A case report of advanced heart failure refractory to pharmacological therapy who was successfully recovered by combinatory usage of cardiac resynchronizing therapy, Impella and MitraClip

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Background

The safety and efficacy of MitraClip for advanced heart failure (HF) patients who are inotrope-dependent or mechanically supported are unknown.

Case summary

The patient was a 71-year-old man diagnosed as dilated cardiomyopathy in 2003. He was admitted due to worsening HF in January 2019 and became dependent upon intravenous infusion of inotropes. During the 8-month hospitalization, his haemodynamics were relatively static with bed rest and continuous inotropes, but he was definitely dependent on them. Our multidisciplinary team decided to perform both cardiac resynchronization therapy (CRT) and MitraClip under Impella support. First, Impella was inserted from left subclavian artery. After a week, CRT was implanted from right subclavian vein, and the QRS duration of electrocardiogram became remarkably narrow. MitraClip was performed 2 weeks after Impella, and functional mitral regurgitation improved from severe to mild, and Impella was removed on the same day. Inotropes could be ceased, and he was discharged 2 months after MitraClip.

Discussion

During inotrope-dependent status, there was a risk that HF would worsen with haemodynamic collapse when performing CRT implantation, and we firstly supported his haemodynamics by Impella. Cardiac resynchronization therapy implantation before MitraClip seemed to be crucial. In fact, the mitral valve morphology before Impella insertion had very poor coaptation of the anterior and posterior leaflets that was not optimal for MitraClip procedure. But the Impella support and correction of dyssynchrony by CRT markedly improved the coaptation of those leaflets. The combination therapy of CRT and MitraClip unloading with Impella maybe a new therapeutic option for advanced HF.

Keywords

MitraClip • Cardiac resynchronizing therapy • Impella • Advanced heart failure • Functional mitral regurgitation • Case report

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Learning points

• To identify management options in inotrope-dependent advanced heart failure patient without indication of left ventricular assist device (LVAD).
• To understand efficacy of combination therapy of cardiac resynchronization therapy (CRT) and MitraClip and need to unload with concomitant Impella support.
• To understand the implication of CRT before MitraClip.

Introduction

The percutaneous edge-to-edge mitral repair system MitraClip (Abbott Vascular, Abbott Park, IL, USA) reduces mortality and heart failure (HF) hospitalization rate of the patients with functional mitral regurgitation (FMR).1–3 However, these reports include those with stable haemodynamics, and the safety and efficacy for advanced HF patients who are inotrope-dependent or mechanically supported remain unknown. We report a case of a patient with inotrope-dependent advanced HF who could successfully wean off the inotropes by the combination of cardiac resynchronizing therapy (CRT) and MitraClip therapy under Impella support.

Timeline

| Time (days after admission) | Events |
|-----------------------------|--------|
| 1                           | Intravenous infusion of dobutamine was started to treat decompensated heart failure with low ejection fraction (20%) and severe mitral regurgitation |
| 11                          | Paroxysmal atrial fibrillation occurred and haemodynamics collapsed |
| 40                          | Right heart catheterization showed that mean pulmonary arterial pressure (mPAP) was 40 mmHg, mean pulmonary arterial wedge pressure (mPAWP) was 26 mmHg, and cardiac index (CI) was 2.0 L/min/m² |
| 40 to 261                   | Haemodynamics were relatively static with bed rest and continuous inotropes |
| 261                         | Impella 5.0 was inserted, and mPAP and mPAWP were immediately improved from 58 to 29 mmHg and from 48 to 20 mmHg, respectively |
| 262                         | Cardiac rehabilitation was started at the bedside |
| 268                         | Cardiac resynchronization therapy was implanted |
| 275                         | MitraClip was performed and Impella was explanted |
| 282                         | Right heart catheterization showed that mPAP was 22 mmHg, mPAWP was 11 mmHg, and CI was 3.3 L/min/m² |
| 303                         | Dobutamine was ceased |
| 342                         | Discharge |

Case presentation

The patient was a 71-year-old man with advanced HF due to dilated cardiomyopathy that required implantable cardioverter-defibrillator for non-sustained ventricular tachycardia. He was admitted to our institute due to worsening HF despite guideline-directed medications including losartan of 25 mg, sotalol of 80 mg, pimobendane of 2.5 mg, metoprolol of 40 mg, eplerenone of 100 mg, and azosemide of 60 mg.

On admission, serum creatinine was 1.49 mg/dL (normal value 0.65–1.07), total bilirubin was 1.5 mg/dL (0.4–1.5), and plasma B-type natriuretic peptide (BNP) was 542 pg/mL (<184). Transthoracic echocardiography showed the left ventricular ejection fraction of 20% along with severe tethering FMR due to enlargement of the left ventricle. Blood pressure, pulse rate, respiratory rate, and oxygen saturation were 116/102 mmHg, 102 b.p.m., 36 b.p.m., and 88% (room air), respectively. The third heart sound was audible with a holosystolic murmur at apex. The jugular vein dilatation and the pedal oedema were observed. The QRS duration of electrocardiogram was 186 ms.

His haemodynamics deteriorated despite optimal medical therapy including intravenous catecholamine following the de novo atrial fibrillation refractory to repeated electrical defibrillation, which was eventually managed by bepridil administration. Catheter ablation was not performed given his too remodelled left atrium. He could not be a candidate for ventricular assist device (VAD) therapy given that he was too old to be listed for heart transplantation.

On the 40th day, right heart catheterization showed that mean pulmonary arterial pressure (mPAP) was 40 mmHg, mean pulmonary artery wedge pressure (mPAWP) was 26 mmHg (v wave was 35 mmHg), and cardiac index (CI) was 2.0 L/min/m². Oral medications were sotalol of 80 mg, bepridil of 100 mg, pimobendane of 5 mg, bisoprolol of 0.625 mg, tolvaptan of 15 mg, spironolactone of 25 mg, and azosemide of 60 mg.

During the 8-month hospitalization, his haemodynamics were relatively static with bed rest and maximal continuous inotropes including 4.5 μg/kg/min of dobutamine, 0.23 μg/kg/min of olprinone, and 0.025 μg/kg/min of noradrenaline, but he was definitely dependent on these inotropes. Our multidisciplinary team eventually decided to perform both CRT and MitraClip under Impella support.

On the 261st day, Impella 5.0 was inserted via the left subclavian artery. Mean pulmonary artery pressure and mPAWP improved from 58 to 29 mmHg and from 48 to 20 mmHg, respectively.

After a week, CRT was successfully implanted via the right subclavian vein with a procedure time of 130 min. Left ventricular lead was inserted in a posterolateral vein, and CRT programming was DDD 60 and AdaptiveCRT mode (Medtronic, Minnesota, USA) that leverages a patient’s intrinsic right ventricular conduction and provides continuous optimization of AV/VV timing settings. QRS width
became remarkably narrow and QRS polarity on lead V5, six turned positive (Figure 1). Nevertheless, FMR remained severe (the jet area in the left atrium was 52.3% and the vena contracta width was 0.73 cm) after Impella support and CRT implantation.

MitraClip procedure was performed safely on the 275th day under Impella support with an operative time of 204 min, and FMR improved from severe to mild (Figure 2 and Supplementary material online, Videos S1–S3). Two clips were implanted at the middle leaflets, and the trans-mitral valve mean pressure gradient was 4.3 mmHg. Haemodynamics remained static with mPAWP of 13 mmHg, CI of 3.8 L/min/m², and blood pressure of 84/46 mmHg without Impella support, which was explanted at the same time.

One week later, right heart catheterization showed that mPAP of 22 mmHg, mPAWP of 11 mmHg, and CI of 3.3 L/min/m² under
continuous infusion of dobutamine ($3 \mu g/kg/min$), which was eventually weaned off on the 303rd day (Figure 4). He was discharged on the 342nd day.

Six months later, he has had no HF symptoms or arrhythmias. B-type natriuretic peptide decreased from 756 to 397 pg/mL, the left ventricular dimension, the left ventricular ejection fraction, and the left atrium dimension improved from 85 to 83 mm, from 17% to 20%, and from 62 to 57 mm, respectively.

**Discussion**

In patients with advanced HF, VAD therapy would be the best strategy, irrespective of the existence of mitral regurgitation. However, such an intensive therapy cannot be applicable for all advanced HF patients, and various clinical and social situations should be considered. Of note, only bridge to transplantation strategy is approved in Japan. This patient had inotrope-dependent advanced HF with no
indication for heart transplantation or VAD but was successfully withdrawn from inotropes and discharged by combinatorial usage of CRT and MitraClip under haemodynamic support by Impella.

The procedure of CRT implantation is invasive and has a risk of haemodynamic deterioration, particularly for those dependent on inotropes, and we performed the procedure under Impella support. Support duration was expected to be several weeks, and we chose Impella L5.0 from the subclavian approach instead of femoral access.

The order of procedures between CRT implantation and MitraClip is quite important. The mitral valve morphology before Impella insertion had very poor leaflet coaptation that was not optimal for the MitraClip procedure according to the German Consensus (Figure 3A and Supplementary material online, Videos S4 and S5). Unloading with Impella by itself did not optimize mitral valve coaptation, whereas the correction of dysynchrony by CRT reverse remodelled the mitral annulus diameter and improved the coaptation of those leaflets (Figure 3B and Supplementary material online, Videos S6 and S7).

MitraClip decreased FMR to less than mild. However, such an immediate improvement of FMR sometimes causes an increase in left ventricular afterload. Consistently, ejection fraction decreased slightly (17–13%), left ventricular dimension also slightly increased (85–88 mm), and BNP increased transiently (Figure 4). The post-procedural afterload mismatch is associated with poor future prognosis. Improved left ventricular function due to pre-procedural CRT therapy would have compensated such a post-MitraClip afterload mismatch. Apart from that, we detected L-R shunts (Qp/Qs 1.49) after MitraClip, so far, this has been accepted considering mPAP was low. This shunt might contribute to symptomatic improvement without haemodynamic compromise.

According to Arora et al., MitraClip had little effect on FMR in patients with the too remodelled left ventricle. Those with inotrope dependent might be refractory to the CRT. Nevertheless, even in patients with advanced HF like this case, the combination therapy using CRT and MitraClip with Impella support might be a novel promising therapeutic option, although not yet clearly stated in the guidelines. Further studies are warranted to validate the safety and efficacy of this strategy.

**Lead author biography**

Mitsuo Sobajima was born in Ibaraki, Japan, in 1976. He is a MD and PhD. He works as a Cardiologist at the Toyama University Hospital, Toyama, Japan. He is also a PhD at the Graduate School of Medicine, University of Toyama. He is actively involved in teaching residents and medical students. His main areas of interest are interventional cardiology including structural heart disease and peripheral artery disease.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

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**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

**Consent:** The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

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