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The short-term outcomes of MitraClip implantation: single-center experience in Turkey

MitraClip implantasyonunun kısa dönem sonuçları: Türkiye'den tek merkezli deneyim

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Background: This study aims to evaluate the procedural success and early outcomes of MitraClip implantation.

Methods: Between July 2012 and February 2013, 15 patients (12 males, 3 females; mean age 60.8±13.0 years; range 35 to 78 years) underwent MitraClip implantation in our clinic. All patients had symptomatic severe functional mitral regurgitation with high surgical risk or were judged to be inoperable by the cardiovascular surgeons.

Results: The success of the procedure was 93.33%. MitraClip was successfully implanted in all patients except one. Following the procedure, severity of the mitral regurgitation decreased by 2.1±0.5 grade on average. The mean NYHA functional capacity improved from 3.9±0.4 to 2.6±0.8 after one month during follow-up. Two patients (13.33%) died within the first month of follow-up due to noncardiac causes.

Conclusion: The MitraClip procedure can be performed safely to the symptomatic patients with severe functional mitral regurgitation who have otherwise high surgical risk or are judged to be inoperable. Our initial experience demonstrated acute echocardiographic and early clinical improvement in these patients.

Key words: MitraClip; mitral regurgitation; mitral valve repair.

Amaç: Bu çalışmada MitraClip implantasyonunun işlem başarısı ve erken dönem sonuçları değerlendirildi.

Çalışma planı: Temmuz 2012 - Şubat 2013 tarihleri arasında kliniğimizde 15 hastaya (12 erkek, 3 kadın; ort. yaş 60.8±13.0 yıl; dağılım 35-78 yıl) MitraClip ameliyatı uygulandı. Tüm hastalar yüksek cerrahi riski bulunan veya kardiyovasküler cerrahlar tarafından ameliyat edilemez kabul edilen, semptomatik ciddi fonksiyonel mitral yetersizliğine sahipti.

Bulgular: İşlem başarısı %93.33 idi. Biri hariç tüm hastalara MitraClip başarılı bir şekilde implante edildi. İşlem sonrasında mitral yetersizlik şiddeti ortalama 2.1±0.5 derece azaldı. Bir aylık takipte hastaların ortalama NHYA fonksiyonel kapasiteleri 3.9±0.4'den 2.6±0.8'e geriledi. İlk bir aylık takipte kardiyak dışı nedenlere bağlı iki ölüm (%13.33) olayı oldu.

Sonuç: MitraClip sistemi, cerrahi yüksek riskli veya ameliyat edilemez kabul edilen semptomatik ileri fonksiyonel mitral yetersizliği bulunan hastalarda güvenle uygulanabilir. İlk deneyimimiz bu hastalarda akut ekokardiyografik ve erken dönem klinik iyileşme göstermiştir.

Anahtar sözcükler: MitraClip; mitral yetersizliği; mitral kapak tamiri.

Mitral regurgitation (MR) is a frequently detected disorder that accounts for 24% of valvular heart disease cases in adults. Approximately 7% of the population older than 75 years has at least moderate MR,[1,2] and with increased surveillance after myocardial infarction (MI), longer life expectancy, and an aging population,

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the prevalence of MR is climbing. Moderate-to-severe MR occurs in 30% of patients with congestive heart failure.[3] Severe MR causes progressive left ventricular (LV) dilatation, dysfunction, and heart failure, and the severity is positively correlated with the development of heart failure and death.

Surgery, especially when repair is possible, is the standard treatment for MR in symptomatic patients or those with LV dilatation and dysfunction.[4] However, in clinical practice, because of associated comorbidities and a high surgical risk, many of these patients do not undergo surgery.[5] Additionally, in patients with functional MR, no survival benefit has been shown,[6,7] and some studies have suggested a high MR recurrence rate.[7-9] Therefore, surgery for secondary MR remains a challenge. Less invasive interventional procedures have been developed to percutaneously correct MR, with the MitraClip procedure (Abbott Laboratories, Abbott Park, IL, USA) having received considerable attention in high-risk patients with both functional and organic MR.

The aim of this study was to present the procedural success and short-term results of 15 patients who underwent MitraClip implantation at our heart center.

PATIENTS AND METHODS

Fifteen patients (12 males, 3 females; mean age 60.8±13.0 years) who underwent percutaneous mitral valve repair using the MitraClip between July 2012 and February 2013 were enrolled in our study. All of the patients had severe functional MR and were deemed to be inoperable or were judged to be a high surgical risk by our heart team.

All procedural and in-hospital events were recorded, and success was defined as the implantation of the MitraClip and at least a one-grade reduction in the MR without any obstruction. After discharge, the patients were evaluated via echocardiography and a six-minute walking test one month after the implantation.

Patient selection

All patients evaluated by our heart team for MitraClip implantation had New York Heart Association (NYHA) class 3-4 functional capacity under optimal medical therapy with severe functional MR. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were performed on all patients to assess the MR severity, leaflet structure, and MR etiology. In addition, they were also evaluated according to the whether they met the appropriate criteria for MitraClip implantation. Mitral regurgitation severity was assessed according to the European Association of Echocardiography (EAE)[10] and was classified as mild (1^+), mild-to-moderate (2^+), moderate-to-severe (3^+), or severe (4^+). Based on the echocardiographic parameters, the patients who had a thick interatrial septum, severe leaflet calcifications (in the grasping region), thick valve leaflets (>5 mm), an immobile posterior leaflet, a coaptation length of less than 2 mm, a short and fixed posterior leaflet, rheumatic etiology, or a mitral valve planimetric area of smaller than 4 cm^2 were excluded from the study. Other exclusion criteria for MitraClip implantation were a short life expectancy, malignancies, and poor quality of TEE images. Table 1 summarizes the echocardiographic parameters for each patient that were used to determine whether the procedure was appropriate. These criteria were based on the anatomic criteria set by the Endovascular Valve Edge-to-Edge Repair Study (EVEREST).[11,12] The originally applied EVEREST criteria served as reference parameters, but not all of them were accepted as being absolute for exclusion. For example, we included patients with a left ventricular ejection fraction (LVEF) of <25%, a LV end-systolic diameter of >55 mm, and patients with renal insufficiency, all of which were excluded in the EVEREST trial. Furthermore, partial calcification of the leaflets, the length and depth of the coaptation, an absolute valve area of <4 cm^2, a poor EF, and a noncentral location of jet origin were not considered to be absolute contraindications for the procedure.

Procedure

The implantation was performed in a catheterization laboratory under general anesthesia with two interventional cardiologists, one echocardiographer, one anesthesiologist, one technician, and one nurse present. Fluoroscopy and real-time TEE, were used during the implantation for guidance to ensure the success of the procedure. Although three-dimensional (3D) TEE is not necessary, it can decrease the length

Table 1. Echocardiographic eligibility criteria for MitraClip implantation

Inclusion criteria	
Coaptation length	≥2 mm
Posterior leaflet length	≥8 mm
Leaflet thickness	≤5 mm
Mitral valve orifice area	≥4 cm^2
Mobile posterior leaflet	
No leaflet calcification at grasping site	
Exclusion criteria	
Rheumatic valve disease	
Presence of cleft	

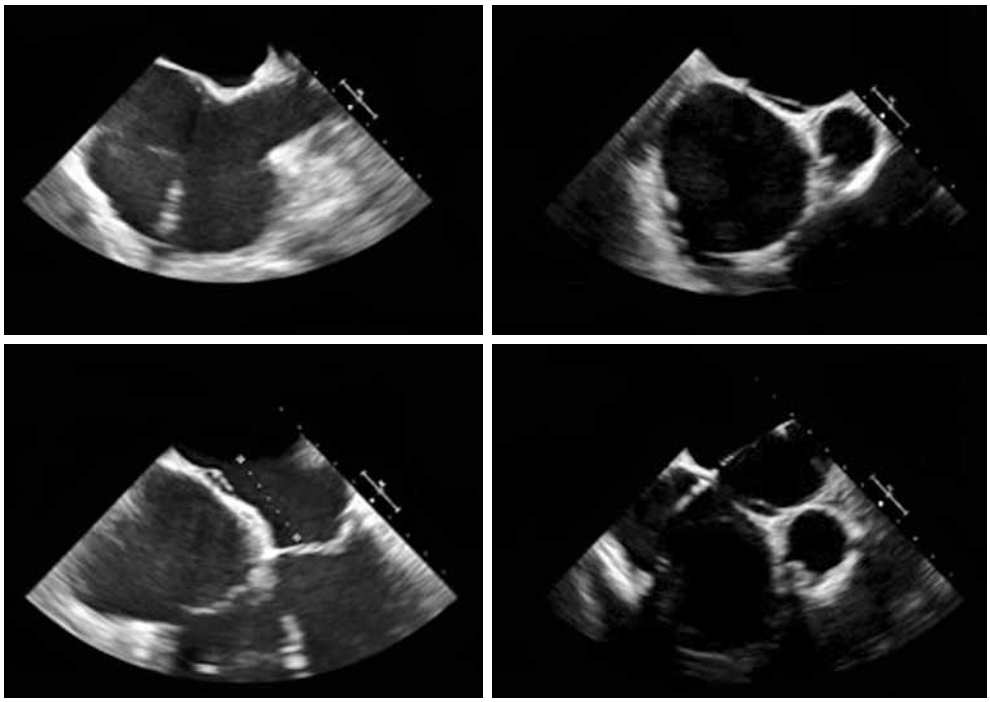

Figure 1. Transesophageal images of optimal transseptal puncture.

of the procedure and increase the success rate. Invasive arterial pressure was monitored through the radial artery, and prophylactic antibiotics were given before implanting the chip. The sheath was placed in the right femoral vein, and a transseptal puncture was performed with a Brockenbrough needle. The localization of this puncture was vital for the progress and success of the implantation, with the ideal point being in a superoposterior location approximately 3.5 to 4 cm from the mitral annulus in the TEE four-chamber view (Figure 1) so that there would be enough space in the left atrium for manipulating the clips. The patient was heparinized after the transseptal puncture, and the activated clotting time (ACT) was followed by a 15-minute interval that was kept between 250 and 350 seconds. After the puncture, a 0.035 extra-stiff exchange guidewire was advanced to the left upper pulmonary vein, and the transseptal sheath was exchanged for a steerable guide catheter and dilator. The clip delivery system was then introduced into the guide catheter, and the MitraClip device was advanced into the left atrium. With the guidance of the fluoroscopy and TEE, the clip was then directed toward the MR jet. The arms of the clip were opened in the left atrium, checked for perpendicularity, and directed toward the ventricle. As soon as both leaflets were inserted on the clip, the grippers were moved down, and the clip was closed (Figure 2). After the MitraClip was used to control the reduction in MR along with the gradient on the mitral valve, and the stabilization of both leaflets had been achieved by the clip, it was detached from the connections and released (Figure 3). In five of the patients, the reduction in the MR was not satisfactory at this point, and a second clip was then inserted. The procedure concluded with the hemostasis of the access site, which was accomplished with figure-of-eight suturing. The patients were prescribed dual antiplatelet therapy

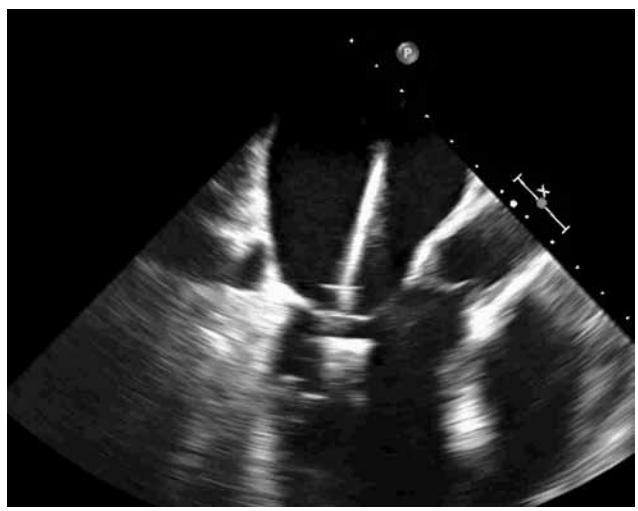

Figure 2. Transesophageal view while grasping the mitral leaflets.

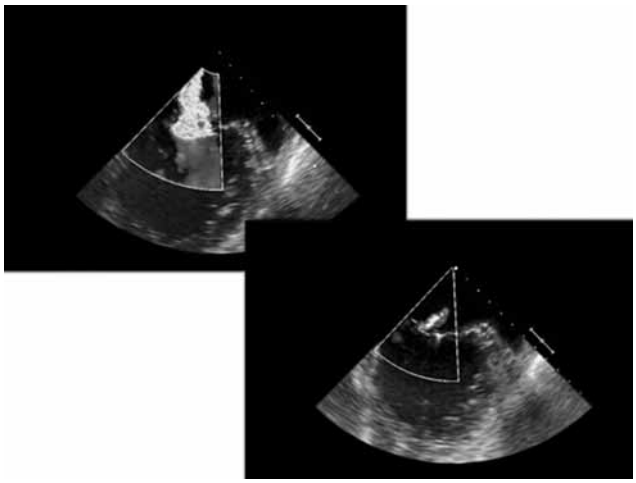

Figure 3. Color Doppler view of mitral regurgitation before and after the procedure.

(aspirin 100 mg and clopidogrel 75 mg) for at least three months afterwards and were informed about infective endocarditis prophylaxis during the first six postprocedural months.

RESULTS

Patient characteristics

The baseline demographics and clinical features of the patients are shown in Table 2. Thirteen patients (86.66%) were NYHA functional class 4 while two (13.33%) were functional class 3 under optimal medical therapy. All except one had a low LVEF (28.7±8.8). The etiology of MR was functional MR secondary to the dilated cardiomyopathy (CMP) in four patients (26.66%), MR secondary to ischemic CMP in 10 (66.66%), and ischemic MR with preserved LVEF in one (6.66%). Furthermore, all had severe (4^+) MR. A one-month follow-up was available for the 13 patients who received clips and survived.

Procedure and in-hospital results

The MitraClip was successfully implanted in 14 (93.33%) of the 15 patients, with one clip being implanted in nine patients (64.28%), and two clips in the other five (35.71%). We could not implant a clip in one patient (6.66%) because the interatrial septum was deviated too much toward the right atrium due to increased left atrial pressure, and the location of the interatrial septal puncture could have possibly led to an unsuccessful result.

The mean procedure time was 183.8±81.0 minutes (range 90-300 minutes) with a mean septal puncture time of 36.2±32.1 minutes. The success rate (correct positioning of the clip with a reduction in MR severity by at least one grade) was 100% in the patients with the implanted clip. There was improvement in the MR severity in all of the patients intraoperatively just after the clip implantation. However, the average MR severity decreased significantly from 4^+ to $1.89\pm0.48^+$ after the intervention, and no significant iatrogenic mitral valve stenosis was detected after the procedure. The mean mitral valve gradient was 3.13±1.16 mmHg.

Procedural mortality was 0%, and all of the patients tolerated the procedure well. However, two died while still in the hospital (13.33%), and one died on the fifth day after the procedure, before the day of externalization, due to a head trauma. In addition, the patient for whom the implantation of the clip failed, died three weeks later due to noncardiac causes

Table 2. Baseline demographics and clinical features (n=15)

	n	%	Mean±SD
Age in years			60.8±13.0
>65 years old	6	40.0	
Gender			
Male	12	80.0	
Hypertension	6	40.0	
Diabetes mellitus	5	33.3	
Creatinine			1.3±0.4
Estimated glomerular filtration rate (ml/min/1.73 m^2)			57.7±16.7
History of coronary artery disease	11	73.3	
Previous coronary artery bypass graft	6	31.5	
Ejection fraction			28.7±8.8
Left ventricle end-diastolic diameter (mm)			64.9±9.3
Left ventricle end-systolic diameter (mm)			54.8±10.8
N terminal pro B-type natriuretic peptide (pg/ml)			3642.3±3220.0

SD: Standard deviation.

(pneumonia and sepsis). The mean length of hospital stay was 5.4±2.3 days, and the mean intensive care unit (ICU) stay was one day for the clip-implanted patients.

One-month follow-up results

At the one-month follow-up, one patient with a past history of gastrointestinal bleeding and chronic renal failure required a blood transfusion along with an endoscopic examination because of gastrointestinal bleeding after externalization. It is possible that dual antiplatelet treatment might have contributed to this event.

Twelve (92.30%) of the 13 surviving patients reported clinical improvement. The average functional status of the patients improved from NYHA class 3.9±0.4 to 2.6±0.8, and their six-minute walking distances improved from 276.2±150.7 to 378.0±168.4 meters. Furthermore, the N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) levels decreased from 3642.3±3220.0 to 2025.8±810.3 pg/ml. The average MR severity was 2.20±0.33^{+} at one month, which was a little higher than the post-procedural MR but still lower than the baseline.

DISCUSSION

We reported 14 successful MitraClip implantation to patients with symptomatic functional MR. Acute improvement in MR severity was achieved in all of the clip-implanted patients. We obtained a mean MR reduction of 2.10±0.48 degrees (Figure 4), and at the one-month follow-up, all of the patients, except for one, reported functional improvement.

Different classifications for mitral valve regurgitation have been identified by Carpentier et al.,[13] and Kumar et al.[14] and it has been categorized etiologically as either primary or secondary according to the presence or absence of leaflet pathology. Surgical mitral valve repair has been successful in cases of organic mitral valve disease, but the role of conventional surgery for patients with severe

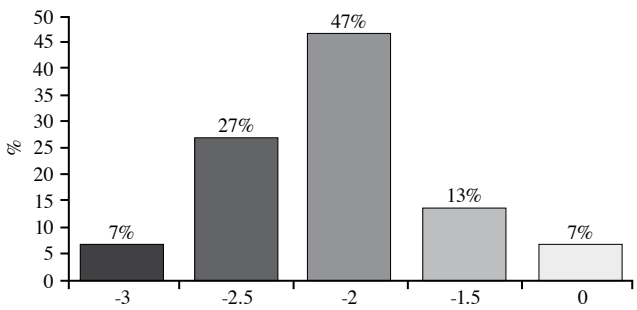

Figure 4. Mitral regurgitation severity reduction by grade in fifteen patients.

secondary MR, compared to those with primary MR, has not been well-defined, and its outcome has been less predictable. Two studies described undersized mitral annuloplasty in patients with end-stage cardiomyopathy and secondary MR.[15,16] The results of that procedure with regard to low operative mortality, enhanced functional capacity, and improved ventricular function have also been reported by in two other studies.[17,18] However, long-term follow-up failed to show any survival benefit of isolated reduction annuloplasty for severe secondary MR with NYHA class 3-4 heart failure.[6] In addition, Mihaljevic et al.[19] could not demonstrate long-term functional status or improved survival in patients with severe functional ischemic MR. The most appropriate indications and effective types of intervention for secondary ischemic MR remain open to debate. In the most recent European guidelines for valvular heart diseases,[4] mitral valve surgery was recommended for symptomatic patients with severe secondary MR and NYHA class 1 if they had an EF of >30% and underwent revascularization and for those with NYHA class 2a if they had an EF of <30% with an option for revascularization and a viable myocardium. Mitral valve surgery is also possible for symptomatic patients with NYHA class 2b under medical therapy with severe secondary MR and low comorbidity if they have an EF of >30% with no option of revascularization. However, medical therapy is still the most preferred treatment for those with an EF of <30% and no possibility of revascularization. In the event that the medical therapy fails, cardiac resynchronization therapy, ventricular assist devices (VADs), and transplantation are other treatment alternatives.[4] These patients may especially be a target for percutaneous valve repair treatment in order to postpone transplantation. Surgical mitral valve repair may also be tried for this purpose, but many of these patients cannot undergo surgery because of associated comorbidities.

Creating a double mitral valve orifice by the approximation of two mitral leaflets was first performed surgically by Alfieri et al.[20] This is a relatively simple type of surgery and can be applied to both organic and functional MR, and its simplicity and effectiveness led to the development of similar catheter-based procedures.[21] The first human application of the MitraClip was performed in 2003, and it has now been successfully implanted in over 6,000 patients worldwide. Soon after it was introduced, the EVEREST I and II studies were published.[10,11,22] The EVEREST I trial evaluated the MitraClip system for its initial safety, and the study population

consisted of patients with moderate-to-severe MR with clinical symptoms or LV dysfunction. It found that percutaneous edge-to-edge mitral valve repair could be performed safely and that in a significant proportion of patients, a reduction in MR could be achieved. The EVEREST II trial was a randomized comparison of mitral valve surgery and percutaneous mitral repair that evaluated the safety and efficacy of the MitraClip procedure compared with conventional valvular surgery.[22] It demonstrated that although percutaneous mitral valve repair was less effective than conventional surgery in reducing MR severity, it was safer than surgery, especially in the first month, and had the same clinical benefits. A subgroup in the EVEREST II trial was made up of 78 high-risk patients, and one-year survival was significantly higher in the high risk study group compared to control group after the MitraClip procedure (76.4% vs. 55.3%, p=0.047).

Franzen et al.[24,25] reported successful outcomes and short-term durability of the MitraClip in functional MR patients, with a significant reduction in MR along with clinical improvement in European clinical trials compared with those in the United States where the majority of treated patients had degenerative MR.

Herein, we report on the safety and efficacy of percutaneous mitral valve repair in patients with functional MR and those patients who underwent successful clip implantation experienced clinical and echocardiographic benefits at the one-month follow-up with regard to reduction in MR severity, improvement in NYHA functional class, NT-ProBNP reduction, and an increased six-minute walking distance.

Conclusion

MitraClip implantation has emerged as an alternative to surgery in symptomatic patients with severe MR and a high or prohibitive surgical risk. It is a safe and effective mode of therapy for these patients and those deemed to be inoperable who have severe symptomatic functional MR and LV dysfunction. In our study, this procedure significantly improved the severity of MR and the functional capacity of patients in a short-term follow-up.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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