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Transcatheter Implantation of the MONARC Coronary Sinus Device for Mitral Regurgitation

1-Year Results From the EVOLUTION Phase I Study (Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for The Treatment of Mitral Regurgitation)

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Objectives This study sought to assess the safety and efficacy of transcatheter valve annuloplasty in patients with mitral regurgitation (MR).

Background Mitral regurgitation is associated with a worsened prognosis in patients with dilated cardiomyopathy. Surgical mitral annuloplasty reduces the septal-lateral dimension of the mitral annulus resulting in improved leaflet coaptation with a reduction in regurgitation. Percutaneous annuloplasty with the MONARC device (Edwards Lifesciences, Irvine, California) implanted within the coronary sinus is designed to reduce mitral regurgitation through a similar mechanism.

Methods A total of 72 patients with MR grade ≥2 were enrolled at 8 participating centers in 4 countries. Clinical evaluation and transthoracic echocardiography were performed at baseline and at 3, 6, and 12 months. Multislice cardiac computed tomography and coronary angiography were performed at baseline and 3 months.

Results The MONARC device was implanted in 59 of 72 patients (82%). The primary safety end point (freedom from death, tamponade, or myocardial infarction at 30 days) was met in 91% of patients at 30 days and in 82% at 1 year. Computed tomography imaging documented passage of the great cardiac vein over an obtuse marginal artery in 55% of patients and was associated with angiographic coronary artery compression in 15 patients and myocardial infarction in 2 patients (3.4%). At 12 months, a reduction in MR by ≥1 grade was observed in 50.0% of 22 implanted patients with matched echocardiograms and in 85.7% of 7 patients with baseline MR grade ≥3.

Conclusions Implantation of the MONARC device in the coronary sinus is feasible and may reduce MR. However, coronary artery compression may occur in patients in whom the great cardiac vein passes over a coronary artery, necessitating strategies in future studies to avoid this occurrence. (J Am Coll Cardiol Intv 2011;4:115–22) © 2011 by the American College of Cardiology Foundation

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Functional mitral regurgitation (MR) frequently develops in patients with heart failure and a dilated left ventricle due to papillary muscle displacement, leaflet tethering, and progressive mitral annular dilation. This may lead to a vicious cycle of worsening heart failure and MR. Late prognosis is determined, in part, by the severity of MR (1–3).

Treatment options for functional MR are limited. Pharmacological therapy and resynchronization pacing may reduce MR and improve outcome in selected patients (1,4,5). Although surgical repair of the mitral valve may reduce MR, mortality and morbidity are significant and recurrence is common (6,7). Patients with MR have a poor prognosis despite medical, resynchronization, or surgical therapy (8–12). Consequently, there is considerable interest in lesser invasive approaches to treat MR in patients with ischemic and dilated cardiomyopathy.

We recently reported our initial experience with a first-generation catheter-based coronary sinus (CS) device designed to address MR (13). We now report the safety and efficacy of a modified second-generation device in patients with clinical and echocardiographic follow-up for 1 year.

Abbreviations and Acronyms

AIV = anterior interventricular vein
CS = coronary sinus
CT = computerized tomography
GCV = great cardiac vein
MI = myocardial infarction
MR = mitral regurgitation
NYHA = New York Heart Association

Methods

Patient selection. Patients were eligible if they had heart failure and dilated cardiomyopathy (ischemic or idiopathic) with MR grade ≥2 (on a scale of 0 to 4) as assessed by color flow criteria on transthoracic echocardiography. Coronary sinus anatomy was considered suitable for the MONARC device if the proximal anterior interventricular vein (AIV) was ≥3 mm and ≤6 mm in diameter, the ostial CS was ≥7 mm and ≤16 mm in diameter, and the length from the great cardiac vein (GCV) to the ostial CS was ≥14 cm and ≤18 cm.

Exclusion criteria included structural valve disease including endocarditis, rheumatic disease, or moderate-to-severe mitral valve prolapse. Patients with pre-existing implantable defibrillators, CS leads for biventricular pacing, left ventricular ejection fraction <25%, prior percutaneous coronary intervention within 3 months, moderate-to-severe mitral annular calcification, serum creatinine >2.0 mg/dl, or inability to comply with all protocol procedures were also excluded. Patients received aspirin 180 to 325 mg and clopidogrel 300 mg before the procedure and continued on daily doses of aspirin ≥81 mg indefinitely and clopidogrel 75 mg for 3 months. Written informed consent and hospital ethics committee approval were required.

Device description. The MONARC system consists of a 12-F guide catheter and dilator, a 9-F delivery catheter, and a nickel-titanium alloy (nitinol) implant. The implant has 3 sections: a distal self-expanding anchor, a springlike "bridge," and a proximal self-expanding anchor. The distal anchor is deployed at the transition between the AIV and the GCV; the proximal anchor is deployed in the ostial CS (Fig. 1). The anchors are designed such that they remain firmly in place acutely and encourage tissue in-growth, which provides a secure platform at both ends of the device. A biodegradable component is incorporated within the springlike bridge and maintains the device in an elongated state at the time of implantation. After implantation, the biodegradable element absorbs over approximately 1 month, creating an active and sustained spring tension between the anchors. Shortening of the device is designed to reduce the septal-lateral dimension of the mitral valve and thereby improve leaflet coaptation (Fig. 1).

The first-generation MONARC device developed a fracture in the bridge segment that resulted in device separation during follow-up in 3 of 5 patients (13). Bridge separation did not cause adverse events but may have reduced the efficacy of the device. Therefore, a nonbiodegradable suture was added to reinforce the bridge segment and reduce the likelihood of separation of the device following implantation. This second-generation MONARC device was tested in the present study. Available device sizes during this study ranged in length from 120 to 159 mm, with proximal and distal anchor diameters of 10 to 18 mm and 6 to 8 mm, respectively.

Implant procedure. The internal jugular vein is accessed percutaneously and a guiding catheter used to cannulate the CS (13). A steerable guidewire is advanced to the AIV over which a calibrated angiographic catheter (Cook Medical Inc., Bloomington, Indiana) is placed to facilitate measurement of the coronary venous anatomy. A MONARC device is selected with anchors 2 to 4 mm larger in diameter than the proximal AIV and CS and a length 2 cm shorter than the distance between these 2 sites. The MONARC delivery catheter is advanced over the guidewire and through the guiding catheter. The distal anchor is deployed at the junction of the AIV and GCV by retracting the outer restraining sheath. The device is tensioned slightly to remove slack, following which the sheath is retracted further to release the proximal anchor.

Study end points. The primary safety end point was the freedom from the composite occurrence of death, tamponade, or myocardial infarction (MI) at 30 days. A secondary safety end point was freedom from the composite occurrence of device embolization or migration from the target area, death, MI, CS thrombosis, or pulmonary embolism at 3 months. The primary efficacy end point was procedural success, defined as device deployment at the intended location without the occurrence of serious adverse events (death, tamponade, or MI). The secondary efficacy end point was a reduction in mitral regurgitation by ≥1 grade.

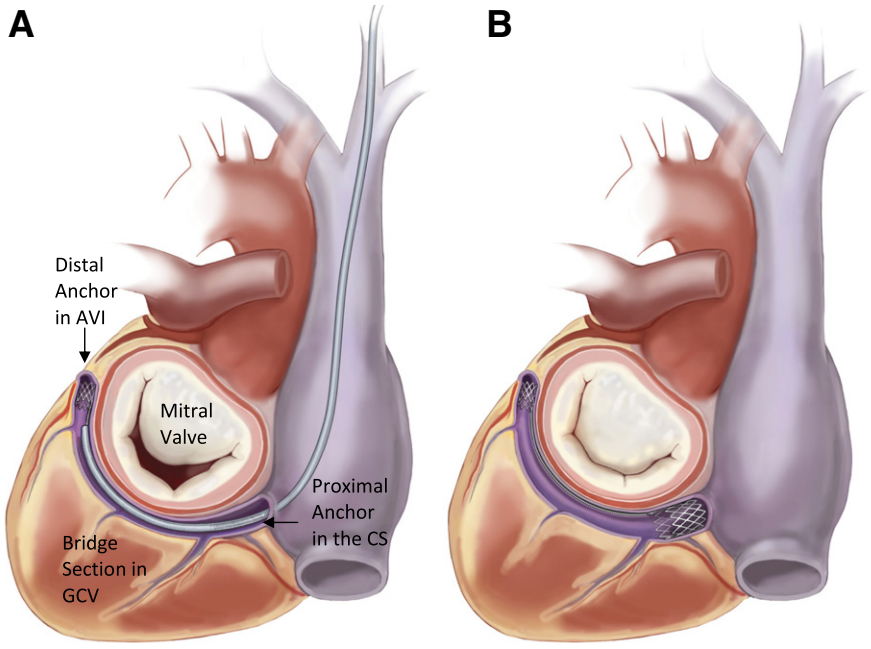

Figure 1. The Mode of Action of the MONARC Device

The MONARC device encircles the posterior leaflet of the mitral valve in systole at implant **(A)** and in its activated state **(B)**. The small distal anchor is positioned in the anterior interventricular vein, the springlike bridge section is positioned in the great cardiac vein, and the large proximal anchor is positioned in the ostium of the coronary sinus. The bridge section shortens during the first month after implantation. The putative mechanism of action is a reduction of the septal-lateral diameter of the mitral annulus with improved coaptation of the leaflets and a reduction in mitral regurgitation. AIV = anterior interventricular vein; CS = coronary sinus; GCV = great cardiac vein.

Patients were followed at discharge and at 1, 3, 6, and 12 months.

Imaging and core laboratory analysis. An electrocardiogram was obtained before and after the implant procedure. Transthoracic echocardiography was performed before the implant, at discharge, and at 1, 3, 6, and 12 months of follow-up. Transesophageal echocardiography was performed before the implant and at 3-month follow-up and analyzed at a core laboratory (Cardiovascular Research Institute, Washington, D.C.). Coronary angiography was performed before the implant procedure and at 3-month follow-up and analyzed at a core laboratory (University of Colorado Health Science Center, Denver, Colorado). Computerized tomographic (CT) scans were performed before and 3 months after the implant procedure and analyzed at a core laboratory (Ohio State University Medical Center, Columbus, Ohio). Chest X-rays were obtained at discharge and at 1, 6, and 12 months of follow-up. Creatine kinase, creatine kinase-myocardial band, and troponins were measured after the procedure and as indicated for suspicion of recurrent ischemia.

Statistical methodology. Analysis of safety end points was performed in all patients. Analysis of efficacy was performed only in patients with implanted devices. Paired *t* tests and Wilcoxon signed rank tests were used to assess the differences from baseline to follow-up of continuous and ordinal variables, respectively. A p value of <0.05 was considered significant.

Results

Baseline features and implantation procedures. A total of 72 patients were enrolled between October 2005 and March 2007 at 8 participating centers in Canada, France, Germany, and Sweden. The mean age was 70.0 ± 9.8 years (range 37 to 90 years); 20 (18%) were women. Diabetes was present in 17 patients (24%), hypertension in 39 (54%), and hypercholesterolemia in 39 (54%). Most patients (68%) had underlying coronary artery disease, as manifested by a history of prior MI (57%), and/or coronary arterial bypass graft (47%) and/or percutaneous coronary intervention (40%). The baseline New York Heart Association (NYHA) class was I in 4%, II in 42%, III in 50%, and IV in 4%. The mean left ventricular ejection fraction was 37.8 ± 10.7% (range 23% to 67%). Mitral regurgitation at baseline as assessed by the core laboratory (transthoracic echocardiography in 59 patients and transesophageal echocardiography in 13 patients) was grade 1+ in 8%, grade 2+ in 54%, grade 3+ in 21%, and grade 4+ in 17%.

Table 1. Major Adverse Cardiovascular Events at 1 Year

Event	Cause
Tamponade (n = 2)	
Day 1	Wire perforation*
Day 6	Wire perforation*
Myocardial infarction (n = 2)	
Day 16	Diagonal artery compression due to distal anchor
Day 19	Obtuse marginal artery compression due to bridge
Death (n = 8)	
Day 22	Arrhythmia (intractable ventricular fibrillation)
Day 24	Heart failure
Day 51	Sudden cardiac death while being treated for erysipelas
Day 52	Fall leading to intracranial hemorrhage
Day 61	Pulmonary embolism
Day 96	Multiorgan system failure following post mitral valve surgery
Day 141	Heart failure
Day 280	Heart failure

*Non–J-tipped wire used.

The device was implanted in 59 of 72 patients (82%). In the other 13 patients, a device was not implanted due to excessive tortuosity of the coronary venous anatomy or the lack of appropriately sized devices. In 1 of the patients with a tortuous sinus, there was an intraprocedural small dissection of the sinus during guidewire manipulation. The case was abandoned. Post-procedural echocardiography confirmed no pericardial effusion. Procedure time was 84 ± 59 min. Hospital stay was 4.1 ± 4.7 days.

Adverse events. Among the 72 enrolled patients, the primary safety end point of freedom from the occurrence of death, tamponade, or MI at 30 days was 91% at 30 days and 82% at 12 months. The secondary safety end point was achieved in 87% of patients at 3 months, 83% at 6 months, and 81% at 1 year.

Major adverse cardiovascular events are summarized in Table 1. Coronary sinus perforation resulted in 2 cases of tamponade early in the study from use of a stiff straight tipped wire; this complication did not recur with a change to J-tipped guidewires. Following discharge, MI occurred in 2 patients. One patient presented at day 16 with compression of a diagonal artery by the distal anchor. A second patient presented at day 19 with compression of an obtuse marginal artery. This site was stented with patency documented at 1-year follow-up.

There were no in-hospital deaths. None of the late deaths (8) were attributable to the procedure or device (Table 1). The survival rate was at 97%, 92%, 89%, and 87% at 1, 3, 6, and 12 months, respectively. Other adverse secondary safety end point events through 1-year follow-up included pulmonary embolism in 1 patient and device migration in 1 patient. There were no cases of device embolization or CS thrombosis.

Device malfunctions and coronary compressions. Routine follow-up coronary angiography at 3 months in 50 of 59 implants revealed 4 cases (8%) of separation of the bridge from the proximal anchor. No adverse clinical events were associated with anchor separation. However, only 1 of these 4 patients had an improvement in the degree of MR (compared with baseline) at follow-up.

Of 50 patients with implanted devices in whom follow-up angiography was performed, some degree of coronary artery compression was noted in 15 patients (30%): 5 were distal anchor-related, 9 were bridge-related, and 1 patient had both. The stenosis severity assessed by the angiographic core laboratory was >50% in 4 patients (8%) (Table 2). Among the 15 patients with angiographic coronary artery compression, 2 (13.3%) suffered a myocardial infarction.

Core laboratory analysis of CS anatomy by CT was available in 42 patients. The CS/GCV was observed to pass over a major obtuse marginal artery in 23 patients (55%), 8 of whom (34.8%) had angiographic coronary artery compression. In contrast, the CS/GCV did not pass over a major obtuse marginal artery in 19 patients, none of whom developed coronary compression.

Efficacy analysis. Among the 59 patients in whom a device was implanted, the in-hospital procedural success rate was 93% (n = 55). In 4 patients, the proximal anchor was released outside the intended range of >0.5 to <2 cm from the CS ostium. Although this was not associated with adverse events, only 1 of these 4 patients had a reduction in MR at last follow-up. The secondary end point occurred in 87% of patients at 3 months, 83% at 6 months, and 81% at 1 year (Fig. 2).

Table 2. Patients With Coronary Arterial Compression. Quantitative Angiographic Analysis Through 12 Months

Patient #	Vessel Diameter Baseline (mm)	Stenosis Baseline (%)	Stenosis 90 Days (%)
102	3.1	0	30
258	3.1	1	31
259	3.7	0	42
007	2.5	10	44
121	2.3	17	45
053*	0.9	37	100
019	1.3	20	48
006	1.8	19	79
119†	2.1	17	99
256‡	1.2	59	100

*Occlusion of a diagonal artery documented at day 16. This appeared due to compression by an anchor in the anterior interventricular vein. Spontaneously recanalized at day 90. †Occlusion of an obtuse marginal artery at day 19. Presented with acute myocardial infarction. Successfully stented. ‡Occlusion of a small obtuse marginal artery. No clinical event.

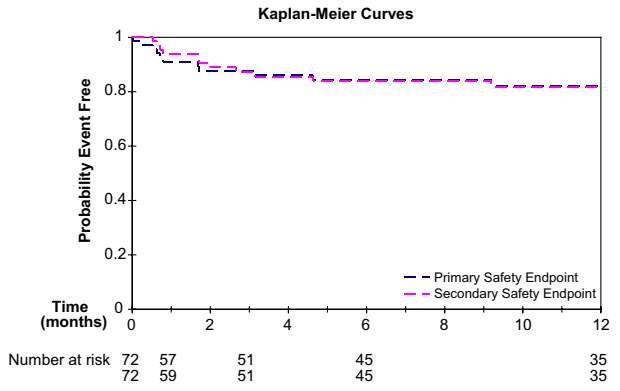

Figure 2. Probability of Event-Free Survival After MONARC Implantation

Kaplan-Meier curves for freedom from the composite occurrence of death, tamponade, or myocardial infarction and freedom from the composite occurrence of device embolization or migration from the target area, death, myocardial infarction, coronary sinus thrombosis, or pulmonary embolism.

The secondary efficacy end point (responder rate) is displayed in Figure 3 for 22 patients with matched data, in whom all transthoracic echocardiograms were completed within the pre-specified protocol windows (the results when all unmatched data were included were comparable—data not shown). In these 22 patients, the mean grade of MR was 2.5 ± 0.7 at baseline and 1.8 ± 0.8 at 12 months ($p = 0.002$). Mitral regurgitation decreased by ≥1 grade from baseline to follow-up in 40.9% of patients at 3 months and in 50.0% of patients at 6 months and 1 year. Moreover, the response rate appeared to be higher in the 7 patients with baseline grade ≥3+ MR compared with the 15 patients with only grade 2+ MR at baseline. The responder rate at 12 months was 85.7% in patients with severe MR at baseline (grade ≥3+) in whom the mean MR grade was reduced from 3.4 ± 0.5 at baseline to 2.1 ± 0.9 at last follow-up. Significantly fewer patients with a baseline MR grade of 2+ responded (Fig. 3).

Effects on left ventricular structure and function. Serial changes in quantitative echocardiographic variables are shown in Table 3. Although not powered or tested for statistical significance, directional reductions were present from baseline to follow-up in mitral valve annular diameter, effective regurgitant orifice area, regurgitant volume, left atrial volume, left ventricular end diastolic volume, left ventricular end systolic volume, and left ventricular ejection fraction.

Changes in NYHA functional class. In the paired analysis, 26 of 47 surviving patients at 6 months (55.3%) had at least 1 NYHA functional class improvement (including 12 patients who were NYHA class I), and 5 patients improved by at least 2 NYHA classes. NYHA functional class progressed at 6 months in only 2 patients. At 12 months, 19 of 41 surviving patients (46.3%) had at least 1 NYHA class improvement (including 9 patients in NYHA class I), and 6 patients improved by at least 2 NYHA classes. Only 1 patient had functionally deteriorated.

Other late clinical events. Five patients who did not have a clinically adequate reduction in MR following MONARC device implantation subsequently underwent mitral valve surgery at days 70, 110, 164, 222, and 232, respectively (ring annuloplasty in 2 patients and mitral valve replacement in 3 patients). Surgery was not influenced by the presence of the study implant. One patient died after surgery from multiorgan failure, and 4 patients had an uncomplicated postoperative course with significant reduction in MR.

Five patients who had persistent heart failure subsequently underwent implantation of a coronary sinus lead for biventricular pacing at days 109, 149, 170, 222, and 357 after device implantation. The placement of the lead was not hampered by the presence of the MONARC implant (14) and served as a convenient landmark for the CS ostium.

Discussion

The 12-month results of the multicenter prospective, nonrandomized EVOLUTION phase I trial (Clinical Evaluation of the Edwards Lifesciences Percutaneous Mitral Annuloplasty System for the Treatment of Mitral Regurgitation) demonstrate the feasibility of a gradually foreshortening indirect acting mitral annuloplasty system delivered into the coronary sinus via a percutaneous jugular venous approach to reduce MR in patients with dilated and ischemic cardiomyopathy. Compared with other percutaneous mitral valve repair technologies, the MONARC procedure is relatively straightfor-

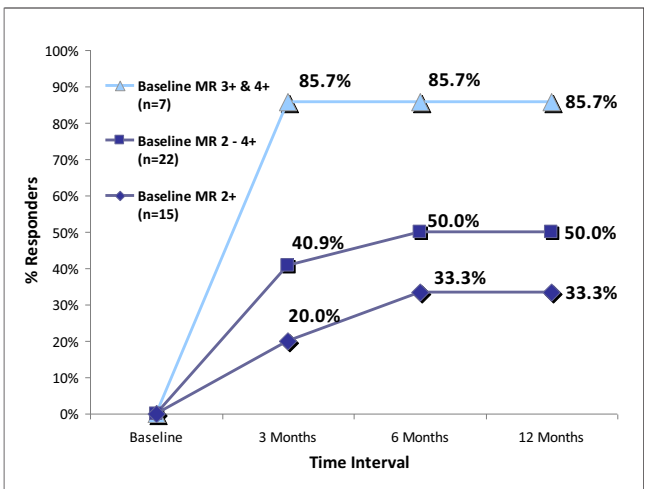

Figure 3. 1-Year Echo Outcome of MR Severity

Percentage of patients with improvement in mitral regurgitation by ≥1 grade. Serial paired transthoracic echocardiograms in patients with complete data (**squares,** n = 26), with baseline mitral regurgitation grade ≥3+ **(triangles)**, and with baseline regurgitation grade 2+ (**diamonds**).

Table 3. Serial Quantitative Echocardiographic Measurements

Time	n	Baseline	Follow-Up	% Δ	p Value	n	Baseline	Follow-Up	% Δ	p Value
	Mitral Valve Annular Diameter (cm)					EROA (cm^2)				
Discharge	46	3.61 ± 0.42	3.51 ± 0.42	−3%	0.01	20	0.31 ± 0.23	0.25 ± 0.19	−24%	<0.01
1 month	43	3.57 ± 0.39	3.50 ± 0.37	−2%	0.16	18	0.27 ± 0.20	0.25 ± 0.17	−8%	0.39
3 months	35	3.54 ± 0.37	3.42 ± 0.42	−4%	0.05	25	0.23 ± 0.18	0.19 ± 0.13	−21%	0.12
6 months	35	3.61 ± 0.40	3.36 ± 0.45	−7%	<0.01	26	0.24 ± 0.18	0.17 ± 0.15	−41%	0.03
12 months	27	3.62 ± 0.42	3.32 ± 0.39	−9%	<0.01	19	0.22 ± 0.11	0.16 ± 0.10	−38%	0.12
	Left Ventricle Ejection Fraction (%)					Regurgitant Volume (ml)				
Discharge	29	37.4 ± 10.9	39.1 ± 10.6	4%	0.12	21	40.4 ± 24.6	31.6 ± 20.3	−28%	<0.01
1 month	32	37.2 ± 10.6	38.6 ± 12.2	4%	0.29	18	37.7 ± 20.9	31.5 ± 16.8	−20%	0.14
3 months	34	34.8 ± 9.9	35.5 ± 10.1	2%	0.59	25	33.7 ± 21.9	28.6 ± 16.6	−18%	0.27
6 months	34	36.2 ± 10.4	37.5 ± 9.2	3%	0.29	25	34.6 ± 21.9	23.2 ± 14.3	−49%	0.02
12 months	26	36.8 ± 9.9	40.2 ± 8.3	8%	0.08	19	31.8 ± 16.1	25.0 ± 15.1	−27%	0.14
	Left Ventricle End-Systolic Volume (ml)					Left Ventricle End-Diastolic Volume (ml)				
Discharge	29	109.9 ± 44.9	104.3 ± 50.2	−5%	0.08	29	170.1 ± 54.7	165.1 ± 64.4	−3%	0.26
1 month	32	111.3 ± 56.3	102.8 ± 46.2	−8%	0.20	32	170.6 ± 71.0	163.3 ± 62.0	−4%	0.23
3 months	34	118.4 ± 50.0	111.2 ± 41.8	−6%	0.25	34	175.8 ± 60.6	169.8 ± 57.7	−4%	0.36
6 months	34	116.0 ± 54.7	111.6 ± 53.4	−4%	0.44	34	175.4 ± 68.2	173.9 ± 74.5	−1%	0.83
12 months	26	114.8 ± 56.8	98.2 ± 37.9	−17%	0.02	26	175.4 ± 72.5	161.9 ± 54.8	−8%	0.05

Time	Left Atrial Volume (ml)				
	n	Baseline	Follow-Up	% Δ	p Value
Discharge	27	129.2 ± 65.0	127.3 ± 65.1	−1%	0.69
1 month	33	113.2 ± 52.0	119.4 ± 50.4	5%	0.14
3 months	33	102.9 ± 43.5	102.7 ± 44.5	0%	0.95
6 months	34	104.4 ± 43.7	100.1 ± 56.1	−4%	0.37
12 months	27	101.5 ± 28.6	98.9 ± 26.9	−3%	0.53

EROA = estimated regurgitant orifice area.

ward and has a short learning curve and procedure time. A majority of patients appeared to have a reduction in MR during follow-up, with the percentage of responders gradually increasing from baseline to 6 months and thereafter stabilizing. Patients with severe MR (grade ≥3+) seemed most likely to benefit.

Major procedural complications included 2 cases of CS perforation occurring due to navigation of the GCV in the early phase of the trial with a straight-tip guidewire. However, the potential for external coronary artery compression when the CS/GCV runs over the obtuse marginal epicardial vessels (which occurs in >50% of patients [15]) emerged as the most important consideration for use of this device. Angiographic follow-up demonstrated some degree of coronary artery narrowing in 30% of patients, which was significant (diameter stenosis >50%) in 8% of patients. This resulted in coronary occlusion in 3 patients, 2 of whom presented with a MI (3.4% of all patients receiving an implant). Patients in whom the anatomic relationship of the coronary venous and arterial anatomy is not a concern may include those with small, occluded, or protected (patent bypass graft) circumflex branches. The present study has also demonstrated that noninvasive screening with CT is able to identify those patients in whom the obtuse marginal vessels course under the CS/GCV who are at risk. Nonetheless, if the potential safety benefits of the MONARC are to be realized, prospective studies are required to demonstrate that procedural and late complications can be avoided.

Whether the gradual nature of MONARC device activation is beneficial compared with acute CS tensioning (16) cannot be answered by this study. The constant and continuous foreshortening of the device over 4 to 6 weeks may allow the heart to progressively remodel. The observation that left ventricular structure and function continued to improve between 3 and 6 months (well after which maximal device contraction has occurred) suggests that the gradual reduction in MR in patients might interrupt the progressive cycle of increasing heart failure and MR, although controlled studies in greater numbers of patients are required to confirm this hypothesis. Finally, compared with other CS technologies, the greater length of the MONARC device with placement of the distal anchor in the AIV may be

important for left ventricular remodeling, as it tends to lift or retract the anterior wall of the ventricle.

Ventricular systole results in significant torquing and bending of CS implants. Bridge fractures with separation, which occurred with the first-generation device (13), were not observed in the present study, attesting to the success of design modifications. However, fractures in the proximal anchor were noted in 4 patients in the present series, which may have contributed to lack of device efficacy. Extending the bridge-section reinforcement to this region of the device may reduce this fracture mode.

Importantly, MONARC device implantation did not appear to interfere with subsequent mitral valve surgery (n = 5) or CS lead placement (n = 5). One patient had previously undergone a Mobius (Edwards Lifesciences) clip implant (17) (an investigational device that used a percutaneous suture to achieve a double outlet mitral valve) and was additionally treated with the MONARC device 3 months later without difficulty. Surgical experience suggests that mitral annuloplasty and edge-to-edge leaflet repair (18) may be synergistic in the treatment of MR.

Additional studies are required to determine the echocardiographic and clinical benefits that may be achieved with the present device. The average 1-grade reduction in MR with the MONARC device is less than what is obtained with surgical mitral valve repair, but may be of some benefit in patients with functional MR, particularly if accomplished with minimal periprocedural morbidity. Moreover, patient inclusion and exclusion criteria may affect the likelihood of a favorable response. The response rate was highest in the patients with more severe grades of MR. More sophisticated echocardiographic assessment may provide additional insight into which patients are likely to benefit with a CS annuloplasty device (1). Surgical series have suggested that improved cardiac performance after mitral valve repair occurs only when the pre-operative left ventricular end diastolic diameter is <65 mm (19).

Study limitations. The present report is the largest study to date of CS annuloplasty. Nonetheless, limitations of this phase I study include the modest sample size, heterogeneity of the study population, incomplete follow-up, and lack of a control group. Analyzable echocardiographic quantitative parameters were not available from all patients at all times. Functional measures of heart failure improvement such as the 6-min walk time and quality-of-life measures beyond NYHA class were not assessed.

Conclusions

The limitations notwithstanding, the present study indicates that implantation of the MONARC device in patients with functional MR is feasible, can be performed at relatively low procedural risk, and may result in a reduction in MR. However, coronary artery compression may occur in patients in whom the CS/GCV courses over the circumflex vessels and may result in late MI. A multicenter evaluation of the MONARC device (EVOLUTION II) is underway to determine the safety and efficacy of this device (with a reinforced proximal anchor) in patients with MR. This study includes pre-procedural CT screening to exclude those at risk for coronary compression of a major epicardial vessel, a concurrent control group, and serial measures of 6-min walk time and quality of life. Ultimately, a randomized controlled trial will be necessary to establish a potential role of the MONARC device in the treatment of patients with MR.

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REFERENCES

1. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. N Engl J Med 2005;352:875–83.
2. Ngaage DL, Schaff HV. Mitral valve surgery in non-ischemic cardiomyopathy. J Cardiovasc Surg 2004;45:477–86.
3. Bax JJ, Braun J, Somer ST, et al. Restrictive annuloplasty and coronary revascularization in ischemic mitral regurgitation results in reverse left ventricular remodeling. Circulation 2004;110 Suppl 1:II103–8.
4. Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation 2001; 103:1759–64.
5. Daubert C, Gold MR, Abraham WT, et al., for the REVERSE Study Group. Prevention of disease progression by cardiac resynchronization therapy in patients with asymptomatic or mildly symptomatic left ventricular dysfunction: insights from the European cohort of the REVERSE (Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction) trial. J Am Coll Cardiol 2009;54:1837–46.
6. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease). J Am Coll Cardiol 2006;52:e18–142.
7. Carpentier AF, Lessana A, Relland JY, et al. The "physio-ring," an advanced concept in mitral valve annuloplasty. Ann Thorac Surg 1995;60:1177–85, discussion 1185–6.
8. Crabtree TD, Bailey MS, Moon MR, et al. Recurrent mitral regurgitation and risk factors for early and late mortality after mitral valve repair for functional ischemic mitral regurgitation. Ann Thorac Surg 2008;85:1537–42.
9. Bursi F, Enriquez-Sarano M, Nkomo VT, et al. Heart failure and death after myocardial infarction in the community. The emerging role of mitral regurgitation. Circulation 2005;111:295–301.
10. Mihaljevic T, Lam BK, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional mitral regurgitation. J Am Coll Cardiol 2007;49:2191–201.
11. Trichon BH, Glower DD, Shaw LK, et al. Survival after coronary revascularisation, with and without mitral valve surgery, in patients with ischemic mitral regurgitation. Circulation 2003;108;Suppl 1:II103–10.
12. Anker MA, Bolling S, Shemin R, et al., for the Acorn Trial Principal Investigators and Study Coordinators. Mitral valve surgery in heart failure: insights from the Acorn Clinical Trial. J Thorac Cardiovasc Surg 2006;132:568–77.

13. Webb JG, Harnek J, Munt BI, et al. Percutaneous transvenous mitral annuloplasty: initial human experience with device implantation in the coronary sinus. Circulation 2006;113:851–5.
14. Mueller D, Tschoepe C, Spencker S. Cardiac resynchronization therapy in a patient with a mitral annuloplasty device. Pacing Clin Electrophysiol 2008;31:1074–6.
15. Maselli D, Guarracino F, Chiaramonti F, et al. Percutaneous mitral annuloplasty: an anatomic study of human coronary sinus and its relation with mitral valve annulus and coronary arteries. Circulation 2006;114:377–80.
16. Schofer J, Siminiak T, Haude M, et al. Percutaneous mitral annuloplasty for functional mitral regurgitation: results of the CARILLON Mitral Annuloplasty Device European Union Study. Circulation 2009; 120:326–33.
17. Webb JG, Maisano F, Vahanian A, et al. Percutaneous suture edge-to-edge repair of the mitral valve. EuroIntervention 2009;5:86–9.
18. Feldman T, Kar S, Rinaldi M, et al., for the EVEREST Investigators. Percutaneous mitral valve repair with the MitraClip system: safety and midterm durability in the initial EVEREST (Endovascular Valve Edge-to-Edge Repair Study) cohort. J Am Coll Cardiol 2009;54: 686–94.
19. Braun J, Bax JJ, Versteegh MI, et al. Preoperative left ventricular dimensions predict reverse remodeling following restrictive mitral annuloplasty in ischemic mitral regurgitation. Eur J Cardiothorac Surg 2005;27:847–53.

Key Words: annuloplasty ■ coronary sinus ■ heart failure ■ mitral regurgitation ■ mitral valve.

APPENDIX

For a description of the EVOLUTION I study organization and list of participants, please see the online version of this article.