capacity as assessed by 6-min walking test increased from 250 ± 107 m to 332 ± 118 m ($p < 0.001$) and quality of life (Minnesota Living With Heart Failure Questionnaire) was also significantly improved ($p < 0.001$).

CONCLUSIONS In this feasibility trial in symptomatic patients with FMR, transcatheter mitral annuloplasty with the Cardioband was effective in reducing MR and was associated with improvement in heart failure symptoms and demonstrated a favorable safety profile. (Cardioband With Transfemoral Delivery System; NCT01841554) (J Am Coll Cardiol Intv 2016;9:2039–47) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

6MWT = 6-min walking test

FMR = functional mitral regurgitation

IDS = implant delivery system

MR = mitral regurgitation

MV = mitral valve

NYHA = New York Heart Association

SAT = size adjustment tool

TEE = transesophageal echocardiography

TSS = transseptal steerable sheath

Mitral regurgitation (MR) is the most frequent valvular disease and affects up to 2% of the population, with an increasing incidence with age (1). Approximately 10% of those ≥70 years of age are affected. Primary disease of the valve or its components (degenerative MR) accounts for the minority of patients and is potentially curable with repair of the valve. In the majority, MR is secondary to left ventricular dysfunction and remodeling, which leads to tethering of the valve, annular dilation, and inadequate leaflet coaptation. Secondary MR may result from both ischemic and nonischemic etiologies (2–4). Because the valve abnormality is only 1 component in the pathology of secondary MR, relief of the MR is not in itself curative. Current guidelines reflect the uncertain benefit of isolated valve surgery for functional MR (FMR) (2,5). Recent reports suggest that even patients in need for surgical coronary revascularization may not benefit from concomitant mitral valve (MV) surgery (6,7). At the same time, even with optimized medical therapy, worsening of the MR is likely due to continued left ventricular dysfunction and remodeling (2,5,8–10).

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Given the central pathologic role of annular dilation in FMR, surgical annuloplasty of the MV was developed, and is often performed in conjunction with surgical revascularization (7). In the absence of an indication and suitability for concomitant nonvalve surgery, many patients are treated medically due to the typically high surgical risk of heart failure patients. There is therefore an unmet need for alternative, catheter-based, minimally invasive, and effective interventional approaches.

To date, 3 different catheter-based direct annuloplasty systems have been tested in early clinical studies: the Mitralign (Mitralign Inc., Tewksbury, Massachusetts) (NCT01852149), the Accucinch (Guided Delivery Systems, Santa Clara, California) (NCT01899573), and the Cardioband device. The Cardioband system (Valtech Cardio, OrYehuda, Israel) uses a transvenous, transseptal route to implant a device on the posterior annulus from the anterolateral to the posterior-medial MV commissure, which reduces the annular dimensions via controlled cinching of the implant, which is performed on the beating heart under transesophageal echocardiographic guidance. The 30-day results were recently reported (11). We herein report on the 6-month data of the first-in-man safety and feasibility study in 31 patients.

METHODS

TRIAL DESIGN, INCLUSION CRITERIA, AND PATIENT SELECTION. The study was a single-arm, multicenter, prospective trial enrolling patients at 5 institutions in Europe. Patients were high-risk adult individuals with symptomatic FMR despite optimal medical therapy including cardiac resynchronization therapy when indicated. Patients with a left ventricular ejection fraction <25% and a left ventricular end-diastolic diameter >70 mm were excluded. Other main exclusion criteria included organic (primary) lesions of the MV, calcification of the annulus, acute endocarditis, coronary artery disease requiring revascularization, dialysis, significant concomitant non-MV disease, life expectancy <12 months, and recent cerebral event.

The anatomical feasibility of Cardioband implantation was assessed by transesophageal echocardiography (TEE) and cardiac computed tomography. Computed tomography scanning was used to size the mitral annulus for device selection, and to plan the procedure (location of transseptal puncture, mitigating the risk of injury to the left circumflex coronary artery, and planning of fluoroscopic views). On the basis of computed tomography analyses, the positioning of transseptal puncture was chosen individually to allow optimal device steering.

The implant size was chosen according to the length of the posterior annulus (from left trigone to right trigone) at maximal diastolic opening of the valve.

CARDIOBAND ADJUSTABLE MITRAL ANNULOPLASTY SYSTEM. The Cardioband implant is a polyester sleeve with radiopaque markers spaced 8 mm apart.

Abbott Vascular; and has received research grant support from Valtech Cardio. Dr. Messika-Zeitoun has served as a proctor for Valtech Cardio; and has received research grant support from Abbott Vascular and Edwards Lifesciences. Dr. Volker has received speaker fees from Valtech Cardio. Dr. Latib has served on the advisory board for Medtronic and Millipede; and as a consultant for Direct Flow Medical. Dr. Kuck has served as a consultant for St. Jude Medical, Abbott Vascular, and Medtronic. Dr. Kreidel has served as a consultant for Valtech Cardio. Dr. Ben-Yehuda has received research grant support from Valtech Cardio. Dr. Maisano has served as a consultant for Valtech Cardio, Abbott Vascular, Medtronic, Edwards Lifesciences, and St. Jude Medical; he is the co-founder of Valtech Cardio; and has received royalties from Edwards Lifesciences. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Nickenig and Hammerstingl contributed equally to this work.

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The sleeve covers the delivery system that deploys anchors. A contraction wire is pre-mounted on the Cardioband sleeve and is connected to an adjusting spool. Activating the spool syncs the implant, thereby reducing the mitral annular dimension. The implant size is adjusted to the patient's needs under TEE guidance and can be reversed. The implant is available in 6 lengths (**Figure 1**).

Three accessories are required for implantation:

1. Transfemoral delivery system: The Cardioband Delivery System consists of the implant delivery system (IDS) and the 25-F transseptal steerable sheath (TSS). The IDS comprises of a steerable guide catheter and an implant catheter (IC) with the Cardioband implant mounted on its distal end.
2. Implantable metal anchors and anchor delivery shafts: Implantable stainless steel, 6-mm-long anchors, are used to fasten the Cardioband implant to the annulus. Between 12 and 17 anchors are implanted using a delivery shaft. The anchors are fully repositionable and retrievable until deployed.
3. Size adjustment tool (SAT): The SAT distal tip is connected over the implant wire and is used to control the implant adjustment spool.

Contracting the polyester sleeve from one side by use of a dedicated cinching tool performs cinching and results in a proportionally reduction of the distances between the implanted anchors (Online Figure 1).

CARDIOBAND IMPLANTATION PROCEDURE. The procedure is performed under general anesthesia with 3D TEE guidance. Femoral vein and arterial access is obtained. Following echo-guided transseptal puncture, systemic heparinization is administered to achieve an activated clotting time between 250 and 300 s. The TSS is advanced over a super-stiff guidewire into the left atrium. The IDS is then advanced through the TSS. The delivery system is steered, until the tip of the IC is placed over the anterior commissure. Verification of the first anchoring location is obtained with TEE. The first anchor is placed close to the leaflet hinge, as anterior as possible in the annulus, close to the anterior commissure. Following confirmation of the location with 3-dimensional TEE, coronary angiography is performed to rule out damage to the left circumflex coronary artery. The first anchor is delivered and implanted using the anchor delivery drive inside the IC through the Cardioband implant fabric and into the annulus tissue. The anchor is released after proper anchoring is verified with push-and-pull testing under echocardiographic and fluoroscopic guidance. The Cardioband implant is deployed until the radiopaque marker of the IC channel reaches the next marker on the implant. The IC tip is then navigated, by actuating the TSS and guide catheter steering knobs, to the next anchoring point along the posterior annulus using echocardiographic guidance. These actions are repeated until the implant catheter tip reaches the last anchoring site on the posterior commissure.

FIGURE 1 The Cardioband Delivery System

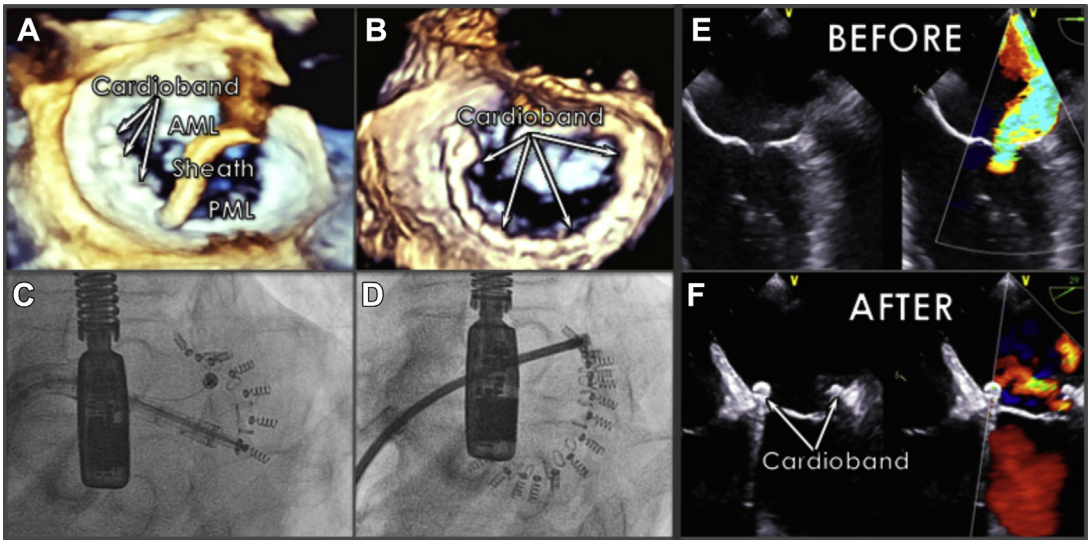
The last anchor is then deployed and the implant is disconnected from the IDS, which is subsequently removed. The SAT is then inserted through the TSS, over the implant guidewire, until its distal end reaches the adjustment spool of the implant. After SAT connection, the implant is contracted by clockwise rotation of the adjustment roller. Adequate reduction of MR severity is assessed by TEE under beating heart conditions. When the appropriate implant size has been reached, the SAT is detached from the adjustment spool leaving the implant with the desired degree of contraction (**Figure 2**).

TRIAL ENDPOINTS. The primary efficacy endpoints included: 1) technical success rate of Cardioband implantation, defined as the ability to advance the implant, load anchors, anchor the implant to the tissue, and retract the implant delivery system; 2) technical feasibility of Cardioband adjustment, defined as the ability to connect the adjustment tool, reduce the implant dimension, and retract the adjustment tool with the guidewire; and 3) Cardioband ability to reduce the annular septolateral dimension and MR as measured by TEE post-procedure, and transthoracic echocardiography at hospital discharge and at the post-operative 30-day visit.

Echocardiograms were analyzed by an independent core laboratory (headed by Paul Grayburn, MD, Baylor Health, Dallas, Texas).

The overall rate of major serious adverse events and serious adverse device effects until hospital discharge and at 30 days post-implantation was the primary safety endpoint. Both the major serious adverse events and the serious adverse device effects

FIGURE 2 Stepwise Deployment of the Cardioband Device and Acute Reduction of MR After Cinching



(A and C): Corresponding views from 3D TOE and fluoro with stepwise development of the device from the lateral commissure of the MV to the P2 segment of the posterior mitral annulus. **(B and D)**: Complete device development. **(E and F)**: Severity of MR before the procedure and after annuloplasty. AML = anterior mitral valve leaflet; fluoro = fluoroscopy; MV = mitral valve; P2 = posterior segment of the MV; PML = posterior mitral valve leaflet; TOE = transesophageal echocardiography.

were collected and adjudicated by an Independent Clinical Event Committee (Cardiovascular Research Foundation, New York, New York). Pre-specified major serious adverse events included death, myocardial infarction, cardiac tamponade, device-related cardiac surgery, and stroke.

The clinical investigation was performed in conformity with the ethical principles set forth by the Declaration of Helsinki, Good Clinical Practice principles, and in accordance with ISO 14155:2011.

STATISTICS. Statistical analysis was conducted using SPSS software version 22.0 (SPSS Inc., Chicago, Illinois). Continuous variables are presented as mean ± SD or as median (interquartile range [quartile 1 to quartile 3]). The distributions of the continuous variables were examined using the Kolmogorov-Smirnov nonparametric test.

Categorical variables are expressed as percentages. Univariable comparisons (differences between pre and post values) were calculated by repeated measures analysis of variance and by Friedman nonparametric test. Paired comparisons between time point measurements were calculated by paired *t* test and by Wilcoxon nonparametric tests. A p value <0.05 was considered statistically significant; reported p values are 2-sided.

Statistical evaluation must be interpreted with cautions because 22 of 33 patients completed follow-up evaluations and study data were acquired from 5 different institutions. Institutional outcomes and recruitment numbers are shown in Online Table 1 and Online Figures 1 to 4.

RESULTS

BASELINE CHARACTERISTICS AND FOLLOW-UP PROCEDURES. The first patient was implanted on February 19, 2013, and last patient on October 23, 2014 (Online Table 1, distribution of patients according to recruiting centers). Mean age was 71.8 ± 6.9 years, 26 patients (84%) were men. Thirty of 31 patients were in had New York Heart Association (NYHA) functional class III to IV and left ventricular ejection fraction was 34 ± 11%. The majority of patients (19 of 31 [61%]) had restricted leaflet motion (Carpentier classification type IIIb), whereas the remaining had predominantly annular dilation (type I MR). Etiology of secondary MR was ischemic in 60% of the patients. Fourteen patients (45%) had previously undergone open heart surgery at least once. Most common comorbidities included moderate to severe renal impairment (92%), atrial fibrillation (77%), diabetes (45%), poor mobility (23%), and chronic pulmonary disease (23%) (**Table 1**).

Six-month follow-up procedures were performed in 22 patients, the reasons for incomplete clinical data

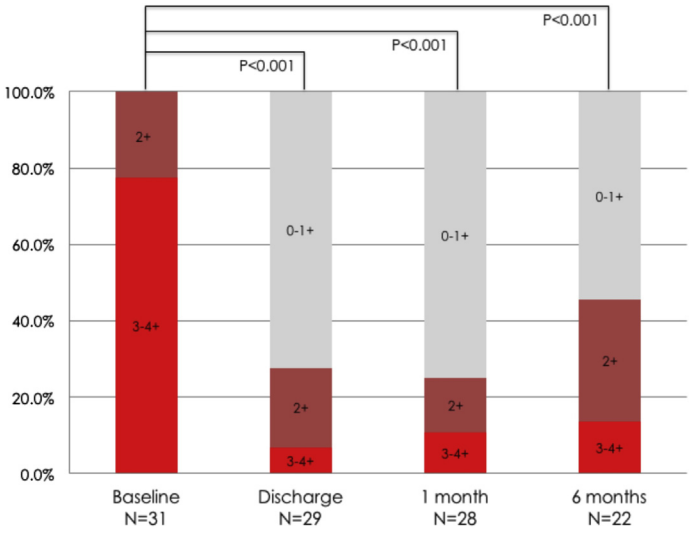
TABLE 1 Baseline Characteristics (N = 31)

Age, yrs	71.8 ± 6.9 (55.0–81.5)
Male	26 (83.9)
Medical history	
EuroSCORE I*	18.1 ± 11.9 (2.9–50.8)
EuroSCORE II*	8.6 ± 5.9 (1.5–21.6)
NYHA functional class III or IV	97
EF, %	34 ± 11 (15–59)
MR etiology	
Ischemic	19 (61)
Nonischemic	12 (39)
Systemic hypertension	20 (65)
Diabetes	14 (45)
Dyslipidemia	18 (58)
Renal insufficiency	
Moderate	9 (35)
Severe	15 (58)
Moderate or severe PH	24 (77)
Arrhythmias	
AFib	24 (77)
AFL	1 (4)
VT	1 (4)
Prior cardiac interventions or surgeries	
CABG	12 (41)
PCI	10 (32)
ICD implant	10 (32)
PM implant	8 (26)
CRT implant (n = 26)	7 (27)

Values are mean ± SD (range) or n (%). *EuroSCORE I and II was not available in 5 subjects.

AFib = atrial fibrillation; AFL = atrial flutter; CABG = coronary artery bypass grafting; CRT = cardiac resynchronization therapy; EF = ejection fraction; EuroSCORE = European System for Cardiac Operative Risk Evaluation; ICD = internal cardioverter-defibrillator; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PH = pulmonary hypertension; PM = pacemaker; VT = ventricular tachycardia.

FIGURE 3 MR Severity From Baseline to 6 Months



MR = mitral regurgitation.

collection were death (n = 3), withdrawal of informed consent (n = 2), implantation of a MitraClip (Abbott Vascular, Santa Rosa, California) (n = 2; those patients had to be excluded from efficacy data collection), 1 patient had a phone visit at 6 months, he denied personal attendance (partial data collection), and 1 patient was lost to follow-up (the patient had moved to another part of the country without available contact details).

PROCEDURAL SUCCESS AND SAFETY. Procedural success rate, defined as delivery of the entire device, was achieved in all patients. The procedure was well tolerated with no periprocedural deaths or severe adverse events. Technical success rate, defined as complete implantation and reduction of septolateral dimension, was achieved in 29 of 31 patients (93.6%). The mean procedural time was 165 ± 44 min (range 100 to 282 min). In 1 case 2 anchors were not implanted at the posterior commissure due to technical difficulties in the early phase of the experience. In the second case the implant size could not be reduced due to technical failure.

Septolateral dimension was reduced from 3.67 ± 0.47 cm before the procedure to 2.46 ± 0.37 mm 1 month after the procedure with a sustained effect at 6 months at 2.41 ± 0.44 cm ($p < 0.001$).

MITRAL REGURGITATION. As adjudicated by the core lab, all patients at baseline had ≥2+ MR, and 77.4% had 3 to 4+ MR. No patient had MR grade 3 to 4+ after the Cardioband implantation. Figure 3 shows the severity of MR over time. At 1 month, 75% of the patients had 0 to 1+ MR, and 10.7% of the patients remained with 3 to 4+ MR. After 6 months, 13.6% had 3 to 4+ MR, 31.8% had 2+ MR, and 54.5% of the patients had 0 to 1+ MR ($p < 0.001$ compared to baseline).

Table 2 shows data for regurgitation volume, vena contracta, proximal isovelocity surface area, and effective regurgitant orifice area, which were all significantly reduced by the Cardioband implantation ($p < 0.01$) at 1 month as well as at 6 months.

Left ventricular volumes were not significantly altered after 6 months when compared with baseline measurement (left ventricular end-diastolic volume index: 93.4 ± 21.3 ml and 89.2 ± 21.9 ml, respectively; $p = 0.8$; left ventricular end-diastolic strain index: 59.7 ± 21.9 ml and 62.0 ± 19.3, respectively; $p = 0.8$). Left ventricular ejection fraction and

TABLE 2 Echocardiography During 6 Months

Parameter	Baseline (1)	30 Days (2)	6 Months (3)	p Value (1-2)	p Value (1-3)	p Value (2-3)
LVEF				n = 24	n = 20	n = 20
	0.37 ± 0.11	0.34 ± 0.10	0.31 ± 0.08	0.382	0.022	0.190
	0.35 (0.30–0.43)	0.33 (0.26–0.41)	0.30 (0.26–0.37)	0.475	0.030	0.212
VCW				n = 13	n = 7	n = 7
	0.57 ± 0.008	0.45 ± 0.10	0.50 ± 0.10	<0.001	0.007	0.125
	0.59 (0.47–0.63)	0.43 (0.38–0.45)	0.48 (0.47–0.57)	0.002	0.018	0.108
PISA radius				n = 12	n = 11	n = 10
	0.78 ± 0.13	0.63 ± 0.24	0.64 ± 0.21	0.021	0.007	0.687
	0.84 (0.68–0.87)	0.58 (0.46–0.77)	0.64 (0.48–0.84)	0.034	0.010	0.646
PISA EROA				n = 12	n = 11	n = 10
	0.28 ± 0.11	0.17 ± 0.13	0.20 ± 0.15	0.047	0.090	0.652
	0.26 (0.18–0.39)	0.13 (0.09–0.25)	0.15 (0.08–0.29)	0.060	0.050	0.646
PISA RVol				n = 12	n = 11	n = 10
	38.5 ± 12.5	26.9 ± 23.1	27.1 ± 20.6	0.080	0.063	0.798
	36.8 (27.7–50.1)	19.5 (12.3–35.0)	24.5 (11.6–37.1)	0.050	0.050	0.575
sPAP				n = 11	n = 10	n = 10
	44 ± 12.7	37 ± 6.5	41 ± 13.5	0.055	0.210	0.162
	40 (36–51.5)	37 (32–42.5)	37 (31.5–47.5)	0.062	0.221	0.307

Values are mean ± SD or median (interquartile range). Regurgitant volume (RVol) was calculated with the effective regurgitant orifice area (EROA) method. Systolic pulmonary artery pressure (sPAP) was calculated with flow measurement over tricuspid insufficiency.

LVEF = left ventricular ejection fraction; PISA = proximal isovelocity surface area; VCW = vena contracta width.

pulmonary systolic pressure did not change significantly over time.

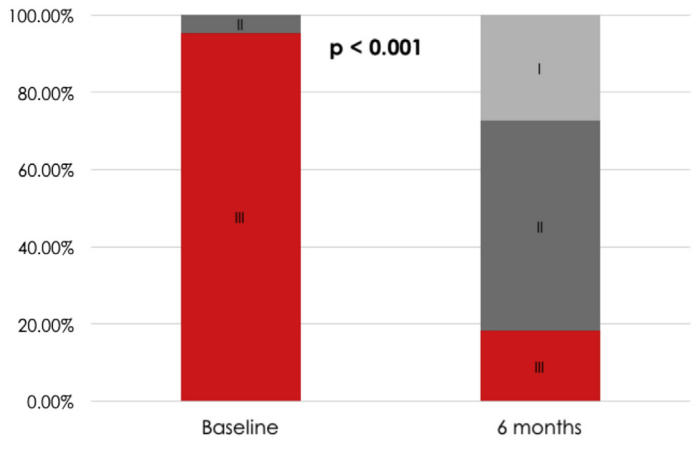
CLINICAL OUTCOME. Rehospitalization for heart failure occurred in 10 patients (32%) within 6 months. Mortality rate was 9.6% at 6 months (3 of 31). One death occurred due to hemorrhagic stroke 9 days after the procedure, 1 death due to multiorgan failure and sepsis 30 days following elective open heart surgery, and 1 death occurred 4 months after the procedure after a planned internal cardioverter-defibrillator battery replacement with sepsis and subsequent severe septic shock. All 3 deaths were unrelated to the device. All were adjudicated as unrelated to the implant or the procedure by the independent Clinical Events Committee. One patient died of intracranial bleeding, 1 of unrelated infection, and 1 in the post-operative period after open heart surgery. At baseline 95.5% of the patients had NYHA functional class III status. After 6 months, 18.2% of the patients had NYHA functional class III symptoms, 54% had NYHA functional class II symptoms, and 27% had NYHA functional class I symptoms ($p < 0.001$) (Figure 4).

The distance on the 6-min walking test (6MWT) increased from 250 ± 107 m at baseline to 332 ± 118 m after 6 months (Figure 5).

Quality of life as assessed by Minnesota Living With Heart Failure Questionnaire improved over the 6-month follow-up from 38.2 ± 21 to 18.1 ± 10.9 (Figure 6).

There was no significant difference between patients with ischemic (n = 18) versus nonischemic (n = 13) in change in degree of MR, 6MWT distance, Minnesota Living With Heart Failure Questionnaire score, and NYHA functional class.

FIGURE 4 Stapled Columns of NYHA Functional Classification Before Treatment and After 6 Months



NYHA = New York Heart Association.

DISCUSSION

The results of this first human feasibility study demonstrated that transcatheter, transseptal direct annuloplasty with the Cardioband device is feasible and safe in surgical high-risk patients with FMR, impaired left ventricular function, and symptomatic heart failure. The observed reduction of FMR severity after 6 months is comparable to that seen with surgery and was associated with significant improvement of exercise capacity and quality of life in the treated patient group. In the context with available treatment strategies, this approach has the potential to become a new therapeutic option for high-risk FMR patients.

PROGNOSTIC IMPACT OF FMR IN FAILING HEARTS. FMR affects up to 25% to 65% of heart failure patients with ischemic or dilated cardiomyopathy (12,13) and observational studies suggest that chronic FMR not only aggravates heart failure related symptoms in patients with depressed left ventricular function but also worsens the outcomes of the affected patients (8–10,14). MR reduction has the potential to improve outcomes in patients with FMR and current

guidelines propose early treatment of FMR if effective regurgitant orifice area exceeds 20 mm^2 (15).

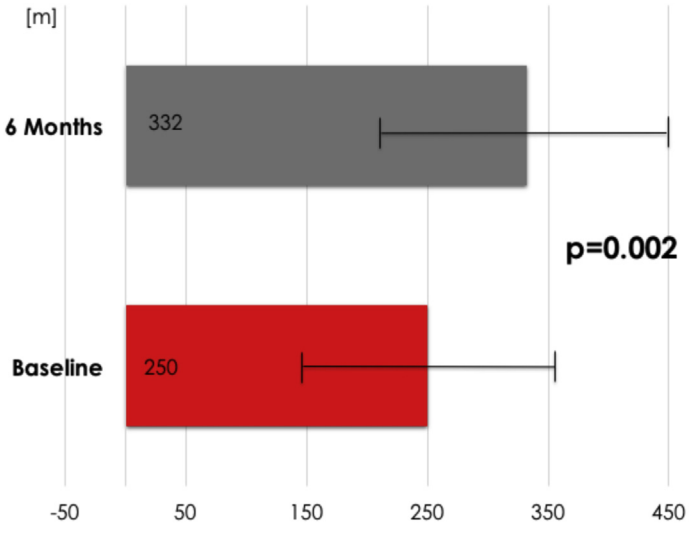
AVAILABLE TREATMENT OPTIONS. Due to advanced left ventricular dysfunction and the frequent presence of comorbidities, isolated surgical repair of FMR is usually not a viable treatment option, and current guidelines do not recommend isolated valve surgery in high- risk heart failure patients. Indeed, the prognostic survival benefit of adding MV surgery even to bypass surgery alone in patients with at least moderate FMR at need for surgical revascularization has not been demonstrated. Although patients may benefit in terms of improved exercise capacity, the recurrence rate of FMR after surgical annuloplasty is reported to be high up to 32% after 1 year (7) and 58.8% at 2 years (16). The perception today is that the success of annuloplasty in FMR is predominantly related to the specific pathoanatomy causing mitral malcoaptation. This is part of the ongoing clinical investigation on refinements in patient selection.

Due to its favorable safety profile, the Cardioband system is a promising new treatment option for high-risk patients. In this early study no intraprocedural or device-related death occurred and serious adverse events were few during and after the intervention. This safety aspect could offer an invaluable advantage of repair strategies in comparison to surgical approaches or current catheter-based methods of valve replacement.

TRANSCATHETER APPROACHES FOR MV DISEASE. In FMR the valve leaflets themselves are not primarily pathologic but fail to coapt due to left ventricular dilation leading to annular dilation or tethering of the valve apparatus. In contrast, (primary) degenerative MR is characterized by a primary leaflet abnormality.

Since its introduction into clinical routine in 2008, approximately 30.000 patients have undergone interventional edge-to-edge repair of MR with the MitraClip system. Although the MitraClip was developed to mimic the surgical approach of creating a double orifice MV in (primary) degenerative MR, the preponderance of use has been in patients with FMR (17,18). In the EVEREST (Endovascular Valve Edge-to-Edge REpair Study) cohort, insertion of the MitraClip led to an anteroposterior annular reduction persistent at 5 years (19) and we were able to show, that this might impact on procedural outcomes in FMR patients (20). The ongoing COAPT (Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy) study is comparing the use of the MitraClip with guideline-directed medical therapy to guideline-directed medical therapy alone in FMR with heart failure.

FIGURE 5 6MWT Before Annuloplasty and After 6 Months

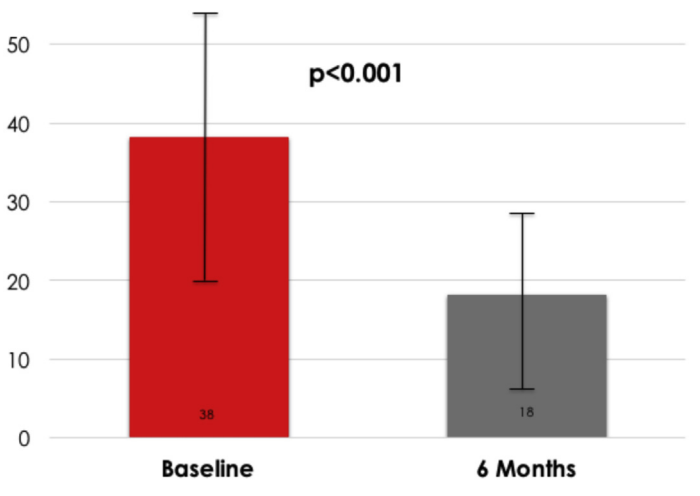


m = meters; 6MWT = 6-min walking test.

Compared to the MitraClip, implantation of the Cardioband led to a similar reduction of MR severity. Direct annuloplasty with the Cardioband has the advantage that it does not preclude future surgical or interventional approaches such as transcatheter MV insertion, or even the combination with the edge-to-edge repair technique.

Indirect annuloplasty by an interventional approach via the coronary sinus with the Carillon system (Cardiac Dimension Inc., Kirkland, Washington) has

FIGURE 6 MLHFQ Score Before Treatment and After Six Months



MLHFQ = Minnesota Living with Heart Failure questionnaire.

been tested in a proof of concept study on 41 patients (21). Despite the fact that this approach seems less invasive, implant success rates were lower when compared with the Cardioband and the reported effects on MR severity and MV anatomy were only moderate. Outcome data including larger series are not available. A possible reason for the unpredictable effect of this technique might be the indirect approach by applying pressure on the MV annulus and the variability of each individuals' sinus anatomy.

In this context the new Cardioband device offers several potential advantages: first, the reduction of annular dimensions appears to be similar to surgical repair strategies. Second, the Cardioband implantation and subsequent cinching reduces FMR very effectively. More importantly, the cinching grade can be adjusted to the acute effect on MR measured by TEE on the beating heart allowing for intraprocedure optimization to maximally reduce MR severity.

Third, we were able to show that FMR reduction was associated with substantial clinical improvement as assessed by 6MWT and NYHA functional class at 6 months. However, rehospitalization for heart failure occurred in 32% of treated patients and one should be aware of the fact that despite significant improvements in MR severity, treated patients still need close clinical follow-up.

STUDY LIMITATIONS. Our report is an early feasibility study and as such enrolled a limited number of patients without a control group and the follow up is limited to 6 months. We therefore cannot assess longer-term durability of the MR reduction as well as long-term clinical outcomes as supposed by the Mitral Valve Academic Research Consortium (22). Due to the limited patient numbers we were not able to analyze the impact of underlying pathoanatomy on procedural success rates and MR recurrence after 6 months (eccentric MR, left ventricular aneurysm). This must be evaluated with future studies in this field. Longer follow-up data are also needed to show the impact of FMR reduction on left ventricular remodeling and function, which will be addressed in this ongoing study when a substation number of patients completed 12-month follow-up procedures. Due to the limited number of included subject statistical results must be interpreted with caution, significant tests could be specious and nonsignificant findings could simply lack of power.

CONCLUSIONS

In patients with impaired left ventricular function, FMR, and heart failure, mitral annuloplasty with the transcatheter Cardioband system is feasible and safe. Annular dimension and FMR are significantly reduced and is associated with decreased heart failure symptoms and increased exercise capacity.

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PERSPECTIVES

WHAT IS KNOWN? FMR increases morbidity and mortality in patients witch chronic heart failure and the current gold standard—surgical annuloplasty—is often denied in such patients because of a prohibitive surgical risk.

WHAT IS NEW? Interventional annuloplasty with a dedicated device is safe and effective in surgical high-risk heart failure patients.

WHAT IS NEXT? Future studies will have to improve patient selection and show long-term durability of interventional annuloplasty and its impact on patients' survival.

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KEY WORDS direct annuloplasty, functional mitral regurgitation, heart failure, transcatheter mitral repair

APPENDIX For supplemental figures and a table, please see the online version of this article.