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Immediate increase of cardiac output after percutaneous mitral valve repair (PMVR) determined by echocardiographic and invasive parameters
Patzelt: Increase of cardiac output after PMVR

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ABSTRACT

Background: Successful percutaneous mitral valve repair (PMVR) in patients with severe mitral regurgitation (MR) causes changes in hemodynamics. Echocardiographic calculation of cardiac output (CO) has not been evaluated in the setting of PMVR, so far. Here we evaluated hemodynamics before and after PMVR with the MitraClip system using pulmonary artery catheterization, transthoracic (TTE) and transesophageal (TEE) echocardiography.
Methods: 101 patients with severe MR not eligible for conventional surgery underwent PMVR. Hemodynamic parameters were determined during and after the intervention. We evaluated changes in CO and pulmonary artery systolic pressure before and after PMVR. CO was determined with invasive parameters using the Fick method (COi) and by a combination of TTE and TEE (COe).
Results: All patients had successful clip implantation, which was associated with increased COi (from 4.6 ± 1.4 l/min to 5.4 ± 1.6 l/min, $p < 0.001$). Furthermore, pulmonary artery systolic pressure (PASP) showed a significant decrease after PMVR (47.6 ± 16.1 before, 44.7 ± 15.5 mm Hg after, $p = 0.01$). In accordance with invasive measurements, COe increased significantly (COe from 4.3 ± 1.7 l/min to 4.8 ± 1.7 l/min, $p = 0.003$). Comparing both methods to calculate CO, we observed good agreement between COi and COe using Bland Altman plots.
Conclusions: CO increased significantly after PMVR as determined by echocardiography based and invasive calculation of hemodynamics during PMVR. COe shows good agreement with COi before and after the intervention and, thus, represents a potential non-invasive method to determine CO in patients with MR not accessible by conventional surgery.

1. Introduction

Interventional therapies for cardiac diseases are generally associated with substantial changes in patient hemodynamics [1]. While in the early years of heart catheterization assessment of hemodynamics was important for the understanding of cardiovascular pathophysiology, the advance in interventional techniques towards more invasive procedures such as percutaneous interventions to treat patients with valvular and congenital heart disease has made it an indispensable roadmap for most procedures. It is important to realize that minimally invasive procedures such as percutaneous mitral valve repair (PMVR) offer a clinical setting to understand hemodynamic principles underlying

Abbreviations: CO, Cardiac output; COe, cardiac output echocardiographically determinded by combination of TTE and TEE parameters; COi, invasively determined cardiac output; DMR, degenerative mitral regurgitation; ECG, electrocardiogram; EF, ejection fraction; FMR, functional mitral regurgitation; LVOT, left ventricular outflow tract; LA, left atrium; LV, left ventricle; MR, mitral regurgitation; NYHA, New York heart association; PMVR, percutaneous mitral valve repair; PA, pulmonary artery; PASP, pulmonary artery systolic pressure; PCW, pulmonary capillary wedge; PW, pulsed wave; SD, standard deviation; TAVI, transcatheter aortic valve implantation; TEE, transesophageal echocardiography; TR, tricuspid regurgitation; TTE, transthoracic echocardiography; VTI, velocity time integral.

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cardiac diseases, because it has less confounding factors with influence on hemodynamics than open surgery using an on-pump approach.

PMVR was developed to treat patients with mitral regurgitation (MR) not suitable for conventional surgery. 5 year-follow up data of the EVEREST II trial confirmed that PMVR is a beneficial therapy in these patients, and there was no difference in the prevalence of moderate-to-severe or severe MR or mortality compared to conventional surgery [2]. Using transthoracic echocardiography (TTE), a reduction of LV volumes and LA volumes specifically at end-diastole by PMVR mirrored the correction of volume overload in degenerative MR [3]. Furthermore, in functional MR positive reverse remodeling was documented after PMVR therapy [3]. In an elegant study, improvements of hemodynamic profiles were recently documented using conductance catheter measurements in a collective of 33 patients undergoing PMVR [4]. These immediate effects caused by the reduction in MR were paralleled by a decrease in end-diastolic volume and systolic pulmonary artery pressure (PASP) at follow up [4]. We observed significant changes in heart geometry induced by mechanical ventilation during PMVR reflecting the complex hemodynamic status in patients with severe MR [5].

During the PMVR procedure, hemodynamic parameters are routinely monitored. Changes in heart geometry associated with MR reduction such as enhanced mitral valve coaptation or modified mitral valve and ventricular architecture are followed by functional hemodynamic effects. This intervention, thus, offers a clinical setting to better understand hemodynamic changes in patients with pathologies of the mitral valve.

While invasive measurements offer direct values of hemodynamic parameters, echocardiographic determination of hemodynamics acquired during outpatient follow up could be more feasible for long-term follow up after PMVR. Thus, this study was carried out to explore changes in hemodynamics after PMVR and the relationship between hemodynamic values calculated based on invasive measurements or based on echocardiography during and after the PMVR procedure.

2. Material and methods

2.1. Study population

We included 101 patients with severe MR, who underwent PMVR using the MitraClip® system (Abbott Vascular) at the University hospital, Department of Cardiology and Cardiovascular Medicine, University of Tübingen between May 2014 and June 2016. In this study, invasive hemodynamics and echocardiographic parameters were assessed to validate success of the PMVR procedure. For instance, we measured hemodynamic parameters using a Swan Ganz catheter as well as TTE and TEE before and after clip deployment. Invasive CO (COi) was correlated with CO calculated by echocardiographic parameters (COe). The study was approved by the local ethics committee (260/2015R) and patients gave informed consent. An interdisciplinary team of interventional cardiologists and cardiac surgeons made the decision for treatment by PMVR based on either the EuroSCORE [6] or on the presence of specific surgical risk factors not covered in the EuroSCORE. Exclusion criteria for PMVR were as previously described [5]. The patients underwent TEE, TTE and clinical assessment before the intervention to document MR severity, mitral valve morphology and NYHA functional class. Heart failure patients had to be on optimal medical treatment according to current guidelines for at least 3 months prior to PMVR treatment.

2.2. Echocardiographic assessment

TTE and TEE were performed at the beginning and at the end of the procedure to acquire hemodynamic and geometric data using a Philips CX 50 and iE 33 machine (Philips HealthCare, Hamburg, Germany). MR and reduction of MR were assessed using TEE at the beginning and at the end of the PMVR procedure. MR severity at baseline and the etiology of regurgitation were determined according to the current European Association of Echocardiography guidelines [7]. The technique described by Foster et al. was used to assess the severity of MR post-intervention [8]. All echocardiographic loops were recorded. Two additional investigators blinded to the results repeated the echocardiographic assessment using the Centricity Enterprise Web 3.0 software (GE medical systems, 540 West Northwest Highway, Barrington IL, USA). The mean of measurements was calculated and reported as final value.

2.3. Calculation of cardiac output based on echocardiography (COe)

We evaluated 101 matching pairs for echocardiographic and invasive measurements of CO. Cardiac output based on echocardiography (COe) was calculated as product of the time-velocity integral in the left ventricular ouflow tract (LVOT VTI), LVOT area and the heart rate (Fig. 1A). LVOT VTI was measured with pulsed wave doppler of TTE in the apical 5 chamber view, with the doppler beam aligned to the LVOT axis. VTI of 3 consecutive beats was measured and the mean was calculated and reported as final result. For determination of LVOT area, the LVOT area was directly measured by planimetry in TEE. In the septo-lateral view in a mid-esophageal position at 120–150°, a second imaging axis (simultaneous biplane mode) was placed orthogonally to the aorta just below the aortic valve in the LVOT. Heart rate was obtained from the monitoring ECG (Fig. 1A and B).

2.4. Hemodynamic measurements

Pressure transponders were calibrated to athmospheric pressure at right atrial height. Arterial blood pressure and arterial blood gas sampling were obtained via cannulation of the radial artery. A Swan-Ganz catheter (7F, Edwards Lifesciences, Irvine, USA) was introduced and pulmonary capillary wedge pressure (PCWP) and pulmonary artery systolic pressure (PASP) curves before and after MitraClip® deployment were obtained as well as PA blood samples. Wedge position was confirmed via fluoroscopy and pulmonary capillary blood sampling in comparison to arterial blood sampling. During PMVR, we monitored changes in hemodynamics via the indirect Fick method.

2.5. PMVR procedure

The procedure was carried out either in general anesthesia or in deep sedation. After sedation of the patient or induction of general anesthesia, the TEE probe was introduced into the esophagus and vascular access to the femoral vein was established. The MitraClip® device was advanced via the transseptal route across the mitral annulus into the left ventricle using fluoroscopic and transesophageal two- and three-dimensional echocardiographic guidance. The device was retracted with the two arms of the clip extended to capture and subsequently closed, to coapt the mitral leaflets thereby emulating the surgical double-orifice technique introduced by Alfieri et al. [9]. After clip deployment, PCW and PA pressure curves, blood samples and final TEE and TTE measurements were obtained a second time.

2.6. Statistical analysis

Statistical analysis was performed with SPSS (version 22, IBM Deutschland GmbH, Ehningen, Germany). Categorical variables are shown as absolute numbers or percentages, continuous variables as means ± standard deviation (SD). Normal distribution of variables was checked using the Saphiro-Wilk test. For normally distributed data paired *T*-Test was used to compare means. For not normally distributed data the Wilcoxon signed-rank test was used to compare means. Intergroup comparisons were performed by ANOVA analysis. The 2-tailed p values were calculated and a value of $p \leq 0.05$ was considered statistically significant. Echocardiographic views were assessed by 3 independent investigators, 2 of whom were blinded to the results. To evaluate reproducibility of echocardiographic measurements, the intraclass correlation coefficient for absolute agreement was used, with good agreement defined as >0.80. For the assessment of intraobserver reliability, 20 randomly chosen patients were analyzed by 1 investigator twice. Absolute agreement among the observations was calculated using intraclass correlation coefficient analysis. To compare agreement of COi and COe Bland Altman analysis [10] was used.

3. Results

Here, we evaluated hemodynamics in 101 patients undergoing PMVR using echocardiographic and invasive parameters. Baseline characteristics for all patients are shown in Table 1 and and Supplemental Table 1. Functional NYHA class III–IV was present in the majority of patients, and there was a high percentage (50.5%) of patients with severely reduced (≤35% ejection fraction) LV-function. 63.4% of patients had functional MR (FMR). Coronary artery disease was previously diagnosed in 78.2% of the patients, 66.3% had atrial fibrillation and 42.6% renal insufficiency. Reduction of MR severity to ≤ 2 post intervention was achieved in 98 patients, 2 patients had residual MR of 2–3, 1 patient had residual MR of 3 (Fig. 2A). The same proportion of patients achieved MR severity ≤2 in DMR and FMR.

3.1. COi is enhanced after PMVR

COi was significantly enhanced after the PMVR procedure as measured by conventional calculation based on invasive parameters according to the Fick method (Fig. 2B). For instance, it increased from 4.6 ± 1.4 l/min to 5.4 ± 1.6 l/min ($p < 0.001$). Interestingly, PASP was reduced from 47.6 ± 16.1 mm Hg to 44.7 ± 15.5 mm Hg ($p = 0.01$, Fig. 2C). There was no significant change in ejection fraction (EF) after

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