Clinical Study

Invasive Hemodynamic Assessment of Cardiac Output State after MitraClip Therapy in Nonanaesthetized Patients with Functional Mitral Regurgitation

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Background. Surgical correction of mitral regurgitation (MR) can lead to postoperative low cardiac output state. We aimed to assess the acute hemodynamic changes after percutaneous MitraClip therapy (a unique model without influence of factors linked to surgical procedure) in patients with functional MR without the influence of general anaesthesia.

Methods. We studied invasive hemodynamic parameters in 23 patients before procedure (conscious, nonsedated patients), during procedure (intubated patients), and the first day after MitraClip implantation (conscious, extubated patients).

Results. Mitral valve clippings significantly increased cardiac index (CI) (from 2.0 ± 0.5 to 3.3 ± 0.6 L/min/m²; p < 0.01). Conversely, there was significant reduction in the mean pulmonary capillary wedge pressure (PCWP) (from 18.6 ± 5.7 to 10.5 ± 3.8 mmHg; p < 0.01), mean pulmonary artery pressure (from 29.8 ± 10.9 to 25.2 ± 10.3 mmHg; p = 0.03), and pulmonary vascular resistance index (from 531 ± 359 to 365 ± 193 dyn·s·cm⁻⁵/m²; p = 0.03).

Conclusions. The functional MR therapy with percutaneous MitraClip device results in significant increase in CI (+66%) and concomitant decrease in PCWP (~42%). None of our patients developed low cardiac output state. Our results support the idea that significant part of low cardiac output state after cardiac surgery is due to surgery related factors rather than due to increase in afterload after MR elimination.

1. Introduction

Cardiac surgery for mitral regurgitation (MR) (either mitral valve repair or replacement) has a well described risk of deterioration of left ventricular (LV) function and acute postoperative low cardiac output (CO) state, especially in patients with preexisting LV dysfunction. The main known causes of low CO state are elimination of MR with resulting sudden increase in afterload but also several factors inherently linked to the injury due to cardiac surgery—depression of myocardial contractility after cardioplegic arrest, use of cardiopulmonary bypass, and interruption of annular-chordal-papillary muscle continuity. The principal mechanism leading to a decrease in LV systolic function after surgical correction of mitral regurgitation is considered to be the increase in afterload due to elimination of the low-impedance regurgitant flow into the left atrium [1–3].

Percutaneous mitral valve repair with MitraClip device provides a unique model to assess the acute hemodynamic changes solely attributable to elimination of mitral regurgitation. To date, we have limited data on acute hemodynamic changes after MitraClip measured by cardiac catheterisation methods. All previous published reports have significant limitations due to the fact that the measurements of CO before and after MitraClip implantation were performed under general anaesthesia and the studied cohorts were heterogeneous as it included patients with both organic and functional MR [4–6].

We therefore aimed to assess the acute hemodynamic effect after MitraClip therapy in patients with functional MR.
only and to assess invasively cardiac output state in a “real-
world” situation without the influence of general anaesthesia.

2. Methods

Our study included 23 consecutive patients with functional
MR indicated for MitraClip therapy according to current
guidelines; all patients were discussed at the Heart Team
meeting. In brief, patients were selected for percutaneous
mitral repair if they had moderate to severe (3+) or severe
(4+) MR and were symptomatic despite optimal medical
therapy, including cardiac resynchronization therapy (CRT)
if indicated, were judged inoperable or at high surgical risk
and they fulfilled standard echocardiographic morphology
criteria predicting procedural feasibility [7]. All patients
have agreed to participate in this study and have signed
informed consent; study was conducted in accordance with
the Helsinki protocol.

2.1. MitraClip Procedure. The procedure was performed
under general anaesthesia using transoesophageal echocar-
diography guidance and fluoroscopy. The MitraClip device
(Abbott, Menlo Park, CA, USA) was advanced following
an echo-guided transseptal approach to the left atrium and
across the mitral valve to the left ventricle. The leaflets were
grasped by pullback and arms of the clip were closed. The
reduction of MR severity was assessed by Doppler echocar-
diography. A second clip was placed if further reduction of
MR was needed. Acute procedural success was defined as
successful clip implantation with MR reduction to grade 2+
or less by echocardiography.

2.2. Invasive Hemodynamic Measurements. The hemody-
namic measurements were performed in 4 exactly defined
time points:

(i) T1: a conscious nonanaesthetized patient immediately
before the operation
(ii) T2: 15 min after induction into the general anaesthesia
(iii) T3: after clipping at the end of procedure still under
GA
(iv) T4: day 1 after procedure in fully conscious patient

Hemodynamic parameters were obtained using an arterial
catheter (most often via radial artery), a balloon-tipped
Swan-Ganz pulmonary artery catheter, and central venous
catheter. Pulmonary capillary wedge pressure (PCWP) was
assessed at end expiration and transducers were balanced
by determining zero level at the midaxillary line. The Vig-
Ilance II Monitor (Edwards Lifesciences, USA) was used to
calculate cardiac output using thermodilution principle and
an average of six measurements was used. Systemic (SVRI)
and pulmonary (PVRI) vascular resistance indexes and left
(LVSWI) and right (RVSWI) ventricular stroke work indexes
were calculated according to standard equations.

2.3. Follow-Up. Clinical follow-up including assessment of
New York Heart Association (NYHA) functional status and
echocardiography was obtained at 1 month after procedure
in all included patients.

2.4. Statistical Analysis. Standard descriptive statistics were
applied in the analysis: absolute and relative frequencies for
categorical variables and mean supplemented by standard
development for continuous variables. Wilcoxon paired test and
Wilcoxon signed-rank test were used for the evaluation of
statistical significance of differences between hemodynamic
measurements at different time points. Paired t-test was used
for comparison of LV ejection fraction at baseline and 1-
month follow-up. The level of statistical significance was set
at p < 0.05. Statistical analysis was computed using software
SPSS 23.0.0.0. (IBN Corp., Armonk, NY, USA).

3. Results

The study analysed hemodynamic data from 23 consecutive
patients who underwent MitraClip procedure in our centre.
Baseline characteristics are summarized in Table 1. The
aetiology of MR was functional in all patients and more
than two-thirds had ischemic heart disease. The majority of
patients had severe left ventricular dysfunction, and half of
them have already history of congestive heart failure.

Procedure-related and clinical follow-up data are pre-
- sented in Table 2. Acute procedural success was achieved
in 21 (91%) patients. None of the patients needed inotropic
support or prolonged mechanical ventilation at day 1 and all
patients were hemodynamically stable. There were no access-
site complications.

3.1. Invasive Hemodynamic Data. Invasive hemodynamic
data in the monitored time points are shown in Figure 1.
Mitravalve clipping significantly increased cardiac index
(CI) (from 2.0 ± 0.5 before procedure to 3.3 ± 0.6 L/min/m²
one day after procedure, p < 0.01). Similarly, MitraClip
implantation significantly increased LVSWI (from 26.6 ± 9
to 37.7 ± 8.5, p < 0.01) and RVSWI (from 7.4 ± 3.4 to
10.3 ± 4.2 mmHg·mL/m², p < 0.01). Conversely, there was
significant reduction in the mean PCWP (from 18.6 ± 5.7
to 10.5 ± 3.8 mmHg, p < 0.01), mean PAP (from 29.8 ±
Table 2: Procedure-related data and one-month follow-up data (n = 23).

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<table>
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<tbody>
<tr>
<td>APS (%)</td>
<td>91</td>
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<tr>
<td>Number of clips (%)</td>
<td>1</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>2</td>
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<tr>
<td></td>
<td>22</td>
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<tr>
<td>Inotropic support (%)</td>
<td>0</td>
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<tr>
<td>In-hospital heart failure (%)</td>
<td>0</td>
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<td>Early mitral valve surgery (%)</td>
<td>0</td>
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<tr>
<td>Hospital stay (days)</td>
<td>13 ± 9</td>
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<td>In-hospital death (%)</td>
<td>0</td>
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One-month follow-up data

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<tr>
<td>LVEF (%)</td>
<td>36 ± 11</td>
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<tr>
<td>Rehospitalisation for HF (%)</td>
<td>0</td>
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<tr>
<td>One-month death (%)</td>
<td>0</td>
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APS, acute procedural success (defined as MR reduction after clip implantation to grade 2 or less); LVEF, left ventricular ejection fraction; HF, heart failure.

Our results are in agreement with previously published work by Siegel et al. [4] from the EVEREST trial, who described increased CI (from 2.6 ± 1.0 to 3.0 ± 1.0) and decreased SVR (from 1259 ± 531 to 1059 ± 479) after MitraClip implantation (n = 107). The principal difference is in patient population, especially with respect to MR aetiology (only 21% with functional MR and baseline LV ejection fraction was 59.8 ± 8.3%). Importantly, all hemodynamic data were obtained only under general anaesthesia with well-known effect on haemodynamic situation. Very similar results were reported by Gaemperli et al. [5], who described in their cohort of 50 patients increased CI by 32% and decreased PCWP by 20%. Also the limitations of this work are similar to the previous one; only 56% of patients had functional MR and baseline LV ejection fraction was high at 47 ± 18% and the last haemodynamic measurement after mitral valve clipping was obtained still under general anaesthesia.

To the best of our knowledge, our work is the first to invasively measure and describe the acute haemodynamic changes after MitraClip implantation in selected and homogenous cohort of patients with functional MR and severely depressed LV systolic function while carefully avoiding the confounding influence of general anaesthesia on haemodynamic situation. There is no deterioration including severe decompensated group of MR patients and in fact improvement in hemodynamic situation very quickly after this procedure. In summary, increase in forward cardiac output after MitraClip implantation indicates that the beneficial effect of end-diastolic unloading outweighs the negative effect of afterload increase. This is in contrast to well established belief (based on surgical experience) that elimination of MR leads to decrease of LV systolic function and low cardiac output state.

The important question remains: will the measured favourable haemodynamic parameters be translated to improved clinical outcomes? There is evidence that patients with increased CO and decreased filling pressures after MitraClip procedure have positive effect on LV remodelling with decrease in LV size and increase in LV ejection fraction [8]. These hemodynamic changes did result in improvement of clinical outcomes. The haemodynamic status is somewhat reflected by biochemical markers like natriuretic peptides and these levels correlate with clinical outcomes [9,10]. The previous experience with MitraClip is encouraging; symptoms of heart failure (NYHA class reduction) and improvement of the life expectancy of high surgical risk patients compared with standard medical care were demonstrated [11–13].

This is in agreement with our experience; there was significant improvement in patient symptoms expressed by NYHA class after 1 month and significant improvement of LV ejection fraction.

5. Limitations

The main limitation of our work is the small number of studied subjects. This project was initiated only after our centre gained initial experience with this new method to avoid the influence of learning curve. We had carefully
Figure 1: Invasive hemodynamic data and changes in the monitored time points. MAP, mean arterial pressure; MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; CI, cardiac index; SVRI, systemic vascular resistance index; PVRI, pulmonary vascular resistance index; LVSWI, left ventricular stroke work index; RVSWI, right ventricular stroke work index; data are presented as mean ± SD.
conducted all measurements but we are not able to account for possible changes in patient hydration. This is difficult as the patient is fasting prior to the procedure; the fluids administered during the procedure include usually poorly quantified catheter flushing and some patients do receive diuretic therapy after the procedure. Another technical issue might be linked to the use of thermodilution measurement; this may be affected by the presence of severe tricuspid regurgitation. However, only 4 of our patients had severe TR. In the postprocedure measurements, the usually present left-to-right shunting from iatrogenic atrial septal defect can underestimate CO.

6. Conclusions

The reduction of mitral regurgitation using percutaneous MitraClip device results in a quick improvement of cardiac output state in patients with functional mitral regurgitation.
These results are independent of the influence of general anaesthesia. None of our patients developed low cardiac output state. Our results support the idea that significant part of low cardiac output state after cardiac surgery for mitral regurgitation is due to surgery related factors rather than being due to sudden increase in afterload. These findings may have important implications for the use of percutaneous MitraClip device in older patients with severe MR and poor LV function who have a high risk of developing postoperative low cardiac output state.

**Competing Interests**

Victor Kocka has received speaker honoraria from Abbott Vascular. Tomas Budesinsky, Frantisek Bednar, and Hana Linkova have received travel support from Abbott Vascular.

**Acknowledgments**

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