Case series of transcatheter edge-to-edge repair using MitraClip™ system with Impella® mechanical circulatory support

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Background
Secondary mitral regurgitation (SMR) is a major comorbidity in patients with heart failure with reduced ejection fraction (HFrEF). Transcatheter edge-to-edge repair (TEER) using the MitraClip™ system is a promising tool for selected patients with SMR and HFrEF. Durable success using this system in patients who have advanced heart failure and unsuitable anatomy remains a clinical challenge.

Case summary
Three patients aged 67–72 years with HFrEF on inotropic support successfully underwent Impella®-assisted TEER at our centre. Following the procedure, two patients were able to be weaned off inotropic support and were discharged, while one patient expired during the index hospitalization.

Discussion
Impella®-assisted TEER may be a feasible strategy for patients with SMR and HFrEF with unstable haemodynamics particularly when cardiac replacement therapy is not applicable.

Keywords
Mitral regurgitation • Valve disease • Haemodynamics • Mechanical circulatory support • Case report

ESC Curriculum
4.3 Mitral regurgitation • 6.2 Heart failure with reduced ejection fraction

Learning points
- Impella circulatory support might be a novel technically feasible tool to support haemodynamics during transcatheter edge-to-edge repair in patients with secondary mitral regurgitation and unstable haemodynamics due to advanced heart failure.
- Further investigation is needed to clarify optimal patient selection for successful Impella-supported transcatheter edge-to-edge repair.

Introduction
Significant secondary mitral regurgitation (SMR) in patients with heart failure (HF) with reduced ejection fraction (HFrEF) is independently associated with a greater risk of adverse events compared with those without significant SMR.¹² Over the last decade, transcatheter edge-to-edge repair (TEER) using the MitraClip™ system has emerged as a breakthrough therapeutic option for patients with chronic HFrEF and SMR as shown in the COAPT trial, where patients undergoing TEER experienced a reduction in both HF hospitalizations and death compared with medical therapy.³
The current ESC guidelines for HF recommend TEER as Class IIa (evidence Level B) for carefully selected SMR patients with non-eligible for surgery and not needing coronary revascularization, who are symptomatic despite optimal medical therapy and who fulfill criteria to achieve a reduction in HF hospitalizations. TEER is also recommended as Class IIb for those who do not fulfill the indication of COAPT trial. ESC/EACTS guidelines for the management of valvular heart disease also comment that, in high-risk symptomatic patients not eligible for surgery and not fulfilling the criteria, suggesting an increased chance of responding to TEER, the heart team may consider in selected cases a TEER procedure after careful evaluation for ventricular assist device or heart transplant. In real-world practice, we often encounter those with SMR and advanced HF requiring inotropic therapy, where TEER is less proved to have a survival benefit but may offer a chance to improve clinical health status.

The Impella® (Abiomed, Danvers, MA, USA) is a temporary percutaneous left-ventricular assist device that allows for transvalvular ventricular unloading. This device is most commonly used in high-risk coronary interventions or as short-term management in patients with cardiogenic shock. Theoretically, Impella® may also be considered as a mode of haemodynamic support in high-risk TEER cases. We present three cases of high-risk patients who underwent Impella®-assisted TEER for severe SMR.

**Case presentation**

Baseline characteristics and clinical course in all three patients who received Impella®-assisted TEER are shown in Table 1 and Timeline.

**Patient 1 (outcome: successfully discharged home)**

The patient was a 68-year-old female with HFrEF due to cardiac sarcoidosis with no other non-cardiac previous history. She presented with dyspnoea on exertion for several weeks, and was subsequently transferred to our hospital for TEER consideration in the setting of severe SMR. Systolic blood pressure (BP) was extremely low of 58 mmHg, and she had significant general malaise and NYHA 3 HF symptom, although no leg oedema or jugular venous distention. Left-ventricular end-diastolic/end-systole diameter (LVDd/Ds) was 77/65 mm and left-ventricular ejection fraction (LVEF) was 27%. Effective regurgitant orifice area (EROA) by proximal isovelocity surface area was 0.39 cm² and regurgitant volume (RV) was 54 mL. Coronary angiography showed no significant disease. The patient was not deemed a candidate for cardiac replacement therapies at our institution due to frailty and advanced age (Timeline).

The mitral valve had a marked tethering of the posterior leaflet due to dyskinesis at the base of the posterior wall, and the resulting coaptation gap posed an additional challenge for TEER (Figure 1). She also had unstable haemodynamics with a systolic arterial BP of 60 mmHg and cardiac index 1.45 L/min/m² despite inotropic support.

Prior to TEER, an Impella® CP was inserted femorally for haemodynamic stabilization. Transoesophageal echocardiography showed improvement in mitral valve coaptation owing to improved ventricular unloading. Interestingly, the valve coaptation further improved at incremental support levels from P2 to P9 (Figure 2).

Following successful TEER under Impella® support, SMR improved from 4+ to 1+ (Figure 3). The Impella® device was weaned off in the immediate post-procedure period following an improvement in intracardiac haemodynamics together with mean arterial BP up to 90 mmHg. The patient was subsequently able to be discharged on oral medical therapy for HFrEF. Her clinical course after TEER has been good and she has not experienced a HF readmission in over a year.

**Patient 2 (outcome: successfully discharged home)**

The patient was a 72-year-old male with severe SMR and HFrEF, with a history of multiple prior admissions due to decompensated HF, who was transferred to our centre for escalation of care. Hypotension...
QRS on electrocardiogram) and was hypotensive without mechanical
support, our heart-valve team decided to proceed with a high-risk TEER under Impella® support.
Following TEER, SMR significantly improved from 4+ to 1+ (Figure S2). The resulting haemodynamic improvements along with an increase in mean arterial BP to 95 mmHg allowed for successful weaning of Impella® and inotropic support in a matter of days. The patient was also able to be discharged on oral medical therapy and have not experienced HF readmission during a year.

**Patient 3 (outcome: in-hospital death)**
The patient was a 67-year-old male diagnosed with dilated cardiomyopathy 11 years prior to hospitalization. He had hypothyroidism and sleep apnoea, but no life-threatening comorbidities other than heart disease. Despite attempts at optimization of medical therapy, the patient had multiple hospitalizations for worsening HF and ventricular tachycardia. He required ventilatory support due to pulmonary oedema at the referring hospital, and was subsequently transferred to our institute for further HF management.

On referral, systolic BP was as low as 100 mmHg, heart rate was over 90 per minute sinus tachycardia. On echocardiography, LVDd/Ds was 79/72 mm and LVEF was 23.5%. SMR was severe with EROA 0.45 cm² and RV 48 mL. His underlying pneumonia and overall clinical status was not optimized at the time of referral. He experienced ongoing haemodynamic deterioration despite considerable inotropic support; the decision was then made by the heart-valve team to place an axillary Impella® 5.0 given worsening cardiogenic shock (Timeline). The patient’s overall clinical status excluded him from consideration for cardiac replacement therapies. Our heart-valve team decided to perform a high-risk catheter ablation for refractory ventricular tachycardia and TEER under Impella® 5.0 support, even though we expected the odds of survival to be low despite these aggressive measures.

With Impella® 5.0 support, transcatheter ablation for ventricular tachycardia and TEER were successively performed. SMR improved from 4+ to 2+, whereas residual MR remained from indentation of the posterior mitral valve leaflet (Figure S3).

His post-procedure course was challenging as Impella® had to be withdrawn early after TEER due to device-related bleeding. Mechanical support was converted to an intra-aortic balloon pump despite an anticipated inadequate support level. He expired on Day 79 due to multi-organ failure.

### Discussion

**Mechanical circulatory support and secondary mitral regurgitation**
Secondary mitral regurgitation due to Stage D HF can be significantly improved by durable left-ventricular assist device implantation, and heart transplantation. However, many patients are not candidates for these therapies due to underlying comorbidities.

Given our findings, TEER may be another feasible option to address severe SMR in patients with refractory HF dependent on inotropes. We acknowledge these patients fall outside of the COAPT trial inclusion criteria and may not achieve the same survival benefit. Although not durable, the Impella® may be a favourable supportive option to haemodynamically assist the candidates undergoing high-risk TEER as our patients.

### Implication of Impella® to support transcatheter edge-to-edge repair

We performed Impella®-assisted TEER in three patients, with only few published reports of this method.7–9 Impella® during high-risk TEER may prevent haemodynamic deterioration during induction of general

#### Table 1 Baseline characteristics and clinical outcomes following transcatheter edge-to-edge repair

| Patient 1 | Patient 2 | Patient 3 |
|-----------|-----------|-----------|
| **Gender** | Female | Male | Male |
| **Age, years** | 68 | 72 | 67 |
| **Aetiology** | Sarcoidosis | DCM | DCM |
| **INTERMACS profile** | 4 | 3 | 1 |
| **Dose of beta-blocker, mg** | 20 | 10 | 10 |
| **RAAS inhibitor** | + | + | + |
| **STS for MVR, %** | 5.0 | 9.9 | 19.7 |
| **Euro II score, %** | 17.8 | 10.1 | 18.9 |
| **Inotrope** | Dob | Dob | Dob/Milrinone |
| **Plasma BNP, pg/mL** | 628.7 | 137.2 | 1751.6 |
| **Serum creatinine, mg/dL** | 1.16 | 0.92 | 2.05 |
| **LVDd/Ds, mm** | 77/65 | 76/69 | 79/72 |
| **LVEDV/ESV, mL** | 203/279 | 330/446 | 279/359 |
| **LVEF, %** | 27.1 | 26.0 | 23.5 |
| **MR severity, grade** | 4+ | 4+ | 4+ |
| **EROA, cm²** | 0.39 | 0.42 | 0.45 |
| **Regurgitant volume, mL** | 54 | 48 | 48 |
| **Coaptation length, mm** | 0 | 1.2 | 2.8 |
| **Coaptation height, mm** | 8.4 | 4.3 | 9.7 |
| **TSP height, mm** | 32 | 36 | 33 |
| **PML length, mm** | 11.0 | 7.8 | 9.3 |
| **MVA, cm²** | 4.2 | 5.4 | 4.9 |
| **PAWP, mmHg** | 10 | 29 | 37 |
| **Mean PAP, mmHg** | 16 | 38 | 47 |
| **Cardiac output, L/min** | 2.24 | 2.61 | 5.11 |
| **PVR, wood unit** | 2.68 | 3.45 | 1.96 |
| **Numbers of clips** | 2 (NTW, NT) | 2 (NTx2) | 2 (NTW,NT) |
| **Residual MR, grade** | 1+ | 1+ | 2+ |
| **MV mean PG, mmHg** | 2.9 | 2.1 | 5.0 |
| **Outcomes** | Home | Home | In-hospital death |

BNP, Type B natriuretic peptide; DCM, dilated cardiomyopathy; DOB, dobutamine; Ds, end-systole dimension; EROA, effective regurgitant orifice area; ESV, end-systolic volume; ICM, ischaemic cardiomyopathy; LVDd, left ventricle end-diastolic dimension; LVEDV, left-ventricular end-diastolic volume; LVEF, left-ventricular ejection fraction; MR, mitral regurgitation; MVA, mitral valve area; MVR, mitral valve replacement; NAD, noradrenaline; NYHA, New York Heart Association; PAP, pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RAAS, renin-angiotensin-aldosterone system; TEER, transcatheter edge-to-edge repair.

*Numbers of clips were 2 (one NTW, one NT) for Patient 1; 2 for Patient 2 (one NTW, one NTx2); 2 for Patient 3 (NTW, NT).*
anaesthesia in tenuous candidates and during times of unexpected intra-procedural complications, including clip entanglement and ventricular arrhythmias. Those with marginal haemodynamics despite inotropic support who are being considered for TEER should be considered for temporary Impella® support to better tolerate the above-described aspects of the intervention.

In patients with advanced LV dilation, the large coaptation gap makes it challenging to grasp both valve leaflets adequately using the
Optimal patient selection

We may be able to expand the indication of TEER beyond the COAPT trial criteria to more advanced HF stages, as stated in the ESC/EACTS guidelines, when concomitant circulatory support is optimally utilized. However, randomized clinical trials of this subset are lacking to make a clear evidence-based recommendation. Patients with ongoing haemodynamic deterioration and end-organ dysfunction despite inotropic support are at high-risk of in-hospital mortality, and correction of just the valvular-related issue in this subset may prove inadequate.

The contribution of SMR to the clinical haemodynamic profile is an important consideration for successful Impella®-supported TEER. In the successful cases (Patients 1 and 2), haemodynamic stabilization was considerably associated with an improvement in SMR. Needless to say, other interventions to improve haemodynamics should also be considered.

Comorbidities including frailty, systemic infection, and malnutrition will undoubtedly make overall clinical improvement a challenge and should be considered in patient selection for this high-risk intervention, as we experienced in Patient 3. Device-related bleeding and haemoysis are two major adverse events which can occur with Impella® devices particularly in patients with above-mentioned comorbidities.13,14

Conclusion

Impella®-assisted TEER might be a technically feasible strategy for those with SMR and marginal haemodynamics, although its indication should be carefully considered and restricted to highly selected cohorts. Dedicated randomized control trials of higher risk patient cohorts outside of current trial indications are needed to better understand immediate clinical benefit and long-term survival.

Lead author biography

Teruhiko Imamura is a clinician engaging in the management of advanced heart failure.

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: This manuscript has been approved by the IRB, and written informed consent was obtained from all patients beforehand in accordance with COPE guidelines.

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