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Research Article

12 months Outcomes of 12 Young Patients after Mitral Clip Implantation

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Abstract

Background: Mitral Clip became a well-established interventional option for severe MR in elderly patients with high surgical risk. **Objective:** to present 12 patients younger than 65 years with high operative risk treated by TMVR. **Methods: E**valuation of 12 patients younger than 65 years from a total of 250 patients treated by MitraClip® in Westfalen Heart Center, Germany. **Results:** Mean age was 57.1 ± 4 years, male gender was 66,7%. High operative risk was estimated by STS score (mean = 8.76 ± 2.89). Severity of MR was detected by biplane vena contracta (bpVCW) in two perpendicular views (mean = 9.73 ± 1.89 mm). Transmitral mean PG was 1.68 ± 0.75 mmHg. 3 patients showed leaflet prolapse, 5 patients had mitral annular dilatation, 3 patients exhibited mitral leaflet thickening and one patient showed papillary muscle displacement as the main aetiology of MR. Procedural success was achieved in all patients with 1 / 2 / 3 clips implanted in 25% / 75% / 0% of cases. Two grades or more reduction in severity of MR (MR grade ≤ II/IV) was accomplished in 75% of patients. Mean postprocedural MPG remained within acceptable levels of 4.33 ± 2.31 mmHg. During follow up, persistent symptomatic improvement was confirmed in all patients who had already shown symptomatic improvement and effective reduction of MR after the procedure. No procedure-related mortality during the first 30 days. **Conclusion:** MitraClip® in patients younger than 65 years provides satisfactory outcomes at 1 year.

Keywords: Transcatheter Mitral Valve Repairm, MitraClip®, Percutaneous, Mitral Valve Intervention, Mitral Valve Disease, Mitral Regurgitation

Introduction

The basic concept of percutaneous edge-to-edge mitral valve repair (MVR) via MitraClip® sprouted from the Alfieri stitch double orifice technique which was introduced as a new surgical technique of MVR. This surgical procedure has been simplified by omitting the ring annuloplasty and this modification was the principle for percutaneous edge-to-edge MVR via MitraClip®[1,2,3]

Until now Endovascular Valve Edge-to-Edge REpair Study II (EVEREST II) is the only study that compares surgical mitral valve repair (MVR) or replacement with percutaneous edge-to-edge MVR via MitraClip®. EVEREST II concluded that "Although percutaneous repair was less effective at reducing mitral regurgitation (MR) than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical

outcomes." So that, percutaneous MVR became the standard interventional procedure for high surgical risk patients with severe MR. These patients have usually a combination of being elderly, markedly reduced left ventricular systolic function and multiple comorbidities rendering them inoperable or at high risk for open heart surgery.[3,4]

The worldwide experience in MitraClip® has been increased within approximately 15 years of clinical experience and more than 60000 patients were treated in addition to durable outcomes and proven quality of life improvements demonstrated up to 5 years.[5]

Carpentier classification describes the mechanism of MR and therefore it aids in planning of mitral valve reconstruction in order to restore normal mitral valve function rather than restoring normal mitral valve anatomy. According to Carpentier classification, MR is categorized based on mitral leaflets motion into 3 main types. Type I refers to normal mitral leaflet motions and the aetiology of MR is annular dilation, cleft leaflet or leaflet perforation. Type II points to increased leaflet motion and includes mitral valve prolapse (MVP), chordal rupture or elongation and papillary muscle rupture or elongation. Type III is attributed to restricted leaflet motion; however, this type is classified into 2 subgroups. Type IIIa where mitral leaflets are restricted in systole and diastole due to leaflet thickening and restriction, commissural fusion or chordal thickening and shortening mostly owing to fibrosis. Type IIIb which shows only systolic mitral leaflets restriction because of LV dilatation leading to apical papillary muscles displacement usually in ischemic heart disease. [6]

Not only advanced age but also severe left ventricular dysfunction and associated comorbidities are the main causes of surgical denial for many patients with severe MR. Also, the survival benefit and clinical outcome of mitral valve surgery in patients with severe functional MR and markedly reduced left ventricular ejection fraction (LVEF) is limited. Recently, mitral valve surgery techniques relay mainly on MVR rather than mitral valve replacement. [7,8]

Aim of the study

The aim of this study is to evaluate 12 months clinical and echocardiographic outcomes of **MitraClip®** in patients younger than 65 years in Westfalen Heart Centre, Germany.

Methodology

We have retrospectively studied all patients who underwent MitraClip® in Central Clinic Bad Berks, Germany and Westfalen Heart Center, Germany, to identify patients younger than 65 years. All patients underwent routine 2D/3D transthoracic and transesophageal echocardiography prior to mitral clip intervention in order to determine severity of MR based on biplane vena contracta width (bpVCW) based on Kahlert et al., 2009 [9], determine aetiology of MR, mitral valve morphology and anatomical suitability parameters for mitral clip implantation especially mitral valve area (MVA), mean pressure gradient (MPG) across mitral valve and posterior mitral leaflet length. Clinical characteristics particularly New York Heart Association (NYHA) class III or IV despite optimal medical treatment were obtained. Presumably surgical risk was detected through calculating the society of thoracic surgeons (STS) score[10] and heart team meeting decisions with surgical refusal in spite of relatively young patients (mean age = 57.1±4 years) for these patients based on high operative risk due to markedly reduced LVEF and/or associated comorbidities (mean STS score = 8.76 ± 2.89).

Mitral clip procedures were performed under general anesthesia in hybrid catheterization laboratories in both hospitals guided by 2D/3D echocardiography. Right femoral vein was the access site for all patients followed by transseptal puncture under fluoroscopic and transesophageal echocardiographic guidance, then intravenous heparin sodium was injected aiming at achieving more than 280 seconds of activated clotting time. After that steerable guiding catheter (24F) was positioned in the left atrium, then mitral clip delivery system was introduced through it. MitraClip® device was directed, rotated and introduced perpendicular to mitral leaflets and positioned in order to grasp mitral leaflets at the targeted point with the aid of 3D echocardiography which enables simultaneous visualization of mitral clip in two perpendicular views by X-plan mode. After each grasping trial and before release of mitral clip from delivery system, sufficient reduction of the targeted MR jet was confirmed in addition to testing efficacy of mitral clip in reducing MR by increasing systolic blood pressure up to 150 mmHg to confirm the final result before clip release. Furthermore, transmitral MPG should be less than 5 mmHg and atropine test may be done to evaluate MPG across mitral valve before release of mitral clip. Second mitral clip implantation was carried out provided only that residual MR was more than grade II and MPG across mitral valve was less than 4 mmHg.

Finally, after removal of steerable guide catheter, venous puncture site was closed by figure of 8-stitch. Usually, all patients spent 24 hours under monitoring in intensive care unit and typically discharged after admission for 5 to 7 days in the inpatient ward. Clinical and echocardiographic outpatient follow up visits of patients were done at regular basis every 6 months to assess persistence of MR reduction and to evaluate improvement of NYHA functional class.

Owing to limited number of relatively young aged patients undergoing mitral clip implantation, statistical analysis was based mainly on descriptive statistics and comparing means. Quantitative variables were presented as mean ± standard deviation, but qualitative variables were expressed in form of percentages.

Results

Out of 250 patients with severe MR treated by MitraClip® in both centers, we identified 12 patients younger than 65 years with mean age of 57.1 ± 4 years and 8 from 12 patients were males (66.7%). All patients were rejected by cardiac surgeons because of high operative risk assessed by STS score, mean STS score equals 8.76 ± 2.89. Severity of MR were assessed by calculating the average of bpVCW in two orthogonal views (bpVCW mean = 9.73 ± 1.89 mm). Mean of preprocedural transmitral pressure gradient was 1.68± 0.75 mmHg. Echocardiographic etiological characteristics of MR based on Carpentier classification are shown in Table 1.

Table (1): Carpentier classification of mitral regurgitation

Carpentier Classification	Number of patients	Percentage
Type I	5	41.7%
Type II	3	25%
Type IIIA	3	25%
Type IIIB	1	8.3%

Eccentric regurgitation jets and multiple regurgitation jets were found in 50% and 16.7% of patients, respectively. As regard of etiological mechanism of MR, 3 patients showed leaflet prolapse as the main etiological factor of MR and in another 5 patients the cause of MR was mitral annular dilatation. 3 patients exhibited mitral leaflet thickening and/or retraction due to fibrosis and only one patient exhibited papillary muscle displacement leading to leaflet tethering as a reason for MR. Neither cleft mitral leaflet nor mitral annular calcification were detected. Right ventricular systolic function measured by tricuspid annular plane systolic excertion (TAPSE) was found to be normal (≥ 18mm) in 33.3% of patients. Also, moderate to severe tricuspid regurgitation (TR) was confirmed in 8 patients. Table 2 shows general echocardiographic parameters.

Table (2): General echocardiographic parameters

	Baseline	Follow up
LVEF (%)	32.9 ± 13.89	34.58 ± 12.69
LVEDD (mm)	61.58 ± 10.55	61.42 ± 10.03
LVEDV / BSA (mL/m2)	87.37 ± 32.18	87.51 ± 33.12
LA Diameter (mm)	48.33 ± 12.98	45.50 ± 12.83
LA Volume / BSA (mL/m2)	40.9 ± 8.94	40.92 ± 8.29
TAPSE (mm)	13.67 ± 5.02	14.42 ± 5.4
RVSP (mmHg)	52.08 ± 12	49.83 ± 14.17

Successful mitral clip implantation was achieved in all patients. However, MR < grad II/IV was accomplished in 75% of patients. Although two clips strategy was required in most of these patients (75%), MPG across mitral valve remained within acceptable levels (4.33 ± 2.31 mmHg). As regard of symptomatic improvement during 12 months follow up, NYHA functional class was improved 2 or more grades in 66.7% of patient in parallel with efficient reduction of MR in 75% of patients. The successful reduction of MR was consistent so that no reintervention was required during the 12 months of follow up. The relation between Carpentier classification and NYHA improvement in addition to persistent MR reduction during clinical follow up is plotted in figure 1 and 2.

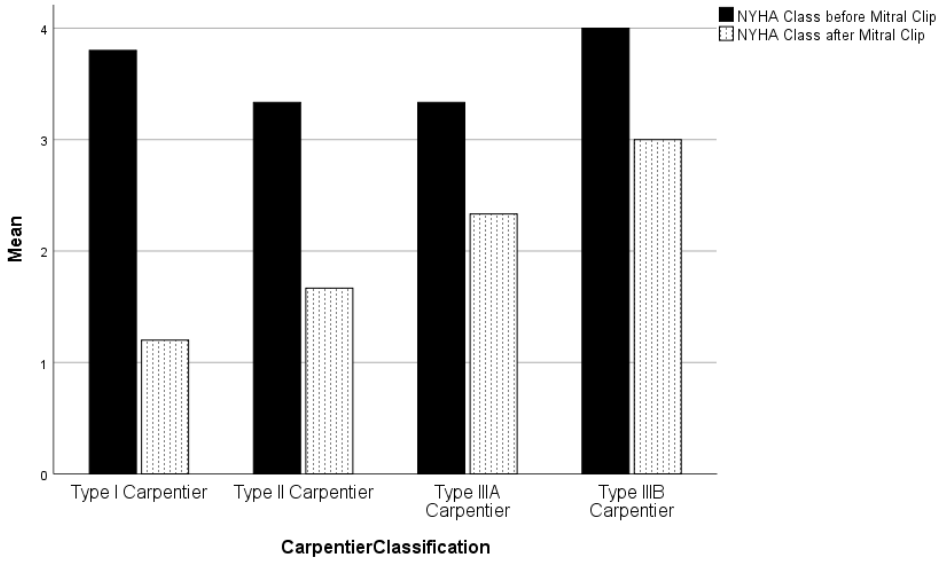

Fig. (1): Relationship between Carpentier class and NYHA improvement 12 months after mitral clip implantation.

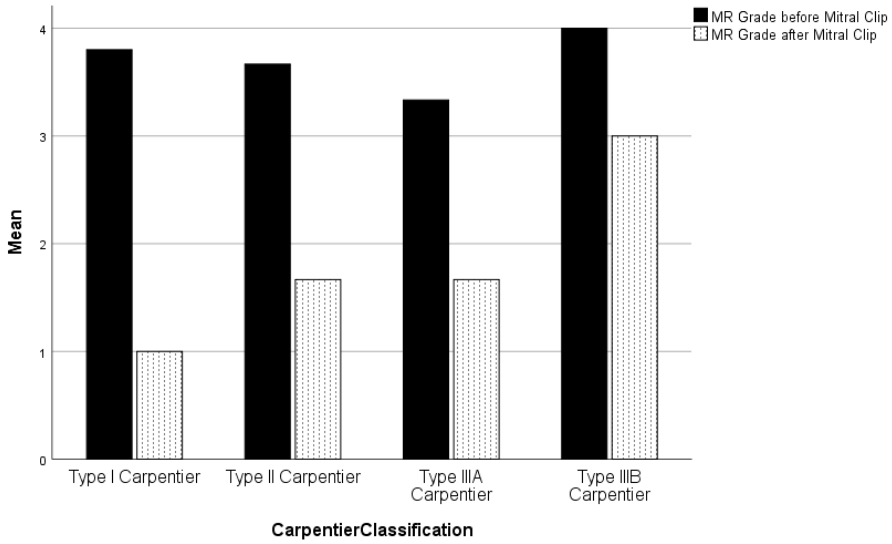

Fig. (2): Relationship between Carpentier class and MR improvement 12 months after mitral clip implantation.

There were no procedure related complications apart from puncture site hematoma in one patient that required evacuation, compression and 2 units of blood transfusion. Early follow up during the first 30 days postprocedural showed no procedure related mortality, but only one cases died owing to septicemia, which was confirmed after exclusion of infective endocarditis. During long term follow up, one patient passed away because of advanced heart failure.

Discussion

After two years of experience in mitral clip procedure and at least 25 cases treated

every year in each center, the interventional teams in both hospitals started mitral clip maneuver in relatively young patients with no surgical options of management due to high STS score. These cases represent our early experience in feasibility of mitral clip in relatively young patients and their early outcome after 12 months of clinical and echocardiographic follow up. Although the fact that a small number of patients was included in the study which hinders any generalization of the results, the most obvious finding was the persistent clinical response and MR reduction during 12 months follow up period in this category of patients. Based on successful mitral clip implantation in all patients of our study and satisfactory 12 months outcome without reintervention, we can state that the procedure is a good alternative option for inoperable severe MR patients younger than 65 years. The same results were confirmed in a number of small studies and case reports.[11,12]

Similar to COAPT population, patients enrolled in our study had large bpVCW (mean = 9.73 ± 1.89 mm), but with markedly dilated left ventricle (LV) and severely impaired LV systolic function, which was not the case in COAPT. Final conclusion of COAPT trial has confirmed that percutaneous repair of secondary severe MR is able to improve symptoms in comparison to optimal medical therapy (OMT) in heart failure with reduced ejection fraction (HFrEF) and explained that secondary severe mitral regurgitation may be an etiological factor in progression of HFrEF. [13]

Also, similar to MITRA-FR population, our patients showed dilated left ventricle (mean of LVEDD = 61.6 ± 10.6 mm) and severely impaired LVEF (mean = 32.9 ± 13.9%), but with larger vena contracta in comparison to patients of MITRA-FR. MITRA-FR trial failed to detect statistically significant difference as regard of symptomatic improvement between OMT and mitral clip therapy in patients with severe MR and HFrEF. [14]

This difference is explained by the fact that COAPT trial investigated primarily disproportionate MR, which can be simply expressed as more severe MR with smaller LV volume and dimensions in contrary to MITRA-FR population, who had principally proportionate MR, which represents larger LV volume and dimensions in combination with relatively less severe MR. [15]

The category of patients with the combination of large vena contracta and markedly increased LVEDD and severely depressed LV systolic function was investigated in our study and we can suggest that symptomatic improvement is achievable in this group of patients after mitral clip therapy.

Improvement of NYHA functional class has been confirmed post mitral clip after 4 years of follow up in EVEREST II, which studied 279 patients, who were classified into percutaneous repair group (mean age = 67.3 ± 12.8 years) and surgery group (mean age = 65.7 ± 12.9 years). Moreover, all patients could be operated which is not the case in all mitral clip studies. The final outcome of EVEREST II after 4 years of follow up stated that mitral clip population had less symptoms, assessed by NYHA class, and better quality of life when compared to surgery population. Nevertheless, the study had obviously confirmed that mitral clip was inferior to surgery when it comes to efficacy in reduction of MR, recurrent severe MR, reintervention and mortality. In addition, another remarkable point that we have learned from EVEREST II was that the probability of recurrence of severe MR is low, if the initial reduction of MR is maintained 6 months after the procedure. [16]

In order to achieve effective reduction of severe MR, the need for more than 1 clip implantation appeared very early in the first world experience of Mitral clip in EVEREST I study, so that the study protocol was modified after the first 10 patients to allow implantation of 2 clips when needed and 4 patients were treated by 2 mitral clips.[17] Our preprocedural strategy relied primarily on implantation of one clip and another clip placement when needed to achieve 2 or more grades reduction of MR with extreme caution to avoid more than 5 mmHg mean pressure gradient across mitral valve. Owing to large bpVCW (mean = 9.73 ± 1.89 mm) in these patients, 2 clips were used in 9 out of 12 patients with a mean of 1.75 ± 0,45 clip / patient. Recent studies reflected the increasing demand for multiple clip strategy. For example, mean clip numbers were 1.7 ± 0.7 clip/patient in COAPT trial.[13] The same pattern appeared in MITRA-FR study, where 9.4% of patients were treated by 3 or more clips, 44,9% received 2 mitral clips and one clip was implanted only in 45.7% of patients.[14]

Absence of mitral annular calcification in all patients was attributed to lower mean age (57.1 ± 4 years) and it was one of factors leading to achievement of clip implantation without elevated transmitral MPG. Jeremy et al., 2018 stated that lack of mitral annular calcification is one of the anatomic predictors of procedural success. Furthermore, presence of annular calcification together with preprocedural MPG and multiple clip placement are independent predictors of postprocedural elevated transmitral MPG.[18] Principally, all patients of our study were carefully selected based on clinical situation and individual anatomic criteria of their mitral valves. Predictors of mitral clip failure were mentioned by Lubos et al., 2014 in a study of 300 mitral clip patients as follows; effective regurgitation orifice area more than 70.8 mm^2, more than 4 mmHg MPG across mitral valve and less than 3 cm^2 mitral valve area. [19]

Another important limiting factor in our study besides small number of patients is the lack of long term follow up to clarify mortality benefit of mitral clip and improvement of heart failure course after reduction of MR.

Conclusion

Percutaneous mitral valve repair via MitraClip® in patients younger than 65 years rejected from surgical repair provides reliable clinical and echocardiography outcomes at 1 year. Future studies should evaluate the outcomes of MitraClip® in this population at longer follow-up.

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Conflict of interest:
All authors have no conflict of interest.

Abbreviations:

- **bpVCW:** Biplane vena contracta width.
- **BSA:** Body surface area.
- **HFrEF:** Heart failure with reduced ejection fraction.
- **LA:** Left atrium.
- **LV:** Left ventricle.
- **LVEDD:** Left ventricular end diastolic diameter.
- **LVEF:** Left ventricular ejection fraction.
- **MPG:** Mean pressure gradient.
- **MR:** Mitral regurgitation.
- **MVA:** Mitral valve area.
- **MVP:** Mitral valve prolapse.
- **MVR:** Mitral valve repair.
- **NYHA:** New York Heart Association.
- **OMT:** Optimal medical therapy.
- **QoL:** Quality of Life.
- **RVSP:** Right ventricular systolic pressure.
- **STS:** Society of Thoracic Surgeons.

- **TAPSE:** Tricuspid annular plane systolic excertion.
- **TR:** Tricuspid regurgitation.

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