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Percutaneous MitraClip device in patients with symptomatic mitral regurgitation: results from three medical centers in Mexico

Dispositivo MitraClip percutáneo en pacientes con regurgitación mitral sintomática: resultados de tres centros hospitalarios en México

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Palabras clave:
Insuficiencia cardiaca, enfermedad valvular mitral, regurgitación mitral severa, MitraClip.

ABSTRACT

Objective: The aim of this study was to evaluate the experience of the use of the MitraClip device in terms of mortality, complications, mitral valve regurgitation reduction, and variations in left ventricle echocardiographic parameters. **Material and methods:** All patients included in the study were treated with the MitraClip device, assessed and considered to be high risk by the Heart Team. Follow-up was conducted 3-9 months after the procedure with transthoracic and transesophageal echocardiography. **Results:** Thirty-three patients were recruited from three medical centers in Mexico. After the procedure, 76% of patients were considered to have had a successful treatment, and during follow-up, 70% remained in this category, whereas only 6% of patients continued to experience mitral valve regurgitations still. Seven patients died, two of them during follow-up and five more dying from postoperative complications. The overall survival was 17.2 ± 1.3 months (CI 14.6-19.9). During the procedure, one detachment and one partial detachment of the device occurred. The procedural success was similar to the one reported in the EVEREST I study and the 2016 TVT registry. In this study, it was found that only one patient had a recurrence of severe MR. It has been described that The Society of Thoracic Surgeons (STS) risk scale and mortality had a strong relationship, which matched the results of this study. In this research, no complications were found, as seen in other trials, such as stroke or dialysis requirements. **Conclusions:** In this population, treatment with the MitraClip device improved the functional class and had few adverse events, signifying this treatment is an achievable option.

RESUMEN

El objetivo de este estudio fue evaluar la experiencia del uso del dispositivo MitraClip en términos de mortalidad, complicaciones, reducción de grado de insuficiencia mitral y las variaciones en los parámetros ecocardiográficos ventriculares izquierdos. ***Material y métodos:*** *Todos los pacientes del estudio fueron tratados con el dispositivo MitraClip, considerados de alto riesgo por el equipo de Cardiología. Se realizó un seguimiento entre 3-9 meses posterior al procedimiento, mediante ecocardiografía transtorácica y transesofágica.* ***Resultados:*** *Treinta y tres pacientes fueron reclutados de tres centros médicos en México. Después del procedimiento, 76% de los pacientes tuvieron un tratamiento exitoso y durante el seguimiento, 70% de ellos permanecieron en esta categoría, donde únicamente el 6% de los pacientes continuaron con regurgitación mitral valvular. Siete pacientes fallecieron, dos de ellos durante el seguimiento y los otros cinco por complicaciones durante el periodo postoperatorio. La supervivencia total fue de 17.2 ± 1.3 meses (IC 14.6-19.9). Durante el procedimiento, se presentó un desprendimiento y un desprendimiento parcial del dispositivo. El éxito del procedimiento fue similar al reportado en el estudio EVEREST I, así como en el registro TVT 2016. En este estudio, se encontró recurrencia de regurgitación mitral severa en un paciente. Se ha descrito previamente una fuerte relación entre la escala Society of Thoracic Surgeons (STS) y la mortalidad, lo cual coincide con estos resultados. En el presente estudio, no se hallaron complicaciones como las descritas en otros estudios publicados, tales como infarto o requerimientos de diálisis.* ***Conclusiones:*** *En esta población, el tratamiento con MitraClip mejoró la clase funcional disminuyendo eventos adversos, aumentando la factibilidad de este tipo de tratamiento.*

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INTRODUCTION

Heart failure has a wide range of etiologies, and mitral valve disease (MVD), together with ischemic heart disease and diabetes, are the leading causes of heart failure; in this context, valvular heart disease remains one of the leading causes of heart failure.[1] In the last fifteen years, due to the increase in life expectancy, there have been changes in the etiology of MVD, while rheumatic causes have diminished, degenerative diseases have increased. In the management of MVD with medical treatment in severe mitral regurgitation (MR), the mortality rate does not improve, only the symptoms. Reports indicated that for every patient who required surgical treatment for the aortic valve, four patients with severe MVD needed surgery, and approximately 6.4% of the population older than 65 years had moderate to severe MVD.[2]

International guidelines recommend treatment with a percutaneous mitral valve repair (pMVR) procedure with the MitraClip device for moderate or severe MR in patients who are not candidates for surgery, such as those with a high surgical risk, with a life expectancy greater than 12 months, who are symptomatic and receiving optimal medical treatment or who have severe MVD that was either degenerative or functional.[3,4]

The safety and viability of the MitraClip system were widely demonstrated in the EVEREST report with a success rate of 75% that diminished the degree of MR after the procedure;[5] on the other hand, the EVEREST II study showed that MitraClip was safer than surgery; however, the surgery was more efficient than the MitraClip.[6] During the four years of follow-up in the EVEREST study, it was found that the patients treated with MitraClip more commonly required surgery to treat residual MR compared to surgery alone. However, no differences were found in the patient mortality for moderate or severe MR.[7]

This research aimed to evaluate the mortality, complications, mitral valve regurgitation reduction and modifications in left ventricular echocardiographic parameters during the follow-up for the MitraClip device.

MATERIAL AND METHODS

Study population

This prospective cohort study of consecutive patients included 33 patients with severe MR (++++) who underwent pMVR with the MitraClip device (Abbot Vascular, Menlo Park, California) in three medical centers, National Medical Center "20 de Noviembre", ISSSTE, Doctors Hospital (in Monterrey) and Angeles Lomas Hospital, between September 2015 and December 2016 for severe primary and secondary MR.

The Heart Team assessed the decision for pMVR. All included individuals were considered to be symptomatic high risk patients (Society of Thoracic Surgeons [STS] mortality risk > 8%) according to the 2014 AHA/ACC Guidelines[3] and to have severe (++++) primary or secondary MR that could not be addressed with a traditional surgical procedure. The inclusion criteria were: symptomatic, New York Heart Association (NYHA) functional class

Table 1: Characteristics of the patients (N = 33).

	n (%)
Age-yr	67.7 ± 10.8
Gender	
Male	18 (54.5)
Female	15 (45.5)
Cardiovascular risk factor	
Hypertension	24 (73)
Diabetes mellitus type 2	9 (27)
Previous heart disease	
Coronary heart disease	21 (64)
Percutaneous coronary intervention	17 (52)
Cardiac resynchronization therapy	9 (27)
Revascularization surgery	5 (15)
Occluder for percutaneous left atrial appendage closure	4 (12)
TAVR	3 (10)
Hemoglobin	13.2 ± 1.8
Hematocrit	40.4 ± 5.6
Creatinine	1.2 ± 0.4

TAVR = Transcatheter aortic valve replacement.

Table 2: Mitral insufficiency modification after MitraClip (N = 33).

Severity of mitral insufficiency at baseline	n (%)
++++	33 (100)
After procedure	
≥ ++	25 (76)
≤ +	6 (18)
Died	1 (3)
Aborted procedure	1 (3)
Clinical follow-up	
≥ ++	19 (58)
≤ +	4 (12)
Died	6 (18)
Lost follow-up	4 (12)

III-IV or patients with NYHA II with at least two hospitalizations due to decompensated heart failure despite optimal medical therapy. Anatomical valve criteria were based on the echocardiographic measurements established in the EVEREST study[5] as follows: valve area > 3.5 cm^2, length of the posterior leaflet > 7 mm, coaptation depth < 10 mm. The exclusion criteria were myocardial infarction within the last 12 months, creatinine > 2.5 mg/dL, endocarditis, rheumatic valvular disease or a mean transvalvular pressure gradient (MVPG) > 3 mmHg. Severe primary MR was defined according to the AHA/ACC guidelines[3] based on the following echocardiographic characteristics: central jet MR > 40%, left atrium (LA) or holosystolic eccentric jet MR, vena contract area ≥ 0.7 cm, regurgitant volume ≥ 60 cc, regurgitant fraction ≥ 50%, and effective regurgitant orifice (ERO) ≥ 0.40 cm^2. Severe secondary MR was defined by ERO ≥ 0.20 cm^2 and regurgitant volume ≥ 30 cc. Mitral insufficiency was classified from mild to severe (+/++++).

Measurement of LV volumes and ejection fraction was performed according to the biplane Simpson's method.

Procedure and devices

The MitraClip was implanted with the usual technique.[6] Additional MitraClip implantations were performed if a moderate or severe residual lateral/medial MR was present.

Definitions

Successful treatment was considered to be a decrease ≥ ++ after the procedure, determined by transesophageal echocardiography.

Cardiac tamponade, intracardiac thrombus, major bleeding, partial or complete detachment were considered as complications during the procedure. Major bleeding was defined as a decrease in hemoglobin > 3 g/dL or the need for a blood transfusion. Partial detachment was defined as the complete loss of connection between a clip and one leaflet. Complete detachment was defined as the disconnection of the clip from both the anterior and posterior leaflets.

Follow-up

After the procedure, follow-up was conducted 3-9 months later with transthoracic and transesophageal echocardiography. In patients who were unable to be present, telephone interviews were conducted to establish their survival status. Transthoracic and transesophageal echocardiography were performed with ultrasound systems (ACUSON SC2000, Siemens Medical Solutions USA, Inc., and Phillips EPIQ 7, Royal Phillips Electronics, Amsterdam, the Netherlands) with the technique reported by Foster and collaborators.[8]

Hospitalization and any-cause of death were considered as events during follow-up.

Statistical analysis

The data were analyzed using Statistical Package SPSS for Windows version 20 (IBM, 2010). Variables were tested for normality with the Kolmogorov-Smirnov test. Parametric variables were expressed as the means (standard deviation). Categorical variables were described as absolute and relative frequencies. The overall change over time for repeated measures was analyzed with the Friedman test. A comparison between groups was determined with a Student's t-test. For the association between variables,

a Pearson correlation was used. A two-tailed p value of < 0.05 was considered significant. The overall survival rates and mean time were assessed by the Kaplan-Meier method. A multiple regression was performed to analyze any risk associated to death.

RESULTS

The general characteristics of the patients were determined *(Table 1)*. A total of thirty-three patients with severe MR (++++) were recruited for MitraClip device implantation in three medical centers in Mexico. The mean follow-up was 4.6 months.

All patients were considered high risk by the multidisciplinary heart team (mean STS mortality risk 8.2). And all of them signed a written informed consent for the procedure. Four patients with degenerative and 29 patients with functional MR.

In twenty-three patients, one clip was placed (70%); in seven patients, two clips were implanted (21%); and in three patients, three clips were deployed (9%).

Mitral insufficiency was compared with a Wilcoxon test immediately after the procedure ($n = 31$, $p \leq 0.001$) and during follow-up ($n = 23$, $p \leq 0.001$). After the procedure, 25 patients (76%) were considered to have successful results, and during follow-up, 19 patients (70%) were deemed to have successful results *(Table 2)*. Two patients (6%) during the follow-up continued to experience severe MVR.

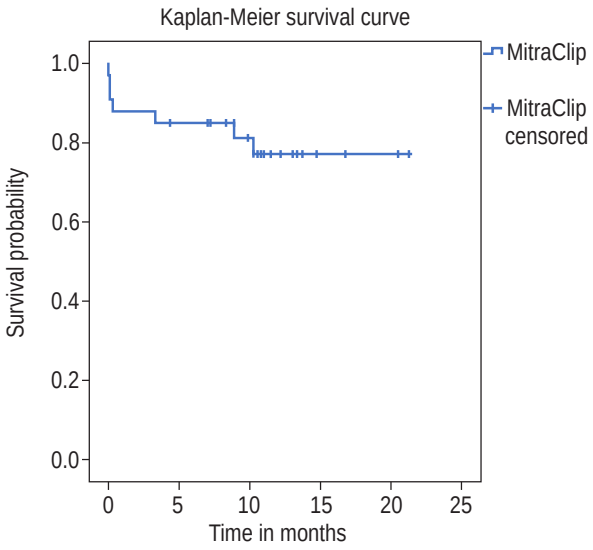

Figure 1:

Kaplan-Meier survival curve for death within 25 months.

Before the procedure, four patients were in NYHA class II (12%), twenty-one patients were in class III (64%), and eight patients were in class IV (24%); after the procedure, seven patients died, and one of them was lost to follow-up. In the remaining patients, the NYHA scale improved as follows: nine patients were in class I (27%), twelve patients were in class II 4 (36%), three patients were in class III (9%), and only one patient remained in class IV (3%); a Friedman test indicated statistical significance ($n = 25$, $p \leq 0.001$).

The overall mortality was seven patients (24%), including two who died during the follow-up, with one of them dying due to heart failure. Five patients died within the first ten days after the procedure, and the causes were pulmonary embolism, hemothorax, esophagus perforation, acute pulmonary edema, and cardiogenic shock. A Pearson correlation was used to determine the association between mortality and hemoglobin (rho = -0.373, p = 0.042), hematocrit (rho = -0.387, p = 0.034) and STS score (rho 0.463, p = 0.11). Kaplan-Meier *(Figure 1)* analysis revealed a median overall survival of 17.2 ± 1.3 months (CI 14.6-19.9).

Echocardiographic parameters were compared with a Student's t-test *(Table 3)*. We found differences in the left ventricle diastolic diameter and the systolic pulmonary pressure *(Table 3)*. A postprocedural mean transvalvular gradient < 5 mmHg was the most predominant measurement in 16 patients (49%), a gradient of 6 mmHg was found in three patients (9%) and a gradient of 7 mmHg was found in 2 patients (6%); the data were lost for 10 patients (30%), 7 patients died and in 3 patients were lost during follow-up. Furthermore, the correlation between postprocedural gradient and mortality was not significant (rho = .065, p = .767), and all of the patients who had a postprocedural gradient ≥ 6 survived during the follow-up, but the correlation with NYHA exhibited only a slight correlation (rho = .446, p = .026) *(Table 3)*.

Major bleeding was recorded in two patients (6%); two patients required rehospitalization during the follow-up due to heart failure. One of them died, which was secondary to a

Table 3: Echocardiographic measurement.

Variable	Before	After	p
LVEF (%)	36.6 ± 11.7 (n = 27)	38.8 ± 15.6 (n = 27)	0.387
LVDD* (mm)	61.2 ± 9.4 (n = 25)	56.8 ± 9.5 (n = 25)	0.027
LVSD (mm)	49.1 ± 10.7 (n = 25)	53.9 ± 38.4 (n = 25)	0.624
LVDV (mL)	169.0 ± 53.9 (n = 25)	174.1 ± 59.6 (n = 25)	0.829
LVSV (mL)	109.2 ± 48.3 (n = 25)	111.7 ± 58.7 (n = 25)	0.448
SPAP* (mmHg)	48.0 ± 17.9 (n = 22)	45.1 ± 15.0 (n = 22)	0.001

LVEF = left ventricle ejection fraction; LVDD = left ventricular diastolic diameter; LVSD = left ventricular end systolic diameter; LVDV = left ventricular diastolic volume; LVSV = left ventricular systolic volume; SPAP = systolic pulmonary artery pressure.
* $p < 0.05$.

left atrial thrombus found during the echocardiography. During the procedure in one patient, he had a complete detachment, and eventually, the patient died of a pulmonary embolism; another patient had partial detachment without clinical consequences. Additionally, one of the patients required repeat MitraClip therapy due to significant recurrent mitral regurgitation.

Logistic regression analysis showed no relationship between mortality and age, sex, diabetes, hypertension, ischemic cardiomyopathy, left ventricular ejection fraction or previous heart surgery.

DISCUSSION

To the best of the knowledge of the heart team, this is the first report on the use of MitraClip in Mexico and in Latin America. The procedural success in these institutions (75%) was similar to the success rate reported in the EVEREST I (74%)[9] trial and the 2016 TVT registry (86%). However, during follow-up, this rate decreased to 54% but was not related to the EVEREST I rate, which remained constant. The following mechanisms could explain this discrepancy: progression of the underlying cardiomyopathy or loss of leaflet insertion into the clip caused by insufficient leaflet grasping, which predisposes the clip to leaflet tear or perforation.[10]

Taramasso and colleagues[11] found that severe pulmonary hypertension and restricted posterior leaflet motion increased the risk of recurrence or persistent MVR after MitraClip implantation in cases of functional mitral regurgitation (FMR). In this study, it was found that only one patient (3%) had a recurrence for severe MR. Since he had functional MR and presented a gradual decrease in the diastolic diameter of the left ventricle (88 mm to 66 mm), it was suspected that he had a loss of leaflet insertion; nevertheless, this patient did not have a negative prognostic impact in terms of survival or symptoms since his NYHA functional class and LVEF presented a slight variation compared to the baseline.

It has been established that STS risk and mortality have a strong relationship,[12] which is consistent with the results presented; nevertheless, in the present study, the association between LVEF < 30% and mortality previously reported in TRAMI[13] did not agree with said results because, in this study, this association was not significant (rho = - 0.234). Although five of the seven patients who died had an LVEF < 30%, this outcome could be explained because the sample was small.

The essential periprocedural morbidity reported was single leaflet device detachment, which was identified in 1.4% of patients by the previous reports;[14] in this study, it was observed that 3% of patients had that detachment type. No complications were found as seen in other trials, such as stroke or dialysis requirements.

The increase in postprocedural MVPG is a significant event predictor for poorer long-term outcomes (2 years) and increased all-cause mortality.[15] Our study showed that patients with increased MVPG did not currently have any clinical deterioration; nevertheless, we could expect a different outcome from a longer follow-up. It was found that implantation of ≥ 2 clips was not associated with higher gradients during follow-up.

Other predictors of 1-year mortality in TRAMI[13] were NYHA class IV, anemia, previous aortic valve intervention, renal failure with serum creatinine ≥ 1.5 mg/dL, peripheral artery disease, left ventricular ejection fraction < 30%, and severe tricuspid regurgitation. In this study, only an association between hemoglobin and hematocrit was found, as previously reported.

This research had some limitations. The data were from an observational study of the

feasibility of the MitraClip device. This study was not a randomized trial and did not have a medically treated control group for comparison. In addition, follow-up was limited, and data during the follow-up could not be obtained. Nevertheless, all the echocardiography was performed with the same echocardiography protocol, which limited the results' variation, and such results are similar to those of more extensive studies.

CONCLUSIONS

The medical heart team can conclude that treatment with the MitraClip device seems viable and safe in a preselected high-risk population. Improvements in the functional class and few adverse events make this treatment a feasible option.

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