JACC: CARDIOVASCULAR INTERVENTIONS VOL. 5, NO. 1, 2012

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. DOI: 10.1016/j.jcin.2011.09.013

Percutaneous Edge-to-Edge Mitral Valve Repair in High-Surgical-Risk Patients

Do We Hit the Target?

Ben J. L. Van den Branden, MD, Martin J. Swaans, MD, Martijn C. Post, MD, PhD, Benno J. W. M. Rensing, MD, PhD, Frank D. Eefting, MD, Wybren Jaarsma, MD, PhD, Jan A. S. Van der Heyden, MD

Nieuwegein, the Netherlands

Objectives This study sought to assess the feasibility and safety of percutaneous edge-to-edge mitral valve (MV) repair in patients with an unacceptably high operative risk.

Background MV repair for mitral regurgitation (MR) can be accomplished by use of a clip that approximates the free edges of the mitral leaflets.

Methods All patients were declined for surgery because of a high logistic EuroSCORE (>20%) or the presence of other specific surgical risk factors. Transthoracic echocardiography was performed before and 6 months after the procedure. Differences in New York Heart Association (NYHA) functional class, quality of life (QoL) using the Minnesota questionnaire, and 6-min walk test (6-MWT) distances were reported.

Results Fifty-five procedures were performed in 52 patients (69.2% male, age 73.2 ± 10.1 years, logistic EuroSCORE 27.1 ± 17.0%). In 3 patients, partial clip detachment occurred; a second clip was placed successfully. One patient experienced cardiac tamponade. Two patients developed inguinal bleeding, of whom 1 needed surgery. Six patients (11.5%) died during 6-month follow-up (5 patients as a result of progressive heart failure and 1 noncardiac death). The MR grade before repair was ≥3 in 100%; after 6 months, a reduction in MR grade to ≤2 was present in 79% of the patients. Left ventricular (LV) end-diastolic diameter, LV ejection fraction, and systolic pulmonary artery pressure improved significantly. Accompanied improvements in NYHA functional class, QoL index, 6-MWT distances, and log N-terminal pro–B-type natriuretic peptide were observed.

Conclusions In a high-risk population, MR reduction can be achieved by percutaneous edge-to-edge valve repair, resulting in LV remodeling with improvement of functional capacity after 6 months. (J Am Coll Cardiol Intv 2012;5:105–11) © 2012 by the American College of Cardiology Foundation

From the Department of Cardiology, St. Antonius Hospital, Nieuwegein, the Netherlands. Drs. Swaans and Van der Heyden are faculty members/proctors for Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received July 6, 2011; revised manuscript received September 9, 2011, accepted September 15, 2011.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 5, NO. 1, 2012
JANUARY 2012:105–11

Mitral valve regurgitation (MR) is an important clinical issue as MR represents >30% of native valve diseases (1). Patients with symptomatic MR have a poor prognosis, with a 5% annual mortality rate in the absence of surgery (2). Optimal medical management can improve symptoms of heart failure but does not affect survival (3). Therefore, surgery is recommended by the current guidelines for patients with symptomatic severe MR or asymptomatic severe MR with evidence of left ventricular (LV) dysfunction or dilation (4,5). Despite those guidelines, a recent European survey established that one-half of these patients are not referred for surgery, mainly because of advanced age and the presence of comorbidity (5,6). Mitral valve (MV) repair is the preferred surgical strategy whenever feasible and is associated with lower morbidity and mortality and better preservation of LV function, compared with MV replacement (7). Reported in-hospital mortality rates range from 1% to 2% in low-risk patients, increasing up to 25% in high-risk or elderly patients (8,9). Therefore, new percutaneous techniques are developed to avoid surgery in high-risk patients. The transcatheter edge-to-edge MV repair using the MitraClip system (Abbott Vascular, Santa Clara, California) creates a double MV orifice by means of a clip in the mid portion of the 2 leaflets and mimics the surgical procedure introduced by Alfieri et al. (10). The first clinical trials with the MitraClip showed very promising results regarding feasibility and safety of the device, and functional improvement of the patient (11–13). We report the 6-month outcomes of our patient cohort treated with this device.

Abbreviations and Acronyms

6-MWT = 6-min walk test
LA = left atrial/atrium
LV = left ventricular/ventricle
LVEDD = left ventricular end-diastolic diameter
LVEDV = left ventricular end-diastolic volume
LVEF = left ventricular ejection fraction
LVESD = left ventricular end-systolic diameter
MR = mitral regurgitation
MV = mitral valve
NT-proBNP = N-terminal pro–B-type natriuretic peptide
NYHA = New York Heart Association
QoL = quality of life
RA = right atrial
RVSP = right ventricular systolic pressure
TEE = transesophageal echocardiography

Methods

Patients. Between January 2009 and November 2010, the interdisciplinary team of cardiac surgeons and cardiologists at our hospital evaluated 52 patients suitable for MitraClip therapy. All patients had moderate-to-severe or severe (grade 3+ or 4) MR and were symptomatic or asymptomatic with LV dysfunction (ejection fraction <60%) or LV dilation (left ventricular end-systolic diameter [LVESD] >45 mm), and consequently had an indication for intervention according to the European Society of Cardiology Task Force recommendation (5). In addition, all patients were at high risk for conventional surgery (logistic EuroSCORE >20% or the presence of specific risk factors associated with excessive morbidity and mortality). Furthermore, echocardiographic parameters played a crucial role in the assessment of the suitability for clip implantation: the coaptation length had to be at least 2 mm, excessive calcification or cleft at the grasping area had to be absent, and in case of a flail leaflet, the flail gap had to be ≤10 mm and the flail width ≤15 mm (11).

All patients underwent a standard pre-procedural screening, containing physical examination, functional capacity assessment (New York Heart Association [NYHA] functional class and 6-min walk test [6-MWT]), quality of life (QoL) assessment using the Minnesota questionnaire, electrocardiogram, chest x-ray, laboratory measurements (including N-terminal pro–B-type natriuretic peptide [NT-proBNP]), transthoracic echocardiography, transesophageal echocardiography (TEE), coronary angiography, and right heart catheterization.

Procedural technique. All procedures were performed as previously described (14). In brief, the clip device system is delivered to the left atrium (LA) via a transseptal puncture, advanced into the LV, and then retracted during systole, grasping the MV leaflets. This results in permanent leaflet approximation and creation of a double orifice. The clip is a 4-mm-wide cobalt-chromium implant with 2 arms. On the inner portion of the clip arms are small "grippers" to secure the leaflets when the arms are closed. Correct positioning of the clip device over the mitral orifice, perpendicular to the line of leaflet coaptation, above the origin of the MR jet, is mandatory to prevent clip disengagement and to obtain an acceptable MR reduction. A second (or third) clip was placed if further reduction of MR was needed. The procedure was performed under general anesthesia and both fluoroscopic and TEE (2- and 3-dimensional) guidance (15).

Follow-up. All periprocedural and mid-term complications were reported. Major complications included hemorrhage requiring blood transfusion, occurrence of cardiac tamponade, need for procedure-related surgical intervention, endocarditis, clip detachment, clip dislodgement/embolization, stroke, and death. Minor complications were defined as MV injury, device thrombosis, bleeding not requiring blood transfusion, femoral arteriovenous fistula formation, and femoral hematoma.

Post-procedural anticoagulation management was based on an individualized protocol.

All patients were discharged on aspirin 100 mg once a day for a period of 6 months and clopidogrel 75 mg once a day for 1 month. In patients on oral anticoagulant therapy before the procedure, clopidogrel was added for 1 month. Infective endocarditis prophylaxis was recommended for 6 months.

Six months after the procedure, all patients underwent clinical examination, laboratory testing, TTE, and assessment

of functional capacity and QoL using the NYHA functional class, the Minnesota questionnaire, and a 6-MWT.

Echocardiographic measurements. The severity of MR at baseline was assessed using a variety of parameters, according to recommendations published earlier (16). At 6-month follow-up, MR severity was graded according to the technique described by Foster et al. (17). Severity scale of 1 to 4 using color flow Doppler (color flow mapping) and color flow jet area (MR jet area/LA area) appeared to be the best reproducible parameters. Vena contracta and regurgitant orifice were recorded if possible but not included as parameters for MR assessment because they have not been validated for a double-orifice valve. The MV orifice area was assessed using the pressure half-time method.

Other echocardiographic parameters included left ventricular ejection fraction (LVEF), LVESD, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic volume, and left ventricular end-diastolic volume (LVEDV) using the biplane Simpson's method, LA dimension and volume, right ventricular systolic pressure (RVSP) using tricuspid regurgitation flow velocity, and right atrial (RA) pressure using vena cava inferior dimensions. Two expert observers performed the endpoint analysis.

Statistical analysis. Descriptive statistics were used to report patients' characteristics. Continuous variables with normal distribution are reported as mean ± SD. Median and range were used when normal distribution was absent. Percentages were used to report categorical variables. Patients' data before and after the procedure were compared with the paired samples *t* test. All tests were 2-sided, and $p < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS software (SPSS, version 14.0 for Windows, IBM, Armonk, New York).

Results

Patient characteristics. A total of 52 patients (mean age: 73.2 ± 10.1 years, male: 69.2%) underwent percutaneous MV repair. Demographic and clinical characteristics are summarized in Table 1. Overall, 81% of the study population had congestive heart failure with advanced NYHA functional class and high log NT-proBNP values (mean: 7.9 ± 1.0 pg/ml). Moreover, the vast majority of patients had several comorbidities that contributed to high logistic EuroSCOREs (mean: 27.1 ± 17.0%). All patients presented with moderate-to-severe (46.2%) or severe (53.8%) MR, mainly secondary to cardiomyopathy (90.4%). Only 5 patients (9.6%) were treated because of primary degenerative MR.

Procedural and in-hospital outcome. Clip implantation was successful in 53 of 55 procedures (96.4%). One clip was placed in 46 patients (83.6%), 2 clips in 6 patients (10.9%), and 3 clips in 1 patient (1.8%). Three patients underwent re-intervention to have a second clip implanted. In 2 patients, the procedure was initially unsuccessful. In the first patient, the heart appeared to be rotated in the thorax after pneumectomy. As a consequence, visualization of the septum was challenging, transseptal puncture was unsuccessful, and the procedure was abandoned. This patient was treated successfully 1 month later after anatomical assessment with

Table 1. Baseline Characteristics (N = 52)

Age, yrs	73.2 ± 10.1
Age >75 yrs	24 (46.2)
Male	36 (69.2)
BMI, kg/m^2	26.5 ± 4.9
Comorbidities	
Diabetes	11 (21.2)
Hypertension	34 (65.4)
COPD	14 (26.9)
Renal insufficiency*	36 (69.2)
Congestive heart failure	42 (80.8)
Coronary artery disease	35 (67.3)
Atrial fibrillation	25 (48.1)
Logistic EuroSCORE, %	27.1 ± 17.0
STS score, %	10.1 ± 7.6
NYHA functional class	
II	1 (1.9)
III	39 (75.0)
IV	12 (23.1)
QoL index score	56.7 ± 22.3
6-MWT distance, m	277 ± 129
Medication	
Loop diuretics	49 (94.2)
Aldosterone antagonists	33 (63.5)
ACEI/ARB	42 (80.8)
Beta-blockers	29 (55.8)
Oral anticoagulation	34 (65.4)
Aspirin	20 (38.5)
Laboratory findings	
Hemoglobin, mmol/l	7.9 ± 1.0
Creatinine, μmol/l	135.0 ± 52.5
Log NT-proBNP, pg/ml	7.9 ± 1.0
ECG	
Rhythm (SR/AF/PM), %	46.2/28.8/25.0
QRS width, ms	137.1 ± 31.9
LBBB	13 (25.0)
MR severity	
3+ (moderate-to-severe)	24 (46.2)
4 (severe)	28 (53.8)
MR etiology	
Functional	47 (90.4)
Ischemic	31 (59.6)
Nonischemic	16 (30.8)
Degenerative	5 (9.6)

Values are mean ± SD or n (%). *Defined as estimated glomerular filtration rate < 60 ml/min/1.73 m^2. 6-MWT = 6-min walk test; ACEI = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin-II receptor blocker; BMI = body mass index; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; LBBB = left bundle branch block; MR = mitral regurgitation NYHA = New York Heart Association; PM = pacemaker rhythm; QoL = quality of life; SR = sinus rhythm; STS = Society of Thoracic Surgeons.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 5, NO. 1, 2012
JANUARY 2012:105–11

Table 2. Procedural and In-Hospital Characteristics

Procedures, n	55*
Successful clip implantation	53 (96.4)
Clips per procedure	
0	2 (3.6)
1	46 (83.6)
2	6 (10.9)
3	1 (1.8)
Procedure time, min	147.7 ± 69.9
Radiation time, min	42.3 ± 21.9
Radiation dose, Gy/cm^2	185.7 ± 116.9
Length of hospital stay, days	5 (3–15)†
Length of intensive care stay, days	1 (1–6)†
In-hospital complications	
Death	2 (3.6)‡
Cardiac	2 (3.6)
Noncardiac	0 (0)
Cardiac tamponade	1 (1.8)
Transseptal complications	1 (1.8)
Procedure related surgical intervention	1 (1.8)
Bleeding requiring transfusion	2 (3.6)
Partial clip detachment	2 (3.6)‡
Clip embolization	0 (0)

Values are n (%) or mean ± SD. *In 52 patients. †Values are median (range). ‡1 death and 1 partial clip detachment occurred in the same patient.

magnetic resonance imaging (suspicion of triatrial heart). In a second patient, no clip was placed because the MR jet was located too far medial to accomplish a satisfactory leaflet apposition. He was treated conservatively. One patient died in the course of a so-called "rescue-clip" procedure as a result of cardiogenic shock and acute heart failure. This 66-year-old male with an LVEF of 15%, underwent the second clip procedure 4 months after the first, because of severe MR with heart failure after a non–ST-segment elevation myocardial infarction. Another patient with dilated cardiomyopathy and pulmonary hypertension died 8 days after the procedure because of end-stage heart failure. In this patient, a total of 3 clips were implanted, of which 1 partially detached from the posterior leaflet during the procedure. Partial clip detachment occurred in another patient before discharge, a second clip was placed successfully 1 week later. In 1 patient, we punctured the LA wall during the first attempt to gain transseptal access. The second transseptal puncture, as well as clip implantation thereafter, was successful. During the procedure, we did not observe pericardial effusion. Unfortunately, 2 h after the procedure, the patient developed clinical signs of cardiac tamponade requiring subxyphoidal drainage. Two patients suffered from femoral bleeding at the puncture site, 1 needed surgery. In another patient, an iatrogenic pharyngeal bleeding (requiring blood transfusion) occurred as a result of TEE probe manipulation. Procedural characteristics and in-hospital complications are listed in Table 2.

Mid-term clinical outcome. Clinical follow-up data were available in 48 patients. One patient moved abroad and was lost to follow-up. Overall 6-month mortality was 11.5%. In addition to the 2 in-hospital deaths, 4 other patients died during follow-up. One patient died of noncardiac cause. All others died as a result of progressive heart failure. Six other patients (12.5%) were rehospitalized because of worsened heart failure, needing intravenous diuretic and/or inotropic therapy. Two of these patients received a cardiac resynchronization device with defibrillator during this admission. Another patient presented with ventricular fibrillation originating from an old myocardial scar; a cardiac resynchronization device with defibrillator was implanted. Complications during follow-up are shown in Table 3. Paired clinical data at baseline and follow-up could be obtained in most patients (Table 4). NYHA functional class diminished significantly from a median of 3 (range: 3 to 4) to 2 (range: 1 to 4) ($p < 0.001$), and 84% of the patients with clinical follow-up was in NYHA functional class I or II (Fig. 1). Five patients (11.4%) did not improve in NYHA functional class. A QoL index score reduction from 56.5 ± 21.9 to 39.4 ± 20.5 ($p < 0.001$) was observed. Furthermore, log NT-proBNP decreased from 7.7 ± 1.0 pg/ml to 7.1 ± 1.2 pg/ml ($p < 0.001$). Because of the improved functional capacity, 6-MWT distances increased from 300 ± 108 m to 339 ± 120 m ($p = 0.02$).

Impact on MR and LV remodeling. Echocardiographic follow-up could be performed in 42 patients (80.8%). Data are summarized in Table 4. Overall, 40 of 42 patients (95.2%) had a reduction in MR of ≥1 grade. Only 2 patients did not improve and remained at grade 3+ MR. In 79% of the patients, a reduction in MR grade to ≤2 was achieved (Fig. 2). Subsequently, RA pressure and RVSP dropped significantly. No clinical or echocardiographic signs of MV stenosis were observed during follow-up.

Compared with baseline, LVEF improved significantly from 36.6 ± 14.1% to 39.3 ± 14.2% ($p = 0.05$). LVEDD decreased from 63.9 ± 10.3 mm to 61.9 ± 10.2 mm ($p = 0.01$). The LV volumes decreased nonsignificantly.

Table 3. Clinical Events During 6-Month Follow-Up (N = 48*)

Complications	
Death	4 (8.3)
Cardiac	3 (6.3)
Noncardiac	1 (2.1)
Mitral valve surgery	0 (0)
Stroke	0 (0)
Mitral valve endocarditis	0 (0)
Partial clip detachment	1 (2.1)
Clip embolization	0 (0)
Rehospitalization for heart failure	6 (12.5)

Values are n (%). 2 patients died in hospital, 1 patient was lost to follow-up, and in 1 patient, no clip was placed.

Table 4. Paired Comparison of Baseline and 6-Month Functional and Echocardiographic Characteristics

	n	Baseline	6 Months	p Value
NYHA functional class	44	3 (3–4)	2 (1–4)	<0.001
QoL index score	44	56.5 ± 21.9	39.4 ± 20.5	<0.001
6-MWT distance, m	31	300 ± 108	339 ± 120	0.02
Log NT-proBNP, pg/ml	38	7.7 ± 1.0	7.1 ± 1.2	<0.001
Echocardiographic parameters	42			
LVEDD, mm		63.9 ± 10.3	61.9 ± 10.2	0.01
LVESD, mm		54.0 ± 12.8	52.9 ± 13.0	0.35
LVEDV, ml		184.0 ± 72.4	172.9 ± 83.9	0.08
LVESV, ml		123.2 ± 65.3	114.4 ± 74.7	0.07
LVEF, %		36.6 ± 14.1	39.3 ± 14.2	0.05
LA volume index, ml/BSA		62.6 ± 23.8	49.8 ± 20.1	0.001
LA dimension, mm		49.4 ± 6.3	49.0 ± 7.9	0.70
MR grade		4 (3–4)	1 (1–3)	<0.001
MR/LA area, %		50.7 ± 15.5	26.4 ± 13.1	<0.001
RVSP, mm Hg		38.8 ± 13.1	31.1 ± 10.9	0.001
RA pressure, mm Hg		7.9 ± 3.8	5.0 ± 3.8	0.005
Mean transmitral gradient, mm Hg		—	3.8 ± 2.0	—
Mitral valve orifice area, cm^2		—	2.9 ± 0.8	—

Values are median (range) or mean ± SD.

6-MWT = 6-min walk test; LA = left atrial; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; RA = right atrial; RVSP = right ventricular systolic pressure; QoL = quality of life; other abbreviations as in Table 1.

Discussion

We report the largest single-center experience for percutaneous edge-to-edge MV repair in a high-surgical-risk population. Our results indicate that this technique can be accomplished with favorable mid-term outcomes with an increase in functional capacity and improvement in echocardiographic parameters.

Patients with severe symptomatic MR might develop progressive heart failure, which is often refractory to medical therapy. Without intervention, these patients have an annual rate of death of 5% or more (18). Especially for patients with functional MR and poor LV function, there are no widely accepted indications for surgery other than as a

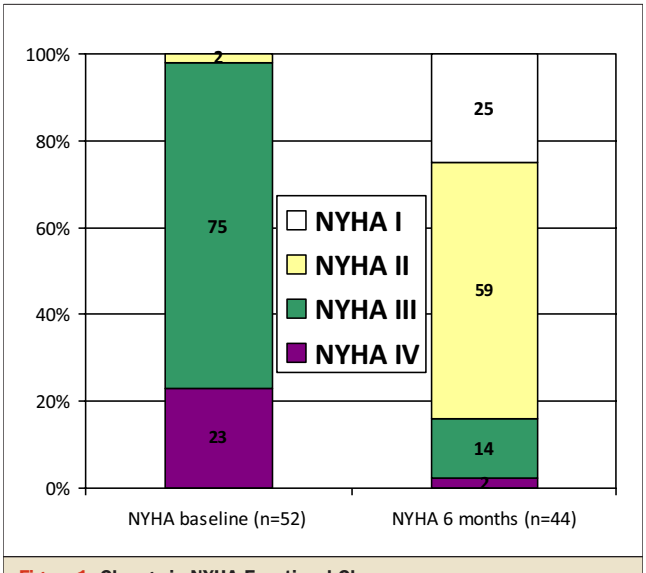

Figure 1. Change in NYHA Functional Class

At baseline, 98% of the patients was in New York Heart Association (NYHA) functional class III or IV. Six months after clip repair, 84% of the patients was in NYHA functional class I or II.

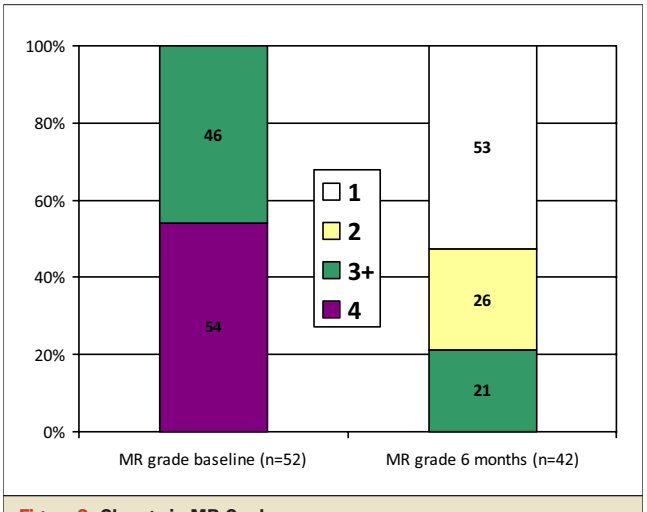

Figure 2. Change in MR Grade

At baseline, all patients had moderate-to-severe (grade 3+) or severe mitral regurgitation (MR). Six months after clip implantation, 79% of the patients had MR grade ≤2.

concomitant procedure at the time of bypass surgery, but its benefits have been variable and outcomes suboptimal (4,5,19,20). The periprocedural mortality rates described in surgical series varies between 2.1% and 11% in patients with depressed LV function, and as high as 25% in very high-risk or elderly patients (21,22). In our study, including high-risk patients with poor LV function, we report an in-hospital mortality of 3.8%. Two patients who were treated in our early experience phase died in-hospital as a result of end-stage heart failure. After reviewing those cases, we must conclude that the risk–benefit ratio for percutaneous repair was suboptimal. Therefore, a stringent selection process is mandatory, including a guideline-supported indication for intervention and extensive pre-procedural echocardiographic assessment. Clinical patient characteristics associated with worse outcome are yet to be determined. In the presence of myocardial fibrosis and irreversible LV adverse remodeling, MR reduction may not provide any benefit (19,23). It has been shown that the degree of LV contractile reserve as assessed by exercise or inotropic stimulation is a predictor of LV function after MV repair (24,25). Therefore, gadolinium-enhanced and dobutamine stress magnetic resonance imaging might be helpful for patient selection.

In the recently published EVEREST II (Endovascular Valve Edge-to-Edge Repair Study II), 279 patients were randomized in a 2:1 ratio to undergo clip therapy or open MV surgery and showed no difference in mortality (6% in both groups) at 12-month follow-up (26). Noteworthy, in this trial, MR of degenerative origin was predominant (73%), and mean LVEF was 60.0 ± 10.1% in the clip group. In the present study, the overall 6-month mortality rate was 11.5%. However, the mean LVEF was 37%, with a predicted periprocedural mortality rate of 27%.

Recently, Franzen et al. (27) showed the effectiveness of MV clip therapy in an end-stage heart failure population. In this multicenter study, 50 patients (LVEF ≤25%, mean logistic EuroSCORE: 34%) with functional MR were included, and at 6-month follow-up, MR ≤2+ was present in 87% of the patients. In the EVEREST II trial, surgery appeared to be more effective in reducing MR compared with percutaneous repair. However, in the subgroup with functional MR (27% in both groups), surgery was not superior (26). In our study population, including 90% functional MR, a reduction in MR of ≥1 grade was achieved in 95%, and 79% of the patients had MR grades ≤2, 6 months after the procedure (11–13). Despite the LV geometric distortion with concomitant annular dilation in most of our patients, clip placement was successful in 96%, which is comparable with the report by Franzen et al. (27). Taken together, patients with functional MR can be treated successfully and seem to benefit most from this new technique. Moreover, Maisano et al. (28) reported that isolated surgical edge-to-edge repair has acceptable outcomes for both degenerative and functional MR with a 5-year freedom from recurrent MR ≥2+ and reoperation of 90%.

As a result of MR reduction, we observed diminished plasma NT-proBNP levels, accompanied with significant improvements in QoL and functional capacity, which may be the primary goal in this challenging high-risk population. The improvement in objective parameters shows that the observed clinical effect can be attributed to improvements beyond a placebo effect. NYHA functional class improved in 89% of our population, which is in line with previous reports (11,27). The EVEREST II trial showed similar improvements in NYHA functional class and QoL in both the clip and surgery subgroups at 12 months (26).

Of note, percutaneous MV repair seems to be associated with positive reverse LV remodeling. We report a significant increase in LVEF, decrease in LVEDD, and obvious improvements in LV volumes. The question remains whether this will affect long-term prognosis, as previous reports showed no evidence that surgery for functional MR prolongs life, despite LV reverse remodeling (29,30).

Our findings underline the growing understanding that percutaneous approaches become a valuable treatment option for an important number of patients with severe (especially functional) MR who cannot undergo surgery (31). In the future, the field of percutaneous transcatheter MV repair will undoubtedly evolve exponentially. In our opinion, because functional MR is primarily a disease of the LV, a combination of the edge-to-edge repair with other percutaneous techniques addressing the annulus and the LV itself will be necessary to provide durable correction and satisfactory long-term outcomes (32).

Study limitations. First, we acknowledge the observational, nonrandomized nature of the study and the relative small number of patients. However, we continue to treat patients not eligible for surgery and will perform long-term follow-up to determine the true value of this new approach. Another limitation is that the follow-up echocardiograms could not be reviewed in a blinded or independent way. Furthermore, we assessed MR severity after clip placement only by MR jet area and the MR/LA jet ratio. However, comparing these parameters pre- and post-procedure should provide a reliable perception of MR reduction.

Conclusions

Percutaneous edge-to-edge mitral valve repair seems to be a valuable alternative for patients with severe, symptomatic MR who are not candidates for open MV surgery. We observed important reductions in MR grade in most patients that contributed to positive LV remodeling with improvement of QoL and functional capacity. However, careful patient selection seems obligatory, especially in case of advanced heart failure.

Reprint requests and correspondence: Dr. Ben J. L. Van den Branden, Department of Cardiology, St. Antonius Hospital, Koekoekslaan 1, 3435 CM, Nieuwegein, the Netherlands. E-mail: b.van.den.branden@antoniusziekenhuis.nl.

REFERENCES

1. Enriquez-Sarano M, Akins CW, Vahanian A. Mitral regurgitation. Lancet 2009;373:1382–94.
2. Agricola E, Ielasi A, Oppizzi M, et al. Long-term prognosis of medically treated patients with functional mitral regurgitation and left ventricular dysfunction. Eur J Heart Fail 2009;11:581–7.
3. Carabello BA. The current therapy for mitral regurgitation. J Am Coll Cardiol 2008;52:319–26.
4. Bonow RO, Carabello BA, Chatterjee K, 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;48:e1–148.
5. Vahanian A, Baumgartner H, Bax J, et al. Guidelines on the management of valvular heart disease: the Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur Heart J 2007;28:230–68.
6. Mirabel M, Iung B, Baron G, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? Eur Heart J 2007;28:1358–65.
7. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. Circulation 1995;91:1022–8.
8. Haan CK, Cabral CI, Conetta DA, Coombs LP, Edwards FH. Selecting patients with mitral regurgitation and left ventricular dysfunction for isolated mitral valve surgery. Ann Thorac Surg 2004;78:820–5.
9. Tribouilloy CM, Enriquez-Sarano M, Schaff HV, et al. Impact of preoperative symptoms on survival after surgical correction of organic mitral regurgitation: rationale for optimizing surgical indications. Circulation 1999;99:400–5.
10. Alfieri O, Maisano F, De Bonis M, et al. The double-orifice technique in mitral valve repair: a simple solution for complex problems. J Thorac Cardiovasc Surg 2001;122:674–81.
11. Feldman T, Kar S, Rinaldi M, et al. Percutaneous mitral 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.
12. Franzen O, Baldus S, Rudolph V, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J 2010;31:1373–81.
13. Tamburino C, Ussia GP, Maisano F, et al. Percutaneous mitral valve repair with the MitraClip system: acute results from a real world setting. Eur Heart J 2010;31:1382–9.
14. Van den Branden BJ, Post MC, Swaans MJ, et al. Percutaneous mitral valve repair using the edge-to-edge technique in a high-risk population. Neth Heart J 2010;18:437–43.
15. Swaans MJ, Van den Branden BJ, Van der Heyden JA, et al. Three-dimensional transoesophageal echocardiography in a patient undergoing percutaneous mitral valve repair using the edge-to-edge clip technique. Eur J Echocardiogr 2009;10:982–3.
16. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.
17. Foster E, Wasserman HS, Gray W, et al. Quantitative assessment of severity of mitral regurgitation by serial echocardiography in a multicenter clinical trial of percutaneous mitral valve repair. Am J Cardiol 2007;100:1577–83.
18. Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. Am J Cardiol 2003;91:538–43.
19. Piérard LA, Carabello BA. Ischaemic mitral regurgitation: pathophysiology, outcomes and the conundrum of treatment. Eur Heart J 2010;31:2996–3005.
20. Mihaljevic T, Lam BK, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. J Am Coll Cardiol 2007;49:2191–201.
21. Geidel S, Lass M, Krause K, et al. Early and late results of restrictive mitral valve annuloplasty in 121 patients with cardiomyopathy and chronic mitral regurgitation. J Thorac Cardiovasc Surg 2008;56:262–8.
22. Nowicki ER, Birkmeyer NJ, Weintraub RW, et al. Multivariable prediction of in-hospital mortality associated with aortic and mitral valve surgery in Northern New England. Ann Thorac Surg 2004;77:1966–77.
23. Di Salvo TG, Acker MA, Dec GW, Byrne JG. Mitral valve surgery in advanced heart failure. J Am Coll Cardiol 2010;55:271–82.
24. Leung DY, Griffin BP, Stewart WJ, Cosgrove DM III, Thomas JD, Marwick TH. Left ventricular function after valve repair for chronic mitral regurgitation: predictive value of preoperative assessment of contractile reserve by exercise echocardiography. J Am Coll Cardiol 1996;28:1198–205.
25. Piechota W, Gielerak G. The prognostic value of stress tests in chronic heart failure. Cardiol J 2007;14:340–6.
26. Feldman T, Foster E, Glower DG, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011;364:1395–406.
27. Franzen O, Van der Heyden JA, Baldus S, et al. MitraClip® therapy in patients with end-stage systolic heart failure. Eur J Heart Fail 2011;13:569–76.
28. Maisano F, Viganò G, Blasio A, Colombo A, Calabrese C, Alfieri O. Surgical isolated edge-to-edge mitral valve repair without annuloplasty: clinical proof of the principle for an endovascular approach. EuroIntervention 2006;2:181–6.
29. Diodato MD, Moon MR, Pasque MK, et al. Repair of ischemic mitral regurgitation does not increase mortality or improve long-term survival in patients undergoing coronary artery revascularization: a propensity analysis. Ann Thorac Surg 2004;78:794–9.
30. Wu AH, Aaronson KD, Bolling SF, Pagani FD, Welch K, Koelling TM. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. J Am Coll Cardiol 2005;45:381–7.
31. Bach DS, Awais M, Gurm HS, Kohnstamm S. Failure of guideline adherence for intervention in patients with severe mitral regurgitation. J Am Coll Cardiol 2009;54:860–5.
32. Chiam PT, Ruiz CE. Percutaneous transcatheter mitral valve repair: a classification of the technology. J Am Coll Cardiol Intv 2011;4:1–13.

Key Words: MitraClip ■ percutaneous mitral valve repair ■ severe mitral regurgitation.