# Cardiogenic Shock Secondary to Acute Mitral Regurgitation With Nonischemic Etiology Successfully Stabilized by Transcatheter Intervention

Jiandong Zhang, MD, Darryl Kalil, MD, Grayson Eubanks, MD, Brian P. Kelley, MD, Bart Singer, MD, Thelsa T. Weickert, MD, and George A. Stouffer, MD, *Chapel Hill, North Carolina*

## INTRODUCTION

Cardiogenic shock secondary from severe mitral valve (MV) regurgitation remains one of the most serious entities in clinical practice, with high mortality and limited options.[1] Data from case series and retrospective studies show that transcatheter therapy is an acceptable alternative approach if the risk of surgical options is prohibitive.[1,2] The etiology and initial presentation of cardiogenic shock as well as the extent of preexisting cardiopulmonary remodeling are critical determinants of the benefit of transcatheter edge-to-edge repair, albeit little is known in this regard. Here we report a unique case of cardiogenic shock due to acute mitral regurgitation (MR) with histopathology-confirmed degenerative etiology, which was successfully managed by transcatheter MV edge-to-edge repair (TMVEER) and subsequent surgical replacement after recurrence.

## CASE PRESENTATION

A 61-year-old woman presented to the emergency department with 4 days of nausea, vomiting, diarrhea, and abdominal pain. The patient led an active lifestyle prior to presentation. The patient had a history of MV prolapse for over 40 years and had undergone periodic transthoracic echocardiography (TTE) for monitoring. The last TTE was done 3 years prior to admission and showed normal left ventricular ejection fraction (LVEF) with moderate MV prolapse and mild MR. On physical exam, the patient was ill, with blood pressure of 132/102 mm Hg, heart rate of 136 bpm, and $SaO_2$ 96% on room air. Cardiac exam was notable for irregular tachycardia and a 3/6 holosystolic murmur heard loudest over the apex; no jugular vein distention or S3 was appreciated. Lungs were clear to auscultation bilaterally, and extremities had normal pulses and no edema. Given the patient's prominent gastrointestinal (GI) symptoms, concern was initially highest for viral or foodborne gastroenteritis. The recent onset of dyspnea and loud murmur also raised suspicion for an acute cardiopulmonary process such as new-onset heart failure due to worsened MR, viral myocarditis, or ischemic etiologies.

However, neither infectious nor ischemic workup was indicative of an acute process. Initial electrocardiogram revealed atrial fibrillation with rapid ventricular response (Figure 1). Chest x-ray revealed cardiomegaly with pulmonary vascular congestion (Figure 2). Hs-troponin was 15 ng/L (reference [ref] < 34), complete blood count was unremarkable, and metabolic profile was notable for sodium, 111 mmol/L (ref, 135-145 mmol/L); total bilirubin, 2.4 (ref, 0.3-1.2 mg/dL); aspartate aminotransferase, 471 U/L (ref, <34); alanine aminotransferase, 483 U/L (ref, 10-49); creatinine, 0.87 mg/dL; and lactic acid, 2.5 mmol/L (ref, 0.5-1.8 mmol/L). Testing for *C. difficile* and other infectious GI pathogens was negative. SARS-CoV-2 by polymerase chain reaction, blood cultures, and hepatitis panel were all negative.

The patient was admitted to the the medicine intensive care unit for management of hyponatremia that did not respond to fluid resuscitation during the first 48 hours. The liver function tests continued to worsen to aspartate aminotransferase 6,510 U/L and alanine aminotransferase 3,879 U/L with international normalized ratio increasing to 4.96, with unremarkable Doppler examination of the liver and hepatitis serology. On day 3, the patient developed hypotension, along with worsening mental status, progressive anuria, and worsening lactic acidosis to 8.9 mmol/L (ref, 0.5-1.8 mmol/L), collectively suggesting progression toward a decompensated stage of shock.

Concurrently, TTE revealed a severe anteriorly directed MR (vena contracta width, 1.4 cm), along with normal LVEF and enlargement of the left atrium (LVEF of 61% was determined by the biplane Simpson method, end-systolic left ventricular internal dimension was measured as 3.7 cm, and left atrial volume index was measured as 63 mL/m$^2$, which was increased from 44 mL/m$^2$ 3 years prior; Figure 3), suggesting more likely a primary MV etiology. Moreover, further views from TTE identified evidence of chordal rupture and a flail P2 segment of the MV (Figure 3, Video 1). Emergent surgical consultation deemed the patient to be of inordinately high surgical risk given severe coagulopathy and cardiogenic shock, with the Society of Thoracic Surgeons score of 35%. An intra-aortic balloon pump was urgently inserted to stabilize rapidly deteriorating hemodynamic conditions during the night of hospital day 3, immediately followed by right heart catheterization. Elevated right (mean right atrial pressure was 24 mm Hg) and left ventricular filling pressures (mean pulmonary capillary wedge pressure of 22 mm Hg with prominent v waves up to 30 mm Hg) were present, as well as decreased cardiac output (Fick cardiac index, 2.1 L/min/m$^2$), despite mechanical and pharmacological support (other hemodynamic

From the Division of Cardiology (J.Z., D.K., G.E., B.P.K., T.T.W., G.A.S.) and Department of Pathology and Lab Medicine (B.S.), University of North Carolina, Chapel Hill, North Carolina.

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Correspondence: George A. Stouffer, MD, 160 Dental Circle, CB 7075, Chapel Hill, North Carolina 27514. (E-mail: *Rick_Stouffer@med.unc.edu*).



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## VIDEO HIGHLIGHTS

**Video 1:** Preoperative video clip from transthoracic echocardiogram. **(A)** Two-dimensional TTE parasternal long-axis view demonstrates the MV leaflets are moderately thickened with moderate posterior leaflet prolapse and a torn chord; the left atrium is dilated, and LVEF is low normal or reduced considering the degree of MR. **(B)** Two-dimensional TTE with color Doppler parasternal long-axis view demonstrates severe anteriorly directed MR. **(C)** Two-dimensional TTE with color Doppler apical 4-chamber view demonstrates severe anteriorly directed MR.

**Video 2:** Preprocedural video clip from transesophageal echocardiogram. **(A)** Two-dimensional transesophageal echocardiogram, midesophageal apical long-axis view at 150° demonstrates posterior leaflet prolapse with a flail P2 segment and chordal rupture. Pre-TMVEER semiquantitative findings included flail gap = 1.3 cm and coaptation length = 1.5 mm. **(B)** Three-dimensional transesophageal echocardiogram midesophageal 60° short-axis surgeon's view demonstrates the flail P2 segment and chordal rupture. Mitral valve area by three-dimensional planimetry is 6.77 $cm^2$.

**Video 3:** Postprocedural video clip from transesophageal echocardiogram. **(A)** Two-dimensional transesophageal echocardiogram, midesophageal apical long-axis view at 142° post-TMVEER demonstrates the device with mild residual MR. **(B)** Three-dimensional transesophageal echocardiogram midesophageal 80° short-axis surgeon's view demonstrates that the TMVEER is well positioned as well as the residual double-orifice mitral opening.

**Video 4:** Follow-up video from TTE. Apical 4-chamber view with color Doppler prior to surgical replacement demonstrates severe anteriorly directed MR with a well-seated device seen on the MV.

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parameters: right ventricular pressure, 47/11 [18] mm Hg; pulmonary artery oxygen saturation, 57%; calculated SVR, 844 dynes*s/cm^5; pulmonary vascular resistance, 4.4 Woods units). The patient was transferred to the cardiac intensive care unit after the procedure. A few hours after the procedure, the patient started to require inotropes and vasopressors to maintain mean arterial pressure greater than 60 mm Hg and soon was intubated due to progressive hypoxia.

The decision was made to attempt transcatheter MV repair of the P2 segment, despite unfavorable anatomic conditions (flail gap, 1.3 cm; coaptation length, 1.5 mm; Figure 2, Video 2). Two *MitraClip G4s* (Abbott, Plymouth, MN) were successfully deployed, resulting in mild residual MR without stenosis (Figures 4 and 5, Videos 2 and 3). The patient was successfully weaned off pharmacological and mechanical support within 24 hours after transcatheter procedure and was extubated a few hours later. The patient was discharged home on day 10 of the hospitalization.

During the first month of follow-up, the patient was doing well. However, during the second month of follow-up, the patient endorsed worsening dyspnea, with TTE findings of recurrent severe MR (Figure 6B, Video 4). The patient successfully underwent surgical MV replacement 3 months later (Video 4). The pathology exam revealed significant myxoid changes (loose collagen in fibrosa from Masson staining, expanded spongiosa area—acellular from hematoxylin and eosin staining and positive for proteoglycan from Alcian blue staining) from resected tissues adjacent to the MitraClips, as well as 2 intact metal clips attached to leaflet and chordae (Figure 7). During 1-month follow-up visit after surgery, the patient was much improved and able to participate in cardiac rehab. The timeline is summarized in Figure 8.

## DISCUSSION

Mitral regurgitation is the most frequent valvular disorder in the United States and Europe.[3] Patients with chronic MR can remain asymptomatic for years. By contrast, patients who develop acute severe MR usually present with symptomatic heart failure symptoms because their heart chambers are unable to adapt to the sudden

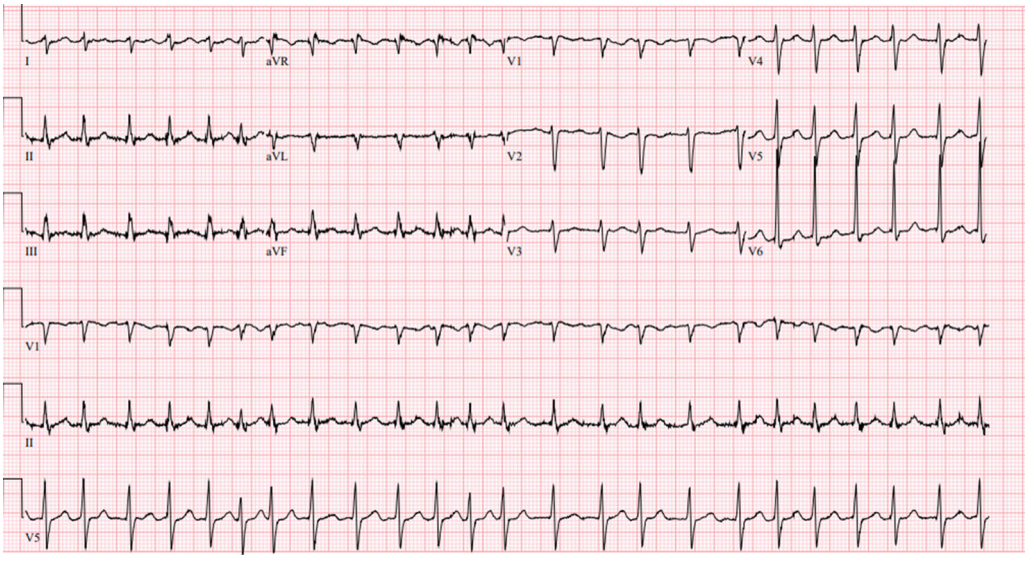


Figure 1 Electrocardiogram, atrial fibrillation with rapid ventricular rate, right-axis deviation.

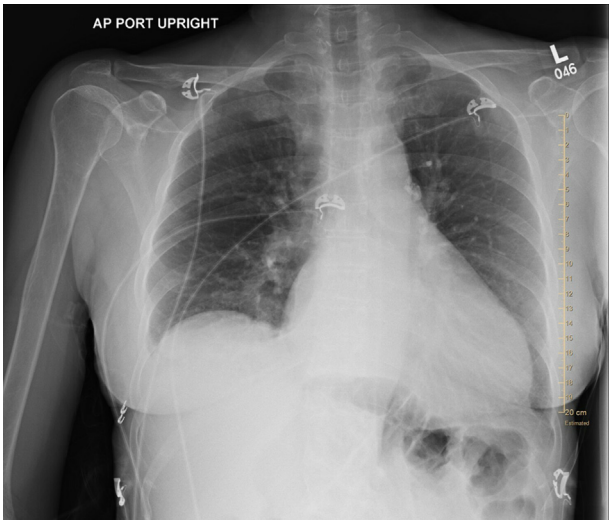


Figure 2 Portable chest x-ray on admission. Cardiomegaly and pulmonary vascular congestion with suspected interstitial pulmonary edema.

increases in volume.[4] However, it remains challenging to make the diagnosis of acute MR at times, especially in initial encounters with atypical presentations.[5]

This case demonstrates an unusual presentation of acute severe MR, initially manifesting as nonspecific GI symptoms and electrolyte abnormalities, followed by rapidly progressive cardiogenic shock in the setting of chronic asymptomatic primary degenerative myxomatous MV. This patient's MV pathology was degenerative MV prolapse, which was demonstrated to be stable on serial echocardiography prior to this hospitalization but is recognized as a pathology that is prone to chordal rupture and acute deterioration. Thus, evaluation for noncardiac causes was prioritized by the primary team in the first 36 hours. It is noteworthy that the narrow pulse pressure (20 mm Hg) on initial presentation is a concerning sign of low cardiac output, suggesting a likely cardiac cause. Retrospectively, it is reasonable to suspect that GI and electrolyte abnormalities were due to compromised perfusion to mesenteric and renal circulation in the early stage of cardiogenic shock, as described in a previous report.[6]

Invasive hemodynamic measurements further supported that the patient had decreased cardiac output from severe MR. Of note, those

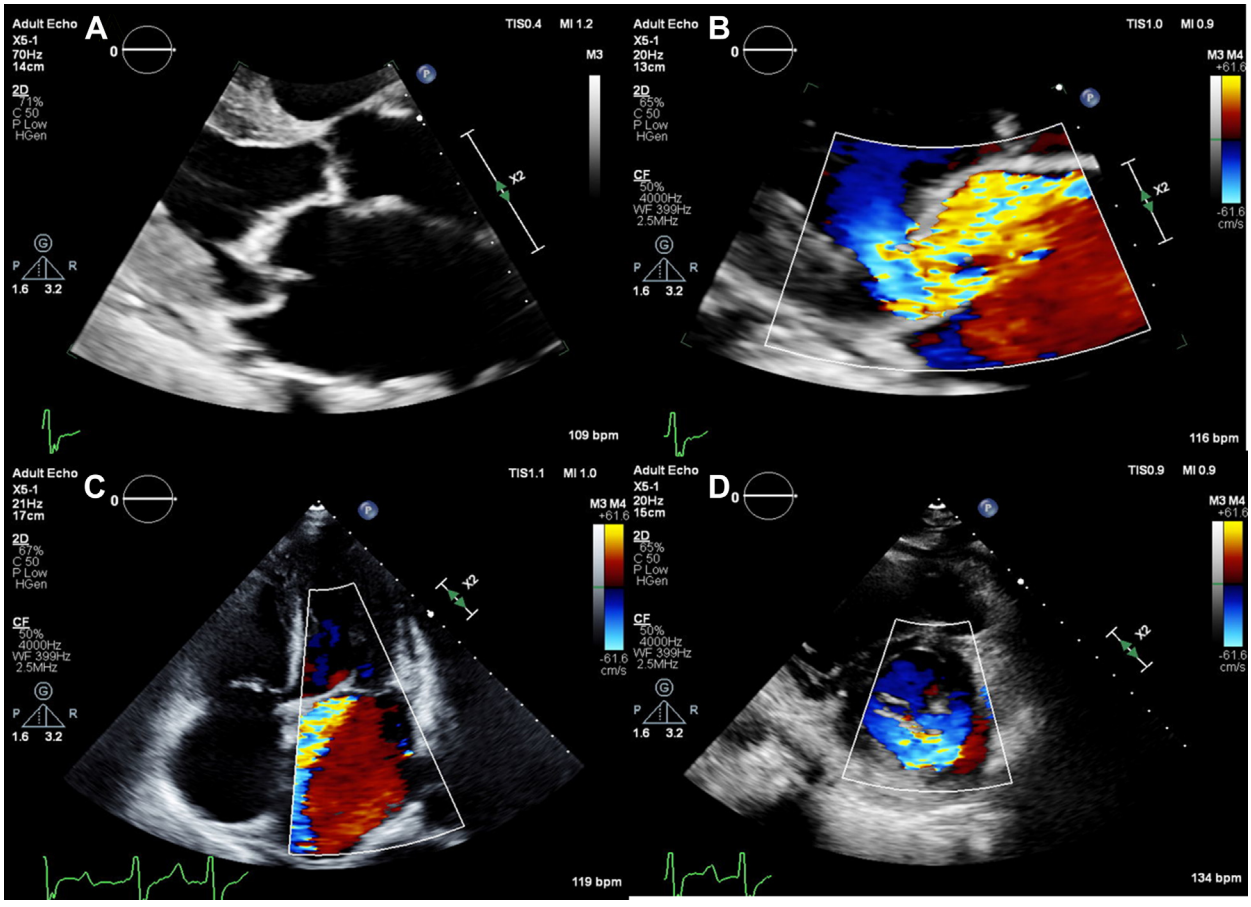


Figure 3 Transthoracic echocardiogram (systolic frame). **(A)** Parasternal long-axis view indicated chordal rupture and a flail segment of posterior leaflet. **(B)** Parasternal long-axis view with color Doppler demonstrates severe anteriorly directed jet of MR. **(C)** Apical 4-chamber view reveals severe anteriorly directed jet of MR. **(D)** Parasternal basal, short-axis view suggests a likely flail P2 segment of the posterior leaflet.

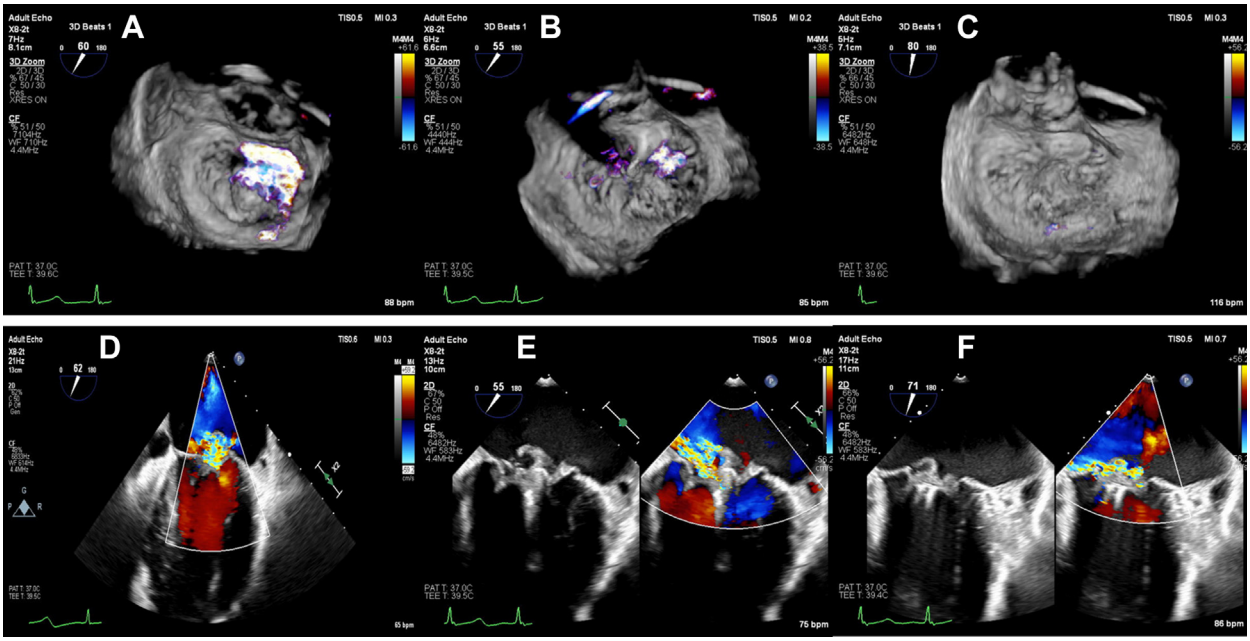


Figure 4 Periprocedural transesophageal echocardiogram, midesophageal views focusing on the MV in systole. **(A)** Three-dimensional reconstruction image prior to TMVEER demonstrates severe anteriorly directed MR. **(B)** Three-dimensional reconstruction image after first TMVEER to A2,P2 demonstrates significantly reduced MR. **(C)** Three-dimensional reconstruction image after second TMVEER demonstrates nearly completely resolved MR. **(D)** Two-dimensional transesophageal echocardiogram with color at 62° view prior to TMVEER demonstrates posterior leaflet prolapse with severe anteriorly directed MR. **(E)** Two-dimensional transesophageal echocardiogram without and with color at 55° view after first TMVEER to A2,P2 demonstrates moderate MR medial to the deployed device. **(F)** Two-dimensional transesophageal echocardiogram without and with color at 71° view after second TMVEER to A2,P2 demonstrates mild MR.

parameters were obtained after the implementation of intra-aortic balloon pump counterpulsation and infusion of dobutamine. Moreover, the enlarged left atrium suggested the condition was likely an acute change on top of chronic MR.

Importantly, the patient's condition continued to worsen despite maximizing both mechanical and pharmacological support, highlighting the immediate need for interventions targeting the severe MR. Emerging data suggest that percutaneous techniques for MV repair are valuable to surgical repair, especially in patients with high surgical risks.[2,7] Evidence for effectiveness of TMVEER in acute severe MR is currently limited to case reports and post hoc analysis and largely focuses on ischemic MR with delayed or lack of reperfusion.[8]

Data from EVEREST II demonstrated the safety and efficacy of TMVEER in stable patients. It provided insight into valve anatomy and patient characteristics that were amenable to TMVEER.[9] Real-world experience using percutaneous edge-to-edge repair of acute MR in the setting of cardiogenic shock is promising. In a matched-cohort analysis of 1,192 patients, Tang *et al*[7] reported that TMVEER is associated with a significantly lower in-hospital mortality and 1-year mortality for patents with MR and cardiogenic shock.[7] Moreover, Jung *et al*[2] reported a similar finding among high-risk patients with cardiogenic shock and moderate to severe MR.[2] Collectively, current data suggest that the concept of using TMVEER to reduce MR severity in cardiogenic shock may translate to improved clinical outcomes.

Through a heart team approach, our patient successfully underwent TMVEER and achieved a very satisfactory improvement of in-hospital course. However, it is important for the heart team to take the following aspects into consideration during decision-making: the balance between complete reduction of MR and eliciting mitral stenosis and options if the clip procedure fails in both the short and long term. Data from the the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy registry in 2017 revealed that 8.3% of patients treated with transcatheter MV clips required repeated clips, while 2.1% of this population required MV surgery within 1 year.[8] Furthermore, the aforementioned data were largely derived from patients in stable conditions, excluding those who were at prohibitive surgical risks and in cardiogenic shock.

Importantly, it remains largely unknown whether the underlying valvar pathology impacts the outcome of TMVEER.[10] Some preliminary studies reported that recurrent MR was most frequently seen in degenerative etiology, flail leaflet, and residual MR after procedure.[11-13] It is reasonable to suspect that myxomatous degeneration likely involves multiple sites of the MV apparatus and is accompanied by a high likelihood of recurrence of MR. In our

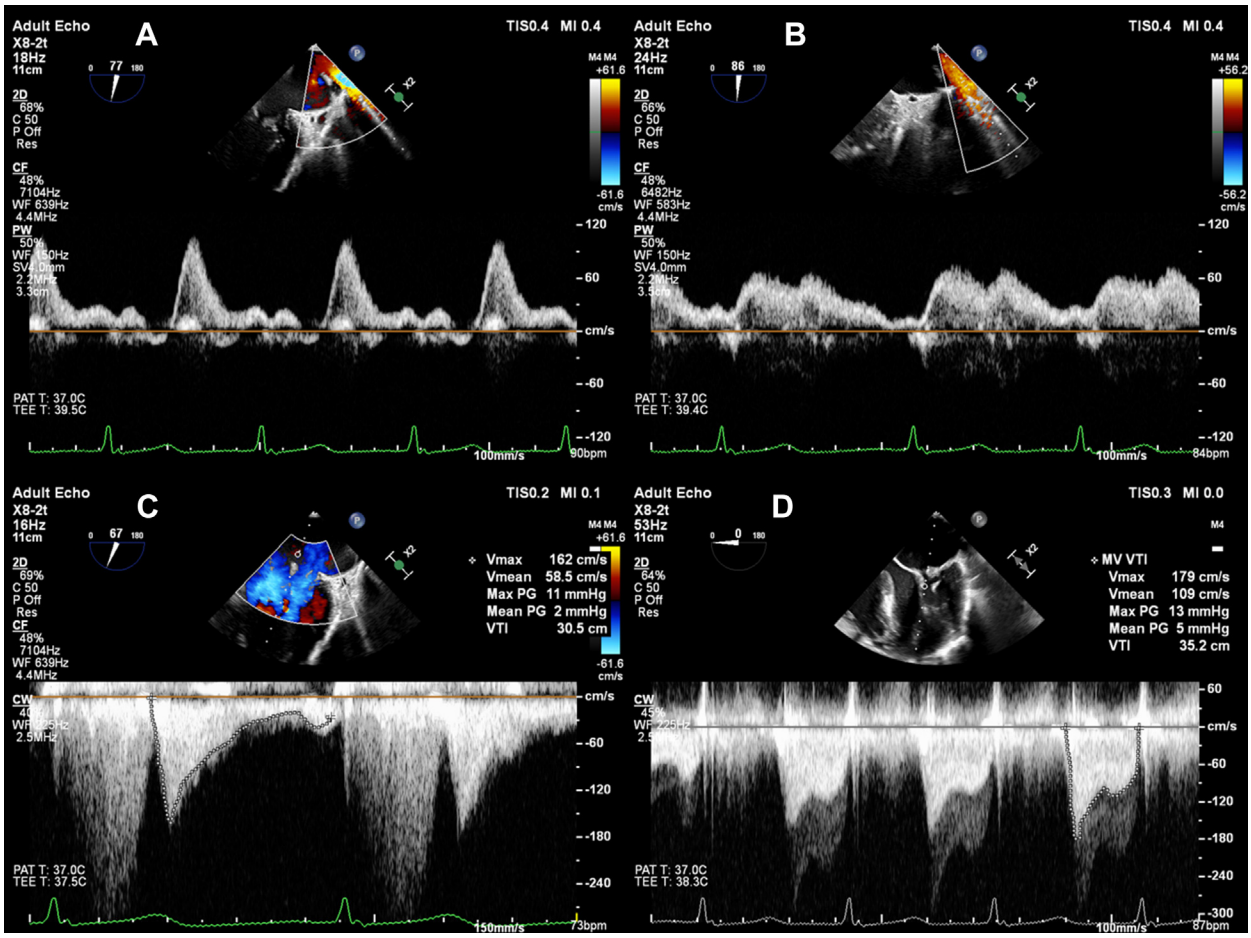


Figure 5 Periprocedural pulsed-wave and continuous-wave Doppler pulmonary vein and MV findings. **(A)** Pulmonary vein flow prior to TMVEER demonstrates blunted systolic velocity (<30 cm/sec). **(B)** Pulmonary vein flow after TMVEER demonstrates restored systolic velocity (>60 cm/sec). **(C)** Trans-MV gradient prior to TMVEER demonstrates a mean gradient of 2 mm Hg, which is increased to 5 mm Hg after TMVEER **(D)**.

patient, the suspicion of ischemic etiology was initially low as assured by normal cardiac injury markers and insignificant electrocardiogram changes. This was further supported by angiographic data obtained prior to surgical intervention (Figure 9).

Limited institutional experience suggests that surgical approaches might improve outcomes compared with medical therapy and repeated TMVEER.[14] Therefore, close follow-up and careful surgical planning are critical in monitoring those patients with degenerative etiology after having TMVEER. Surgical repair late after TMVEER is attractive but technically challenging due to fibrotic remodeling around the attached area and structural distortion of the leaflets and subvalvular apparatus.[15]

After thorough discussion between the heart team and the patient, surgical replacement was successfully conducted. Postsurgical pathological analysis confirmed that 2 clips were intact in situ. Further additional staining revealed exaggerated fibrotic and degenerative changes. Together, our available data suggested the recurrence of MR after TMVEER was likely due to the progression of degenerative changes with possible alterations in spatial structures by the recent TMVEER procedure, rather than ischemic or mechanical detachment.

## CONCLUSION

Timely recognition of the etiology and mechanism of MV pathology played a fundamental role in selecting the appropriate management. TMVEER is a promising option for patients with cardiogenic shock due to MV regurgitation, especially when the risks of surgical intervention are prohibitive. Careful planning for long term surgical management is warranted even for patients with immediate satisfactory postprocedural results, particularly in those with degenerative etiologies.

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## SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2022.07.004.

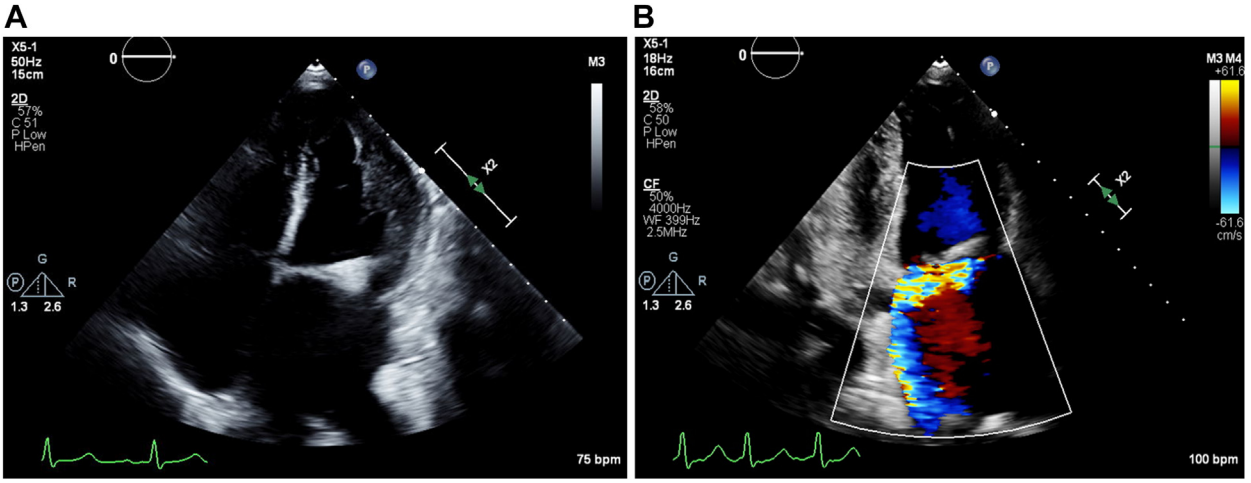


Figure 6 Follow-up TTE, apical 4-chamber view, systolic frame, without **(A)** and with **(B)** color Doppler prior to surgical replacement demonstrates severe anteriorly directed MR with a well-seated device seen on the MV.

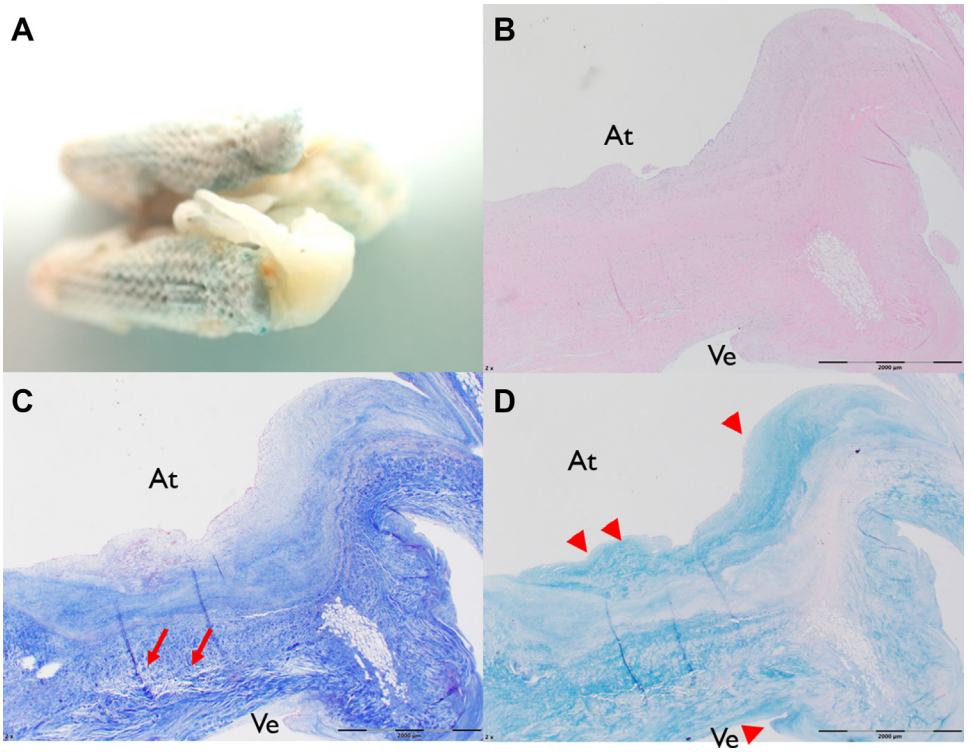


Figure 7 Representative histopathological images from resected tissues. **(A)** Gross pathological image of the resected MV demonstrates the leaflet and chordal tissue and the attached TMVEER devices. **(B)** Hematoxylin and eosin staining demonstrates no significant infiltrating cells in spongiosa area. **(C)** Masson trichrome staining demonstrates diminished and loose collagen in the fibrosa layer *(arrows)*. **(D)** Alcian blue staining demonstrates excessive deposition of proteoglycan in the fibrosa and spongiosa areas of the atrialis and ventrialis tissues (*arrowheads*). Collectively, those pathological features suggest likely degenerative changes rather than inflammatory or ischemic changes.

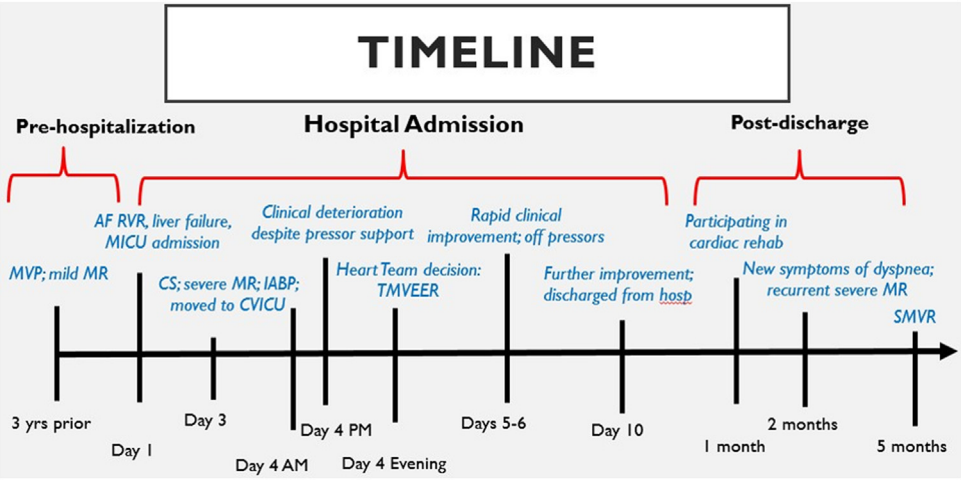


Figure 8 Timeline.

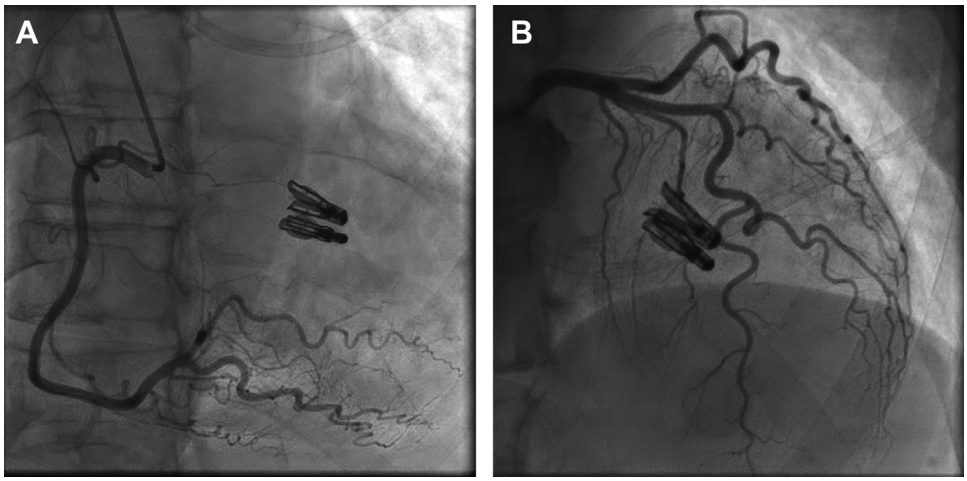


Figure 9 Representative images of angiography. **(A)** Right coronary angiography. **(B)** Left coronary angiography. No significant stenosis was appreciated from either the left or right coronary artery system.

## REFERENCES

1. Parlow S, Weng W, Di Santo P, Jung RG, Lepage-Ratte MF, Motazedian P, et al. Significant valvular dysfunction and outcomes in cardiogenic shock: insights from the randomized DOREMI trial. Can J Cardiol 2022;38:1211-9.
2. Jung RG, Simard T, Kovach C, Flint K, Don C, Di Santo P, et al. Transcatheter mitral valve repair in cardiogenic shock and mitral regurgitation: a patient-level, multicenter analysis. JACC Cardiovasc Interv 2021;14:1-11.
3. Writing Committee Members, Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol 2021;77:450-500.
4. Alegria-Barrero E, Franzen OW. Mitral regurgitation—a multidisciplinary challenge. Eur Cardiol 2014;9:49-53.
5. Watanabe N. Acute mitral regurgitation. Heart 2019;105:671-7.
6. Sundaram V, Fang JC. Gastrointestinal and liver issues in heart failure. Circulation 2016;133:1696-703.
7. Tang GHL, Estevez-Loureiro R, Yu Y, Prillinger JB, Zaid S, Psotka MA. Survival following edge-to-edge transcatheter mitral valve repair in patients with cardiogenic shock: a nationwide analysis. J Am Heart Assoc 2021;10:e019882.
8. Cannata F, Sanz-Sanchez J, Cozzi O, Briani M, Bertoldi L, Fazzari F, et al. [Percutaneous mitral valve repair in acute mitral regurgitation]. G Ital Cardiol (Rome) 2021;22:32S-8.
9. Attizzani GF, Ohno Y, Capodanno D, Cannata S, Dipasqua F, Imme S, et al. Extended use of percutaneous edge-to-edge mitral valve repair beyond EVEREST (Endovascular Valve Edge-to-Edge Repair) criteria: 30-day and 12-month clinical and echocardiographic outcomes from the GRASP (Getting Reduction of Mitral Insufficiency by Percutaneous Clip Implantation) registry. JACC Cardiovasc Interv 2015;8:74-82.
10. Medvedovsky AT, Tahiroglu I, Tonchev I, Planer D, Danenberg HD, Beeri R, et al. MitraClip therapy in patients with acute severe mitral regurgitation. Eur Heart J 2020;41:ehaa946.1956.
11. Sugiura A, Kavsur R, Spieker M, Iliadis C, Goto T, Ozturk C, et al. Recurrent mitral regurgitation after MitraClip: predictive factors, morphology, and clinical implication. Circ Cardiovasc Interv 2022;15:e010895.

12. Petrus AHJ, Dekkers OM, Tops LF, Timmer E, Klautz RJM, Braun J. Impact of recurrent mitral regurgitation after mitral valve repair for functional mitral regurgitation: long-term analysis of competing outcomes. Eur Heart J 2019;40:2206-14.
13. Dodoo SN, Okoh AK, Oseni A, Odiete O, Okafor HE. Adverse events following transcatheter edge-to-edge repair (TEER) Using MitraClip: lessons learned from the Manufacturer and User Facility Device Experience (MAUDE) Registry. Cardiovasc Revasc Med 2022;39:101-5.
14. El-Shurafa H, Arafat AA, Albabtain MA, AlFayez LA, Algarni KD, Pragliola C, et al. Residual versus recurrent mitral regurgitation after transcatheter mitral valve edge-to-edge repair. J Card Surg 2021;36:1904-9.
15. Kaneko T, Hirji S, Zaid S, Lange R, Kempfert J, Conradi L, et al. Mitral valve surgery after transcatheter edge-to-edge repair: mid-term outcomes from the CUTTING-EDGE International Registry. JACC Cardiovasc Interv 2021;14:2010-21.