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Original article

Long-term survival after MitraClip® therapy in patients with severe mitral regurgitation and severe congestive heart failure: A comparison among survivals predicted by heart failure models

Thomas Schau (MD)[a,1,*], Akihiro Isotani (MD)[a,1], Michael Neuss (MD)[a], Maren Schöpp (MD)[a], Martin Seifert (MD)[a], Christin Höpfner (MD)[a], Daniel Burkhoff (MD, PhD)[b], Christian Butter (MD)[a]

[a] Heart Center Brandenburg in Bernau, Bernau, Germany
[b] Columbia University, New York, NY, USA

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ABSTRACT

Background: The aim of the study was to investigate mortality following transcatheter mitral valve repair with the MitraClip System (MC) (Abbott Vascular, Santa Clara, CA, USA) in patients with mitral regurgitation and moderate-to-severe symptomatic heart failure in comparison to mortality predicted by the Seattle Heart Failure Model (SHFM) and the heart failure calculator of the meta-analysis global group in chronic heart failure (MAGGIC).

Methods and results: This retrospective study included 194 consecutive patients, who received a MC implantation between 2009 and 2013 at our institution. The observed mortality was compared with that predicted by the SHFM and the MAGGIC after 1 year: 24% observed, 18% by SHFM ($p = 0.185$) and 20.9% by MAGGIC ($p = 0.542$). At 2 years: 32% observed vs. 33% by SHFM ($p = 0.919$). The subgroup of patients with end-stage heart failure and N-terminal pro-B-type natriuretic peptide (NTproBNP) >10,000 pg/ml ($n = 41$) had significantly worse mortality after 1 year (49%) than predicted by SHFM (24%, $p = 0.034$) and MAGGIC (24.8%, $p = 0.041$).

Conclusion: In the overall patient cohort defined by 3+ to 4+ mitral valve regurgitation with New York Heart Association III and IV symptomatic heart failure, mortality following MC is consistent with that predicted by SHFM and MAGGIC for patients that are not at high risk. However, the subset of patients with severe heart failure defined by NTproBNP >10,000 pg/ml had worse than predicted mortality and may not benefit from MC therapy, mainly due to a high 30-day mortality.

Introduction

Percutaneous edge-to-edge mitral valve repair using the MitraClip (MC) device (Abbott Vascular, Santa Clara, CA, USA) has evolved as a new tool for the treatment of severe mitral valve regurgitation (MR). This technique has been evaluated in patients at low and high risk for surgery [1–4]. The EVEREST II study demonstrated superior safety compared to surgical mitral valve repair with inferior clinical efficacy but similar clinical outcomes in patients with low- or moderate-risk surgical profiles [2]. However, patients with advanced age, multiple comorbidities, and heart failure are currently the first to be considered for nonsurgical techniques. A few studies have already looked into feasibility and safety in patients with high surgical risks during short-term follow-up [5–8]. First results of patients not amenable to cardiac surgery suggest an improvement in symptoms and echocardiographic parameters [9–12]. Moreover, the long-term outcome after MC implantation compared to conservative medical therapy is not known in patients with severe heart failure and severe MR.

The purpose of the present retrospective study was therefore to evaluate survival following MC by comparing observed mortality to that predicted by the well-established, previously validated, and widely referenced Seattle Heart Failure Survival Model (SHFM) [13,14] and the recently published heart failure risk calculator from the meta-analysis global group in chronic heart failure (MAGGIC) [15].

* Corresponding author at: Heart Center Brandenburg in Bernau, Ladeburger Straße 17, 16321 Bernau, Germany. Tel.: +49 3338 694 610; fax: +49 3338 694 644.
E-mail address: t.schau@immanuel.de (T. Schau).
[1] These authors contributed equally to this publication (share first authorship).

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Methods

Study population

From March 2009 through May 2013, 194 consecutive patients were scheduled to be treated with MC implantation at our institution. All included patients had a EURO-score >20 or other severe comorbidities which increased the surgical risks dramatically [for example chronic obstructive pulmonary disease (COPD) with permanent oxygen supplementation, prior radiation to thorax due to malignancy, etc.]. All patients were evaluated by a multidisciplinary team consisting of a heart failure specialist, an interventional cardiologist, an echocardiographer, a cardiac surgeon, and an anesthesiologist.

All patients had symptomatic, severe >2+ MR despite optimal medical therapy, which included cardiac resynchronization therapy (CRT) when QRS duration was greater than 150 ms. The main exclusion criteria were severe clinical comorbidities that limited expected life expectancy below 6 months (e.g. end-stage cancer). Patients were also excluded if the morphology of the mitral valve made MC implantation technically impossible or unlikely according to the EVEREST criteria (i.e. short or calcified posterior leaflet without possibility of leaflet grasping or beginning mitral stenosis).

Patients underwent transthoracic and transesophageal echocardiography to quantify MR and left ventricular (LV) size and to judge morphologic suitability for MC implantation. The transthoracic and transesophageal echocardiograms were obtained using commercially available ultrasound diagnostic systems (Vivid 7 and Vivid E9, GE Medical Systems, Milwaukee, WI, USA and Philips IE 33, Royal Philips Electronics, Amsterdam, The Netherlands) by experienced echocardiographers. The LV end-diastolic diameter (LVEDD) was measured by transthoracic echocardiography in the long axis parasternal view. The LV end-diastolic volume (LVEDV) was quantified in the standard apical four chamber view using Simpson's method.

MC implantation procedure

The endovascular edge-to-edge mitral valve repair procedure has been described in detail previously [1,2]. All procedures were performed using the 24 Fr CDS01 or CDS02 MitraClip device. All clips were implanted under general anesthesia and fluoroscopic and transesophageal echocardiographic guidance. Hemostasis of the femoral vein access site was achieved by Z-suture and compression of the vein for 12 h. Patients were transferred to our intermediate care or, if necessary, intensive care unit after the procedure (for ≤24 h) for post-procedure observation.

Follow-up data

Most patients had regular follow-up visits at our outpatient clinic. In a few cases (n = 10), clinic visits were not possible due to long distance between home and hospital, the health status, or some other personal reasons. In these few cases patient data were collected via telephone calls to patients, their relatives, and/or their family physicians/cardiologists.

Prediction of survival by Seattle Heart Failure Model

The SHFM is a score used to predict the probability of survival in patients with heart failure [13,14]. It is a well-validated scoring system that relies on a combination of the following clinical parameters: age, gender, New York Heart Association (NYHA) class, LV ejection fraction (EF), coronary artery disease, systolic blood pressure, medications, laboratory tests of sodium, cholesterol, hemoglobin, lymphocytes, and uric acid. These parameters were available from the patients' records. Lymphocytes and uric acid were not determined in each case. For missing individual values of lymphocytes, the mean value of the overall population was used. Regarding the uric acid, the missing values were replaced by the upper limit (417 μmol/l) of the normal range (202–417 μmol/l), which was the mean value of heart failure patients in unpublished studies in our hospital. This method of assigning missing patient data has been described previously [13]. The daily diuretic dose was calculated in equivalents of daily furosemide dosage (mg/day) to account for different diuretic agents. The SHFM score was calculated for each patient on the date of the MC implantation. A predicted survival curve was then calculated for the cohort from the mean SHFM score of all patients. This curve was then compared with the actual survival observed in the study cohort.

Prediction of survival by the meta-analysis global group in chronic heart failure score

The recently published MAGGIC score [15] relies on a combination of the following clinical parameters: age, gender, body mass index, NYHA class, LVEF, systolic blood pressure, laboratory test of serum creatinine, co-morbidities such as COPD, diabetes mellitus, smoking, and medications. These parameters were all available from the patients' records. The predicted 1-year survival was calculated for every patient. The median predicted 1-year survival was compared with the observed survival.

Subgroup analyses

Analyses were performed to investigate potential risks in the following subgroups of interest: patients with extremely high values of N-terminal pro-B-type natriuretic peptide (NTproBNP; >10,000 pg/ml), functional (FMR) vs. degenerative (DMR) MR, LVEDD, and LVEDV. The optimal cut-off for NTproBNP was found as the point with the most significant log rank test-split in a former publication [12]. ROC analysis was also used to determine cut-off values for heart size based on LVEDD and LVEDV values that most discretely separated outcome among groups. These ROC analyses yielded cut-off values of 70 mm for LVEDD and 260 ml for LVEDV. These subgroup analyses were chosen because none of these grouping factors are included in the SHFM or the MAGGIC. An additional subgroup analysis stratified patients for different predicted initial risks, specifically a lower SHFM score vs. higher ared to the median value of the entire cohort.

Statistical analysis

The primary endpoint of this study was a comparison between observed all-cause mortality and that predicted by the SHFM and MAGGIC scores using Kaplan–Meier analysis. We performed an intention-to-treat analysis; therefore, the patients with unsuccessful MC implantation were included because they received general anesthesia. Observed and predicted survivals were compared at the 1- and 2-year time-point after MC implantation using 2 × 2 matrix and X^2-test.

Continuous variables are expressed as mean ± SD when normal distribution was confirmed or otherwise as median plus interquartile range (IQR). Categorical variables are presented as absolute numbers and percentages. Normality was assessed with Shapiro–Wilk test. Comparisons among groups were made using Wilcoxon, X^2-test or Fisher's exact test as appropriate. The open-source software 'R' version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) was applied for all statistical tests.

All patients were informed about specific risks and alternative treatments and they gave informed written consent.