OBJECTIVE ARTICLE

Percutaneous mitral repair with MitraClip system; safety and efficacy; initial Egyptian experience

Hazem Khamis a,*, Ahmed Abdelaziz b, Ahmed Ramzy c

a October 6th University, Egypt
b Cairo University, Egypt
c Benha University, Egypt

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KEYWORDS
Mitral regurgitation; Percutaneous repair; Mitral clip

Abstract  Objectives: To evaluate the feasibility, efficacy, and safety of the MitraClip system in patients with severe MR.
Background: Mitral valve repair for mitral regurgitation (MR) has been performed by the use of a surgically created double orifice. Percutaneous repair based on this surgical approach has been developed by the use of a MitraClip device.
Methods: Five patients with 3 to 4+ MR were selected in accordance with the American Heart Association/American College of Cardiology guidelines between March 2013 and May 2013 and underwent percutaneous mitral repair with the MitraClip system with 6 months follow up after the procedure. The primary acute safety endpoint was freedom from major adverse events (MAEs) at 30 days. The primary efficacy endpoint was acute procedural success defined as clip implant with the reduction of MR to equal or less than grade II, based on current guidelines.
Results: No transseptal complications were reported (0%). There was no procedural mortality. No patients experienced MAE at 30 days. No cases of clip detachment or embolization were observed. Acute procedural success was achieved in all treated patients (100%). There was an improvement in the severity of MR in all patients as assessed acutely. Acute MR reduction by 3 grades was achieved in 2 patients and by 2 grades in 3 patients (reduction ≥2 grades in 100%).
Conclusions: Our initial results with the MitraClip device in a very small number of patients indicate that percutaneous edge-to-edge mitral valve repair is feasible and may be accomplished with favorable short-term safety and efficacy results.

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1. Introduction

Severe mitral regurgitation (MR) caused by primary valve disease or as a consequence of underlying left ventricular (LV) dilatation substantially contributes to morbidity and mortality.1-4 Optimal medical management or cardiac resynchronization therapy can improve symptoms and reduce MR...
severity in a number of patients. However, if these measures fail, mitral valve surgery is the standard therapy. Notably, a large percentage of patients in need of valve reconstruction or replacement do not undergo surgery because of a high perioperative risk.

Among the therapeutic options for severe MR, medical therapy is largely palliative, directed at controlling symptoms and manifestations of heart failure. Surgical intervention is well tolerated in a population judged by surgeons to be at acceptable risk; a number of registries and retrospective analyses have provided evidence consistent with the superiority of surgery over medical therapy, of mitral valve repair over replacement, and, where replacement has been needed, of preservation of the subvalvular apparatus. However, in patients at high surgical risk due to multiple comorbidities, the mandate for surgery is less compelling.

Moreover, until the EVEREST II trial randomized patients to medical therapy versus percutaneous mitral valve repair, the evidence base was remarkably lacking in high-level clinical trials studying the outcomes of any intervention for severe MR, surgical or percutaneous. Unfortunately, the clinician with a high-risk patient still does not have a solid evidence base with which to choose between medical therapy and surgery, given substantial peri- and postoperative morbidity and mortality in this population.

In this context, a variety of less invasive percutaneous treatment options for mitral valve repair have been developed; most of these techniques are still at an early stage of clinical evaluation.

The MitraClip® (Abbott Vascular, Santa Clara CA, USA) was the first percutaneous system for MV repair (CE Mark granted in 2008) and has been used in over 6000 patients since 2003. Recently, the first randomized controlled study in the field of percutaneous MV repair, the EVEREST II trial, compared MitraClip with surgical MV repair and demonstrated the superior safety of the MitraClip repair and similar improvements in clinical symptoms.

The performance of the MitraClip transcatheter procedure has been restricted to selected centers that fulfill certain setup and multidisciplinary training requirements. Our hospital was the first to employ this novel procedure in Egypt. Herein, we describe our initial experience, focusing on patient selection, setup requirements and acute clinical outcomes of this technique in high-surgical-risk patients.

2. Methods

2.1. Study design

It is a single center, prospective, single armed study that included the first five patients for whom percutaneous mitral valve repair was done via mitral valve clip system at (Wadi El Neel hospital).

2.2. MitraClip system and procedural technique

We explained the procedure in detail as this is the first study using this novel technique in Egypt, so, other interventionists can get use of it.

- The MitraClip system includes a MitraClip device, a 24-F Steerable Guide Catheter (SGC), and a Clip Delivery System (CDS). The Clip is pre-assembled to the tip of the disposable delivery catheter. Opening, closing, locking, and detaching the clip are all controlled by the delivery catheter handle mechanism, which is firmly lodged on a metal, sterilized external support placed outside the patient, on the bottom of a small table above the upper leg Fig. 1.
Percutaneous mitral repair with MitraClip system: safety and efficacy; initial Egyptian experience

- The procedure was performed under general anesthesia to avoid any discomfort due to Trans-esophageal echocardiography (TOE) monitoring. We used both 2D & 3D echocardiography for monitoring and assessing the procedural success.
- Invasive arterial pressure was monitored through the femoral artery. The right femoral vein was cannulated with an 8-F introducer sheath then exchanged with an 8-F Mullins sheath (St. Jude Medical, Minnesota, USA) over a 0.32 guide wire, and a transeptal puncture was performed using a Brockenbrough needle under TEE guidance.
- This is a critical point of the procedure, because the puncture has to be located in the postero-superior part of the inter-atrial septum in order to obtain enough room in the left atrium for a safe and optimal orientation of the steerable distal part of the CDS.
- Once the left atrium was entered with the 8F sheath, the upper left pulmonary vein was cannulated using a 260 cm Amplatz Super stiff guide wire. After administration of 100 IU/kg of unfractionated heparin, the 24-F SGC was introduced in the left atrium and the dilator was carefully and slowly retrieved for avoiding vacuum air bubbles.
- The CDS was then advanced in the left atrium, and the distal steerable part was manipulated in the atrium for obtaining a perpendicular and central position with respect to the mitral valve leaflets coaptation line.
- The correct trajectory of the clip and the perpendicularity of the two arms with respect to the mitral leaflet coaptation line are checked using three echocardiographic views: (i) The three-chambers in which the left atrium, left ventricle, and aortic root are visualized.
  (ii) The dual chamber view, in which both left atrium and ventricle are obtained.
  (iii) The trans-gastric short axis view to visualize the coaptation line of the mitral leaflets.
- Once the system had been aligned, the clip with opened arms was advanced into the left ventricle and under TEE guidance the arms grasp the leaflets.
- When a double-orifice had been created and the echocardiography confirms the regurgitation reduction is optimal and stable without any significant diastolic gradient across the MV; grasping of both leaflets, there are two options: if the position is suboptimal, the clip can be repositioned and repositioned; if the result is good and the grasp is stable, the clip arms are closed, locked, and detached and the SGC and CDS are withdrawn.
- The guiding catheter was removed, and venous femoral access was closed using a ‘figure-of-eight’ superficial stitch.
- Post-procedural pharmacologic management included aspirin 100 mg lifelong and clopidogrel 75 mg for 3 months in patients without atrial fibrillation. Patients with atrial fibrillation were prescribed aspirin 100 mg and vitamin K antagonists.

2.3. Patient selection

2.3.1. Inclusion criteria

- Patients with moderate-to-severe (3+) or severe (4+) primary or secondary MR with symptoms (NYHA class ≥ II), or if asymptomatic, with compromised LV function (ejection fraction < 60% or end-systolic dimension > 45 mm).
- High risk for surgery (logistic EuroSCORE more than 20%).
- Mitral regurgitation will be graded according to the criteria of the American Society of Echocardiography (ASE) guidelines by the use of quantitative (regurgitant volume, regurgitant fraction) and qualitative (color Doppler and pulmonary venous flow) criteria.
- Key anatomic inclusion criteria included a regurgitant jet origin associated with the A2 to P2 segments of the mitral valve and, for patients with secondary MR, a coaptation length of at least 2 mm, a coaptation depth of no more than 11 mm, and for patients with leaflet flail, a flail gap < 10 mm and a flail width < 15 mm.

2.3.2. Exclusion criteria

- Evidence of an acute myocardial infarction in the 12 weeks prior to the intended treatment.
- Mitral valve orifice area less than 4.0 cm².
- Severe mitral annular calcification.
- Any leaflet anatomy which may preclude clip implantation, proper clip positioning on the leaflets, or sufficient reduction in MR.
- Need for emergency surgery for any reason.
- Hypertrophic cardiomyopathy.
- Echocardiographic evidence of intra-cardiac mass, thrombus, or vegetation.
- History of a stroke or documented TIA within the prior 6 months.
- Patients in whom TEE is contraindicated.

2.4. Study endpoints

- The primary acute safety endpoint is freedom from any of the major adverse events (MAEs) at 30 days, defined as the composite of death, myocardial infarction, non-elective cardiac surgery for adverse events, renal failure, transfusion of more than 2 units of blood, ventilation for more than 48 h, deep wound infection or septicemia.
- The primary efficacy endpoint is acute procedural success defined as clip implant with a reduction of MR to equal to or less than grade II, based on current guidelines. Grade III MR was assigned as recommended by the American Society of Echocardiography based on a validated integrative method and the consensus of two expert observers. In case of disagreement, the opinion of a third observer was obtained and the final decision was made by consensus. As vena contracta width and regurgitant orifice area have not been validated for a double-orifice valve, these parameters were not included among methods to appraise the severity of MR.

We proceeded with the procedure after approval from the local ethics committee at the Wadi El Neel hospital. The procedural details were explained to all included patients and a written consent was signed.
3. Results

3.1. Patient characteristics

Five patients were treated, including 3 patients (60%) with primary or combined primary and secondary disease and 2 patients (21%) with pure secondary MR. Clinical features are shown in (Table 1). The median age was 63 years (range 50–72 years), and 60% of patients were older than 65 years of age, the logistic euro-SCORE was 21 ± 5%. Among patients with secondary MR, there was a history of coronary artery disease in 40% and previous bypass surgery in 40%.

3.2. Procedure results

We placed one clip in 4 patients (80%) and a second clip was needed in only one patient (20%). No transseptal complications were reported (0%). The procedure time for 4 patients was in the range of 115–160 min, but it reached 180 min in 1 patient. The mean procedure time was 146 min and the mean fluoroscopy time was 43 min.

In-hospital outcomes are shown in Table 2. There was no procedural mortality. No patients experienced MAE at 30 days. One patient with a history of transient ischemic attack had a non-embolic stroke with a neurological deficit lasting >72 h, which resolved within 30 days. No cases of clip detachment or embolization were observed. There were no other complications (see Figs. 2 and 3).

Acute procedural success was observed in all treated patients (100%). There was an improvement in the severity of MR in all patients as assessed acutely. Acute MR reduction by 3 grades was achieved in 2 patients and by 2 grades in 3 patients (reduction P 2 grades in 100%). No significant iatrogenic mitral stenosis was detected after the procedure (mean mitral valve gradient <4 mmHg in all patients). In addition to the reduction in MR severity, clinical status, as assessed by NYHA functional class, improved in 4 patients (80%); at discharge, these patients were in NYHA functional class I.

4. Discussion

Mitral valve repair can be accomplished with a procedure that involves the percutaneous implantation of a clip (MitraClip)
that grasps and approximates the edges of the mitral leaflets at the origin of the regurgitant jet. This technology was developed in an attempt to replicate the surgical approach for mitral valve repair, which involves approximation of the mitral leaflets with a suture to create a double orifice.

This report describes the initial experience at the first Egyptian center that started a program of MR treatment with the MitraClip system. We intended to evaluate this therapy in high-surgical-risk patients with grades 3–4 MR. The majority of our patients presented with pronounced LV dysfunction or multiple co-morbidities.

Our study has demonstrated that MitraClip therapy is feasible and effective, with procedural success achieved in all patients (100%). There was no procedural mortality or MAE at 30 days. Successful placement of the MitraClip device was associated with a reduction in MR severity by $\geq 2$ grades in all patients.

In addition to the reduction in MR severity, clinical status, as assessed by NYHA functional class, improved in 4 patients (80%) at discharge. These patients were in NYHA functional class I. Thus, our data show a reduction in MR and corresponding improvement in the clinical status in patients with limited other therapeutic options. However, it needs to be studied whether the reduction in MR leads to reversal of ventricular remodeling and ultimately improves prognosis in the long term.

In comparison with Whitlow et al. who also studied the use of MitraClip in high risk patients, there was relatively high procedure-related mortality for a percutaneous approach (8%). MR graded 2+ or higher was 46% through hospital discharge and 69% at 1 year. Both are high; in EVEREST II, MR grade of $\geq 2+$ was 46% at 1 year (17% after surgery). Only 44% had a $\geq 2$ grade reduction in MR, whereas 19% had no change or a 1-grade increase. A somewhat more optimistic perspective comes from looking at severe MR only; there was an 87% reduction to less severe over 12 months, overall left ventricular dimensions appeared to improve, and New York Heart Association functional class decreased to I or II in 71% of those who were III or IV at the baseline.

However, interpretation of these follow-up data can be misleading: the reader needs to take into consideration the importance of the de facto censoring of 31% of the patients (including the 24% who died before 1-year follow-up). Thus, comparisons shown by Whitlow et al. can result in the reader over-interpreting the benefits of MitraClip in this patient population.

Moreover, the 30-day mortality in the 177 patients with secondary MR treated with the MitraClip in the EU ACCESS registry was 2.8%, while in the 149 secondary MR patients treated with the MitraClip in the EVEREST II high-surgical risk cohort, it was 4.7% (1.1% in the 50 patients with secondary MR randomized to MitraClip in the EVEREST II trial). MitraClip is the only percutaneous technology effective for both functional and degenerative MR. The procedure is performed via a venous route and the device is removable and repositionable. These important attributes contribute to the safety of this procedure. Notably, in spite of the fact that the degree of reduction in MR is lower than that of surgery, the clinical benefits with respect to LV remodeling were observed to be similar to the surgical group.

5. Limitations of the study

Although this study represents the first experience with MitraClip therapy reported to date in Egypt, the total number of 5 patients is still small. A larger number of patients and adequate long-term follow-up is needed to assess the true value of...
this therapeutic approach. Functional improvement was categorized by NYHA functional class, which is most widely used in clinical practice. Measurements such as a 6-min walk test may provide a more objective perspective, but were not performed at discharge.

6. Conclusion

Our initial results with the MitraClip device in a small number of patients indicate that percutaneous edge-to-edge mitral valve repair is feasible and may be accomplished with favorable short-term safety and efficacy results. A universal finding with the MitraClip therapy, which we also encountered in our initial experience, is that MR is significantly reduced but rarely eliminated. However, when treating high-risk patients a suboptimal repair obtained with low risk can be an acceptable outcome.

Conflict of interest

None declared.

References

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