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STRUCTURAL

Elevated Mitral Valve Pressure Gradient After MitraClip Implantation Deteriorates Long-Term Outcome in Patients With Severe Mitral Regurgitation and Severe Heart Failure

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ABSTRACT

OBJECTIVES This single-center study was performed to analyze the effect of an increased transvalvular gradient after the MitraClip (MC) (Abbott Laboratories, Abbott Park, Illinois) procedure on patient outcome during follow-up.

BACKGROUND Percutaneous transcatheter repair of the mitral valve with the MC device has been established as a novel technique for patients with severe mitral regurgitation and high surgical risk. This study investigated the influence of an increased pressure gradient after MC implantation on the long-term outcome of patients.

METHODS A total of 268 patients were enrolled, who received MC implantation between April 2009 and July 2014 in our institution (75 ± 9 years of age, 68% men, weight 76 ± 15 kg, median N-terminal pro-B-type natriuretic peptide 3,696 [interquartile range: 1,989 to 7,711] pg/ml, left ventricular ejection fraction 39 ± 16%, log European System for Cardiac Operative Risk Evaluation score 20% [interquartile range: 12% to 33%]). Pressure in the left atrium and left ventricle were measured during the procedure using fluid-filled catheters. The pressure gradients over the mitral valve were determined simultaneously invasively and echocardiographically directly after MC deployment. A Kaplan-Meier analysis was performed and correlated with the pressure gradients. We used a combined primary endpoint: all-cause-mortality, left ventricular assist device, mitral valve replacement, and redo procedure.

RESULTS The Kaplan-Meier-analysis showed a significantly poorer long-term-outcome in the case of an invasively determined mitral valve pressure gradient (MVPG) in excess of 5 mm Hg at implantation for the combined endpoint ($p = 0.001$) and for all-cause mortality ($p = 0.018$). For the echocardiographically determined MVPG the cutoff value was 4.4 mm Hg. Propensity score matching was used to balance baseline differences between the groups. In a Cox model the increased residual MVPG >5 mm Hg was a significant outcome predictor in univariate and multivariate analysis (hazard ratio: 2.3; 95% confidence interval: 1.4 to 3.8; $p = 0.002$, multivariate after adjustment for N-terminal pro-B-type natriuretic peptide, age, and remaining mitral regurgitation).

CONCLUSIONS It is recommended that the quality of the implantation result be analyzed carefully and repositioning of the MC be considered in the case of an elevated pressure gradient over the mitral valve. (J Am Coll Cardiol Intv 2017;10:931-9)

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

HR = hazard ratio

MC = MitraClip

MR = mitral regurgitation

MVOA = mitral valve opening area

MVPG = mitral valve pressure gradient

MS = mitral stenosis

NT-proBNP = N-terminal pro-B-type natriuretic peptide

MitraClip (MC) (Abbott Laboratories, Abbott Park, Illinois) is a new percutaneous transcatheter therapy of mitral valve (MV) repair for patients with severe mitral regurgitation (MR). Safety and feasibility of the therapy in comparison to standard surgical treatment was established in the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II trial. This trial demonstrated also similar mortality in comparison to surgery during 5 years of follow-up (1,2). Compared to the EVEREST II trial, patients treated in Europe on average had a higher surgical risk, more frequently functional than degenerative MR, and valve morphology considered unsuitable for treatment within the EVEREST II trial (3–7). Some publications and registries suggest improvement of clinical and echocardiographic parameters in such patients not amenable to cardiac surgery (8,9).

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First papers report that the long-term outcome of patients may depend on the grade of the remaining MR (10). The relevance of a remaining transvalvular gradient over the MV after the procedure on the long-term outcome is completely uncertain. It was the aim of this study to investigate how the MV pressure gradient (MVPG) influences the long-term outcome of patients after MC implantation.

METHODS

STUDY POPULATION. This retrospective study included 268 consecutive patients with severe MR who underwent MC implantation between March 2009 and April 2014 in our heart center. A patient flow chart is given in **Figure 1**. All patients were evaluated by an interdisciplinary heart team for MC implantation and referred to interventional treatment due to high surgical risk (mostly European System for Cardiac Operative Risk Evaluation score >20% or other severe comorbidities). Patients had symptomatic heart failure (New York Heart Association functional class III or IV) despite established optimal medical therapy. All patients gave written consent. This retrospective study was performed according to ethical guidelines of our institution.

PROCEDURES. The MC implantation procedure has been described previously (1,2). All procedures were performed using the 24-F CDS01 or CDS02 MC device (Abbott Vascular, Santa Clara, California) following the standard instruction for use.

ECHOCARDIOGRAPHIC MEASUREMENT. Transthoracic and transesophageal echocardiography were performed by experienced sonographers using commercially available ultrasound systems (Vivid 7 and Vivid E9, GE Medical Systems, Milwaukee, Wisconsin; and Philips IE 33, Royal Philips Electronics, Amsterdam, the Netherlands). The echocardiographic loops recorded during the procedure were retrospectively read and analyzed for this study by an experienced board-certified echocardiographer independently of the implantation procedure and the treatment process of the patients.

Initial MR was graded comprehensively using semi-quantitative methods measuring the color Doppler regurgitation area, assessment of vena contracta width, and the quantitative method of the proximal isovelocity surface area according to the guideline of the American Society of Echocardiography using 4 MR grades (11). After the intervention, MR severity was assessed with the technique previously reported (12). The MR was determined 1 or 2 days after the implantation procedure before discharge by transthoracic echocardiography. Mitral stenosis (MS) was evaluated by recording the transmitral mean pressure gradient calculated from the continuous Doppler waveform in transesophageal echocardiography during the implantation procedure simultaneously to invasive MVPG measurement directly after clip deployment (13).

MV orifice area (MVOA) was traced at the level of the leaflet tip in maximum opening during diastole using transgastric view or in orthogonal flexi-slices of midtransesophageal 3-dimensional views, if available. Because 3-dimensional transesophageal echocardiography was provided by GE Medical Systems only at the end of 2012, we decided to use mainly 2-dimensional echocardiography and to confirm these data by 3-dimensional echocardiography, if available.

INVASIVE MEASUREMENT OF TRANSMITRAL PRESSURE GRADIENT. For the invasive measurement of the transmitral pressure gradient a 5-F pigtail-catheter (Merit Medical Systems, South Jordan, Utah) was placed in the apex of the left ventricle through a 6-F sheath in the left radial artery and the left ventricular pressure was measured using a pressure transducer (Medex, Smiths Medical, Ashford, United Kingdom). In the first patients the left atrial pressure was determined by connecting the MC steerable guide catheter to a fluid filled pressure line that was connected to a pressure transducer. In some patients the left atrial pressure could not be reliably measured using this approach. Data from these patients were not used for data analysis (**Figure 1**). Later during our study a 4-F pigtail catheter was introduced into the left atrium in parallel to the MC steerable guide