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Predictors of outcome in patients undergoing MitraClip implantation: An aid to improve patient selection

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ABSTRACT

Background: MitraClip implantation (MCI) reduces mitral regurgitation (MR) and symptoms in patients considered inoperable or with high-surgical risk. Data to determine the benefit from MCI for an individual patient are limited. The aim of this study is to determine predictors associated with the prognosis after MCI to improve the patient selection for this procedure.
Methods: We included 84 consecutive patients (age: 76 ± 10 years, 51% male) who underwent MCI in our institution for symptomatic severe MR. All patients underwent transthoracic echocardiography before MCI; clinical and echocardiographic follow-up was obtained after MCI.
Results: The 2-year survival was 81%. Predictors for two-year mortality in multi-variate analysis were baseline NT-proBNP ≥ 5000 μg/L (HR: 5.4, 95% CI: 1.8–16.2), previous valve surgery (HR: 4.5, 95% CI: 1.7–12.2), tricuspid regurgitation (TR) ≥ grade 3 prior to MCI (HR: 2.8, 95% CI: 1.2–6.8) and absence of MR reduction after MCI (HR: 2.1, 95% CI: 1.2–3.8). The 2-year survival of patients with 0, 1 or ≥2 of these predictors was: 87%; 78% and 38% respectively (log-rank $p < 0.001$). The functional class at 1 month and mid-term follow-up was worse in patients with two or more of these predictors present at baseline compared to patients with zero or one of these predictors (1 month: $p = 0.007$ and mid-term: $p < 0.001$).
Conclusion: Heart failure, previous valve surgery, co-presence of TR and the degree of MR reduction after MCI are the independent predictors of survival and functional status after MCI in high risk patients. The pre-procedural characteristics may be used to optimize patient selection, while maximal MR reduction should be attempted to optimize the outcome of MCI.

1. Introduction

Mitral regurgitation (MR) is a common valvular heart disease with high morbidity and mortality rates, especially in the aging population [1–4]. Surgical mitral valve repair is the preferred treatment for severe MR [5], but many patients are not eligible for surgery because of high age and comorbidities [6], which increase surgical risk and reduce prognosis. For this specific patient population the less invasive, transcatheter MitraClip implantation (MCI) was developed, a technique based on the surgical Edge-to-Edge repair technique. [7] Several studies have already demonstrated that MCI is a safe procedure by which a reduction of MR to grade ≤2 and functional improvement of the patient is achieved in most of the patients [8–12]. Even in selected patients with severe systolic heart failure, MCI can reduce MR significantly and results in an increase in both left ventricular ejection fraction and functional improvement [13]. According to the current European guidelines, MCI is an optional treatment for inoperable or high surgical risk patients [5]. However, it is unclear which patient category will benefit most from this novel catheter based technique. The aim of the present study is to determine independent predictors of functional and clinical outcome of patients treated by MCI in order to improve the selection of patients eligible for this procedure.

2. Methods

2.1. Study population and screening

Between May 2009 and July 2013, 84 patients underwent a MitraClip procedure at our institution. Prior to the procedure, all patients suffered from severe symptomatic MR (despite optimal medical therapy and chronic resynchronization therapy (n = 6)) of functional, degenerative or mixed origin and all were declined for surgical treatment due to

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anticipated high surgical risk by a multidisciplinary heart team. All were de novo MitraClip procedures. High surgical risk was defined as a logistic European System for Cardiac Operative Risk Evaluation I (EuroSCORE I) mortality of >15% or specific surgical risk factors associated with excessive morbidity and mortality which are not included in the current EuroSCORE. Subsequently, all patients were evaluated for eligibility for MitraClip implantation. Patients considered suitable on transoesophageal echocardiography (TEE) underwent a standard pre-procedural screening (including: assessment of functional capacity (New York Heart Association (NYHA) functional class), laboratory measurements (including NT-proBNP), transthoracic echocardiography (TTE) and when indicated coronary angiography). Baseline characteristics such as age, gender, relevant medical and surgical history were collected from medical records. All patients gave written informed consent for MCI and to data being collected and utilized as per the ethical guidelines of the institute.

2.2. MitraClip procedure

The MitraClip device as well as the implantation procedure has been described previously [14]. The procedure was performed under general anesthesia and TEE- and fluoroscopic guidance. In cases where a further reduction of MR grade after the first clip was desirable, a second or third MitraClip was implanted, provided that the mean mitral valve pressure gradient (MVPG) remained <5 mm Hg.

2.3. Post-procedure and follow-up

All patients underwent a TTE 1–2 days after MCI in order to determine the exact severity of MR without anesthesia. Clinical and echocardiographic follow-up was obtained 1 and 6–12 months (mid-term follow-up) after the procedure (including assessment of NYHA status). Patients were invited for a 6 month and 12 month follow-up. If follow-up was available at both 6 and 12 months, data of 12 month follow-up were used for our analyses (for 20 patients (32%) echocardiographic data was available at 6 month follow-up and for 43 patients (68%) this was available at 12 month follow-up). Information on vital status is present up to 2 years after MCI in all 84 patients; 3 patients were deceased at 1 month follow-up and 12 patients were deceased at mid-term follow-up.

2.4. Echocardiographic protocol

TTE and TEE were performed using a Vivid 7 and 9 machine (GE Healthcare, Horten, Norway). All views were obtained according to the recommendations of the American Society of Echocardiography. [15,16] The MR grade was based on qualitative and quantitative data by color Doppler and continuous wave Doppler interrogation of the regurgitant jet in 2 orthogonal views; color flow jet area in the left atrium, pulmonary vein flow (in the case of no atrial fibrillation), vena contracta width, effective regurgitant orifice area (using the proximal isovelocity surface area method), regurgitant fraction and regurgitant volume were used in our institution [5,17]. Accordingly, MR severity was scored from 1 to 4 (1: mild, 2: mild–moderate, 3: moderate–severe, 4: severe). Vena contracta width could not be used after clip placement, due to the double-orifice valve. After clip implantation we measured MR severity according to the MR score reported previously [18]. Left ventricular (LV) function and left atrial volumes were measured using the biplane Simpson's method [19]. The right ventricular (RV) systolic pressure (RVSP) was obtained from the systolic RV-right atrial gradient, using the modified Bernoulli equation (calculated from the peak velocity of the systolic trans-tricuspid regurgitant flow). From the dimension of the inferior vena cava and its collapsibility the right atrial pressure was calculated (measured in the subcostal view) [20]. Due to the absence of pulmonary valve or pulmonary artery stenosis in all patients, the RVSP corresponds well to the systolic pulmonary pressure (sPAP). Tricuspid regurgitation (TR) was qualitatively graded using color-flow Doppler according to the guidelines of the American Society of Echocardiography as follows: normal/trivial (grade 1), mild (grade 2), moderate (grade 3) or severe (grade 4) [20].

All echocardiographic measurements were reviewed by two experienced investigators.

2.5. Statistical analysis

Categorical data are reported as percentages and counts and continuous data as mean ± standard deviation. Comparison of categorical data was conducted with a Chi square (two-sided p-value was used), Fischer's exact or McNemar test where appropriate. A two-tailed paired *T*-test test was performed on continuous data to detect significant differences presuming that the normality assumption has been met. Non-parametric tests were used for data that were not normally distributed and these data were presented as median with the 25th and 75th percentile. With uni- and multivariate analyses (all variables with a p-value < 0.1 in univariate analysis were included in the multivariate analysis) determinants for all-cause mortality were determined by a Cox model. We used a NT-proBNP level ≥ 5000 μg/L in our analyses as a cut-off point because this level is also used as risk-marker in patients with decompensated heart failure [21]. We created a model in which all predictors of the multivariate analysis were included; every available predictor was weighted with 1 point. In this model with predictors we binarized the determinant 'MR reduction' to 0–1 grade MR reduction and 2–3 grade MR reduction and 0–1 grade MR reduction was counted as 1 predictor. The Kaplan–Meier method was used for survival analysis and the log-rank test was used to compare groups.

A p-value < 0.05 was considered statistically significant for all tests. Data analysis was performed with the SPSS (version 20, SPSS, Chicago, IL) software package.

3. Results

3.1. Patient and procedure characteristics

Between May 2009 and July 2013, 84 consecutive patients underwent MCI at our institution. The mean age of the 84 patients was 76 ± 10 years and 51% of the patients were male. All patients had pre-procedural MR grade 3 or 4 and the MR etiology was functional in 54%, degenerative in 38% and mixed in 8% of the patients. The majority of patients were NYHA class III or IV (96%) prior to the MitraClip procedure. The mean EuroSCORE of all patients was 16 ± 11%. The remainder of the patient baseline characteristics is given in Table 1. In the majority of the patients (68%) one MitraClip was implanted, 2 clips were implanted in 31% of the patients and 3 clips in 1% of the patients. In 76% of the patients the MR was reduced to grade ≤2 on the post-procedural TTE.

3.2. Echocardiographic and functional follow-up data

The median time of the echocardiographic mid-term follow-up was 364 days. MR was significantly reduced at follow-up as compared to baseline; 63% of the patients had MR grade ≤ 2 (p < 0.001) at 1 month follow-up and 56% (p < 0.001) at mid-term follow-up. Compared to baseline NYHA class also significantly improved at follow-up, 71% of the patients was NYHA class I or II at 1 month (p < 0.001) and 70% at mid-term follow-up (p < 0.001).

Most echocardiographic parameters remained equivalent between baseline and follow-up except for the mean MVPG, which significantly increased (baseline: 2.5 ± 1.7 mm Hg, 1 month follow-up: 4.0 ± 2.1 mm Hg (p < 0.001, compared to baseline), mid-term follow-up: 4.3 ± 2.8 mm Hg (p = 0.003 compared to baseline)). The sPAP was significantly decreased at 1 month follow-up (Table 2).