ESC European Society of Cardiology

European Heart Journal - Case Reports (2022) **6**, 1–5
https://doi.org/10.1093/ehjcr/ytac370

CASE SERIES
Heart failure

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

Shuhei Tanaka [1], Teruhiko Imamura [1]*, Nikhil Narang[2], Atsuko Fukuo[1], Makiko Nakamura[1], Nobuyuki Fukuda[1], Hiroshi Ueno[1], and Koichiro Kinugawa [1]

[1]Cardiovascular Center, Toyama University Hospital, Toyama, Japan; and [2]Advocate Christ Medical Center, Oak Lawn, IL, USA

Received 22 November 2021; first decision 19 January 2022; accepted 5 September 2022; online publish-ahead-of-print 7 September 2022

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

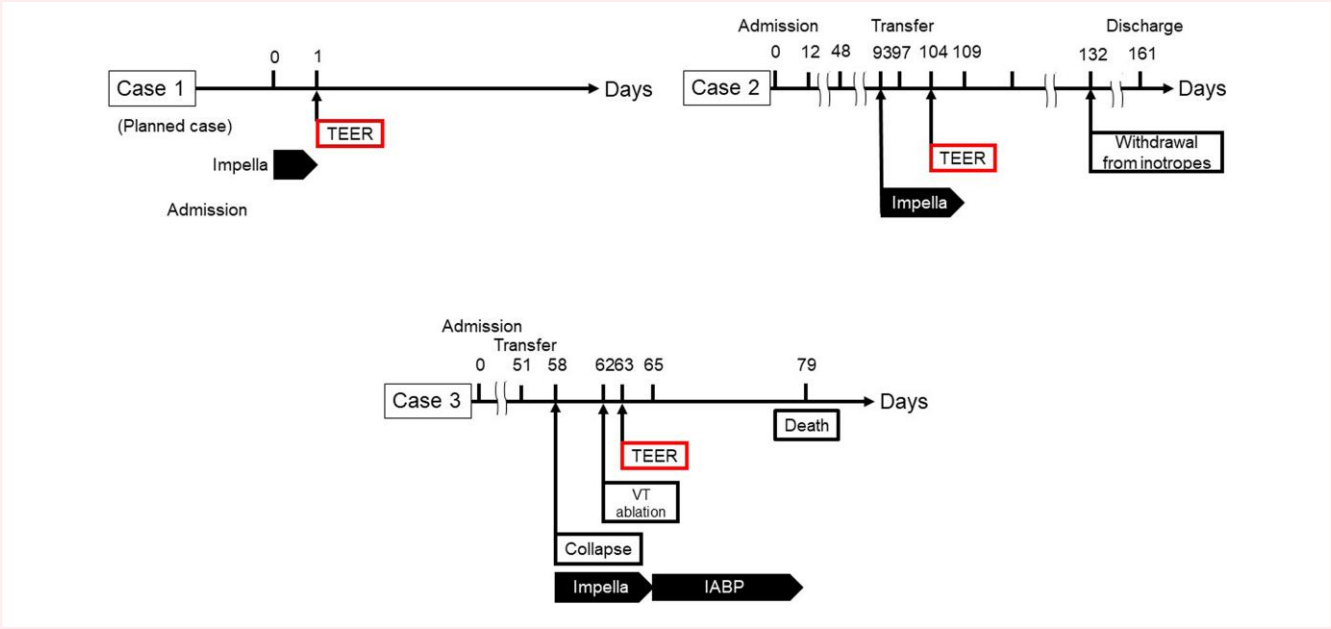
Significant secondary mitral regurgitation (SMR) in patients with heart failure (HF) with reduced ejection fraction (HFrEF) is independently associated with a greater risk of adverse events compared with those without significant SMR.[1,2] Over the last decade, transcatheter edge-to-edge repair (TEER) 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]

* Corresponding author. The second Department of Internal Medicine, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan. Tel: +8176-434-2281, Fax: +8176-434-5026, Email: teimamu@med.u-toyama.ac.jp

Handling Editor: Sameh Shaheen
Peer-reviewers: Enrique Garcia-Sayan; Henrik Fox; Jonathan Adam Batty; Takeshi Kitai
Compliance Editor: Lavanya Athithan
Supplementary Material Editor: Michael Waight

Timeline

Summary of clinical courses



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 fulfil criteria to achieve a reduction in HF hospitalizations. TEER is also recommended as Class IIb for those who do not fulfil the indication of COAPT trial.[4] 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.[2] 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.[5]

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.[6]

Theoretically, Impella® may also be considered as a mode of haemodynamic support in high-risk TEER cases.[7–9] 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 cm^2 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/m^2 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*), (*Figure S1*). 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

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

	Patient 1	Patient 2	Patient 3
Baseline characteristics			
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, cm^2	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, cm^2	4.2	5.4	4.2
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
Procedures data			
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
Outcome	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.

persisted, NYHA Grade 4 HF symptom was present and haemodynamics were unstable despite considerable inotropic support; he was eventually referred to our institute following an insertion of an axillary Impella® 5.0 for consideration of bridge to TEER.

The patient had no comorbidities other than hypothyroidism, but severe LV dysfunction (Dd/Ds 76/69 mm, LVEF 26%) and severe SMR (EROA 0.42 cm^2, RV 48 mL) even under Impella® support. Given that the patient was not a candidate for biventricular pacing (narrow 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 cm^2 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[10,11] 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 report of this method.[7–9] Impella® during high-risk TEER may prevent haemodynamic deterioration during induction of general

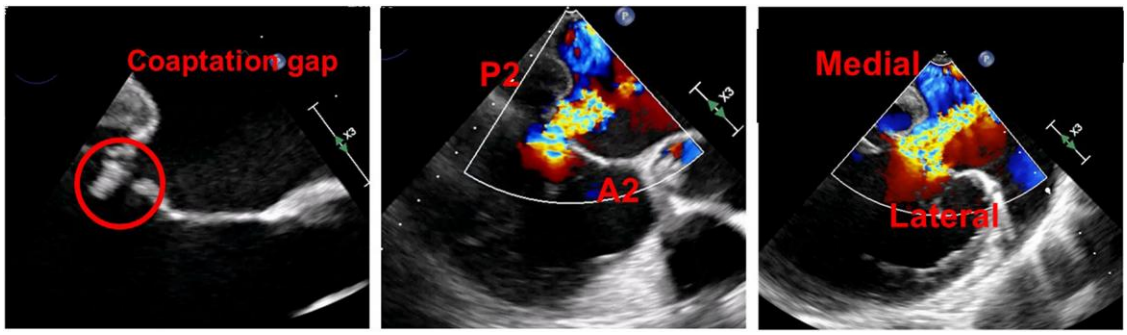


Figure 1 Transoesophageal echocardiographic findings before transcatheter edge-to-edge repair and Impella insertion in Patient 1.

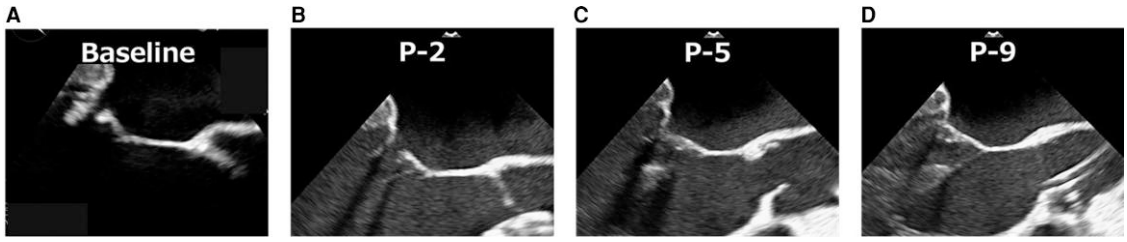


Figure 2 Transoesophageal echocardiographic findings of mitral valve coaptation at each Impella support level in Patient 1. Before Impella insertion (*A*) and at Impella P-2 support (*B*), there was a large junction gap. When the support level was increased (*C*, P-5; *D*, P-9), the junction of both leaflets coapted, although the tethering of the posterior leaflet remained unchanged.

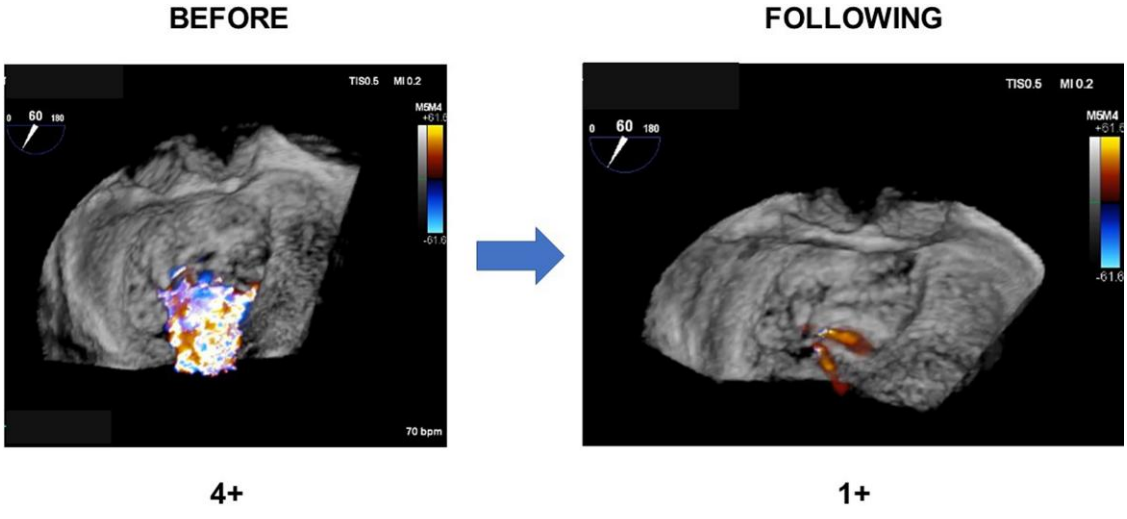


Figure 3 Transoesophageal echocardiographic findings before and following Impella-assisted transcatheter edge-to-edge repair in Patient 1.

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

MitraClip™ system. As observed in this series, Impella® support improves this geometric abnormality by continuous ventricular unloading, allowing for a better chance of procedural success.[12] Adjustment of Impella® support level might further optimize the coaptation gap and increase the procedure successful rate (*Figure 2*).

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 haemolysis 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.

Acknowledgements

The authors acknowledge Naoya Kataoka, Ryuichi Ushijima, Mitsuo Sobajima, Shigeki Yokoyama, Toshio Doi, and Kazuaki Fukahara for data collection and clinical engagement and Nikhil Narang for editing our draft.

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.

Conflict of interest: None declared.

Funding: None declared.

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