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CASE REPORT
Other

Haemolysis resolution after transcatheter valve in valve within a prior mitral annuloplasty ring: a case report

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Background Transcatheter mitral valve in ring procedure has emerged as a minimally invasive alternative to re-do surgery among patients with failed mitral annuloplasty rings. Uncommonly, haemolysis presents as a complication after the percutaneous valvular procedures and often require aggressive measures to correct paravalvular leaks and mechanical collision.

Case summary We report a case of an 82-year-old female who underwent a transcatheter valve in ring procedure (Edwards Sapien S3, Edwards Lifesciences) for symptomatic severe mitral regurgitation from a bioprosthetic annuloplasty ring failure complicated by acute haemolytic anaemia a week after the procedure manifesting as dark coloured urine, profound icterus, and acute renal injury. She was treated with a post-dilation balloon valvuloplasty leading to reduction in haemolysis, but the patient was readmitted with acute haemolysis episode again. At this time, a decision was made to perform a repeat valve in valve TMVR with a 29 mm S3 Edwards Sapien valve which led to a resolution of haemolysis.

Discussion In this case, the leaflets of previously placed S3 valve sealed the blood flow through the valve frame thus diverting the blood flow away from the area of collision leading to resolution of haemolysis.

Keywords Haemolytic anaemia • Transcatheter mitral valve in ring • Mitral valve disease • Haemolysis • Case report

ESC curriculum 4.3 Mitral regurgitation • 7.4 Percutaneous cardiovascular post-procedure

Learning points

- By gaining an understanding of the mechanism of the haemolysis, appropriate intervention for haemolytic anaemia can be selected.
- Valve in valve procedure (Sapiens S3 within a S3) led to the elimination of any RBC collision-mediated haemolysis in this case.
- A close monitoring of the serum haemoglobin trends after mitral procedures can help to identify subclinical or overt haemolytic anaemias.

Introduction

Haemolytic anaemias related to cardiac prosthesis is an uncommon phenomenon post-valvular interventions and surgeries. Majority of time, haemolysis is subclinical; however, it can lead to severe transfusion-dependent anaemia and renal failure. Prior studies have reported a varied prevalence and clinical course for cardiac prosthesis-related haemolytic anaemias (CPHA).[1,2] CPHA is caused by

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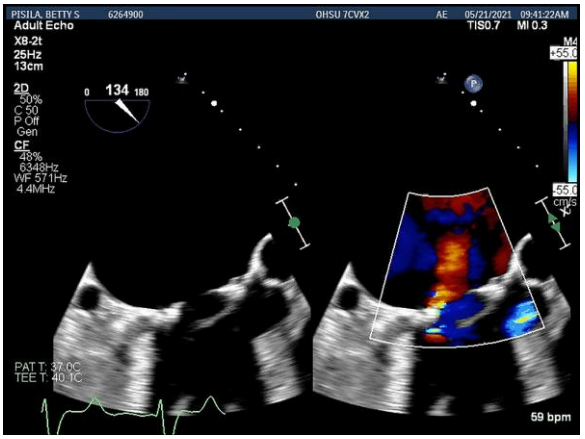
paravalvular leaks (PVLs) or from the collision of red blood cells (RBCs) flow with immobile structures causing fragmentations of RBCs.[3,4] Elimination of PVLs and diverting blood flow away from prosthesis frame can resolve haemolysis. Surgical replacement of the prosthesis is considered the definitive treatment for refractory cases of CPHA.[1,2] We report a case of haemolysis anaemia after a transcatheter valve in ring procedure which resolved after a repeat valve in valve (VIV) transcatheter mitral valve replacement (TMVR).

Timeline

Timeline	Event
Day 0	Valve in ring procedure performed for severe mitral regurgitation. (26 mm S3 within a 30 mm Physio ring)
Day 7	Patient presented with nausea, vomiting and visible icterus, new anaemia, and acute kidney injury. Transesophageal echocardiogram (TEE)showed moderate paravalvular leak and mild central regurgitation from the recently placed prosthesis
Day 19	Mitral balloon valvuloplasty performed to reduce the paravalvular regurgitation. (29 mm balloon)
Day 24	Readmitted with fatigue and was found to have continued haemolysis. A repeat TEE done showing collision of blood flow across the valve frame.
Day 31	A valve in valve transcatheter mitral valve replacement performed (29 mm Sapien S3 within a previously placed 26 mm S3)
Day 37	Discharged home with resolution of haemolysis, improved renal function and stable haemoglobin.



Video 1 A video showing the TEE of the severe mitral regurgitation through the mitral annuloplasty ring.

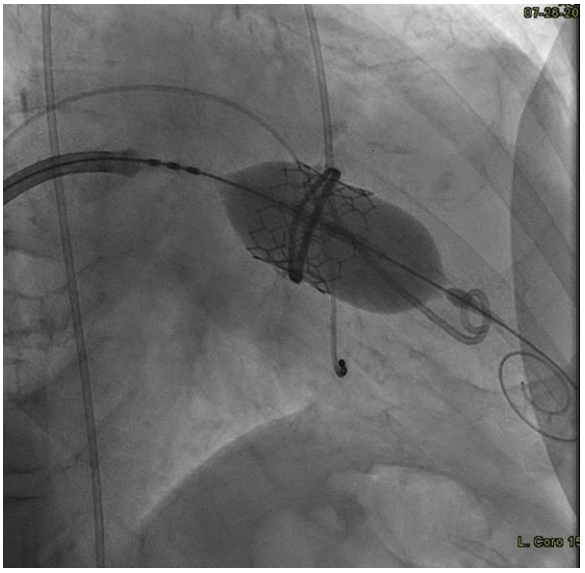


Figure 1 Fluoroscopic image of the deployment of 26 mm edwards S3 (blue arrow) within the edwards physio II 30 mm ring.

Case description

An 82-year-old female who had prior history of persistent atrial fibrillation, heart failure with reduced ejection fraction, valve repair with 30 mm Edwards Physio II ring (Edwards Lifesciences, Irvine, California), hypertension, chronic kidney disease presented with symptoms of heart failure and a transesophageal echocardiogram (TEE) showed severe MR from the annuloplasty ring failure with a severe medial jet of MR with a proximal isovelocity surface area (PISA) of 1.04 cm2, effective regurgitant orifice area of 0.4 cm2, and a regurgitant volume of 67 mL (*Video 1*). Patient was not a candidate for transcatheter edge to edge repair therapies because of the high baseline mean gradients of 5–8 mm Hg. The Society of thoracic surgery surgical core was 7.2% hence after the heart team discussion, a valve in ring procedure with 26 mm Edwards Sapien S3 valve (Edwards Lifesciences, Irvine, California) was planned (*Figure 1*). A post-dilation with an additional 2 ml volume in the 26 mm balloon was performed to reduce the moderate PVL seen on the intraprocedural TEE (*Figure 2*, *Video 2*). One week after the VIR procedure, the patient presented with nausea, visible icterus, and ongoing fatigue and was found to have severe unconjugated hyperbilirubinemia with a total serum bilirubin of 7.6 mg/dL (direct bilirubin of 0.8 mg/dL) (Normal value of total bilirubin: 0.3–1.0 mg/dL), undetectable serum haptoglobin, elevated serum lactate dehydrogenase (LDH) of 2 923 unit/liter (Normal Value 50–150 U/L) and serum creatine of 2.79 mg/dL (Normal value 0.5–1 mg/dL). A TEE was performed to assess the prosthetic mitral valve in ring showing a mild to moderate PVL at the anterolateral aspect of the valve (*Video 3*) hence a balloon post-dilation with a 29 mm balloon was performed to expand the valve and reduce PVL. At the end of procedure, the PVL reduced to trace (*Figure 3*, *Video 4*). Patient was readmitted after one week with similar symptoms and additional fatigue and weakness. The LDH was elevated to 2 539 unit/liter, and serum bilirubin to 6 mg/dL. Patient underwent a repeat TEE to assess for a cause of the ongoing haemolysis. This TEE showed only trace PVLs however a flow across the valve frame and collision of blood flow through the valve frame and anterior mitral leaflet was noted (*Figure 4A*, *Video 5*). Patients' hospital course was complicated by

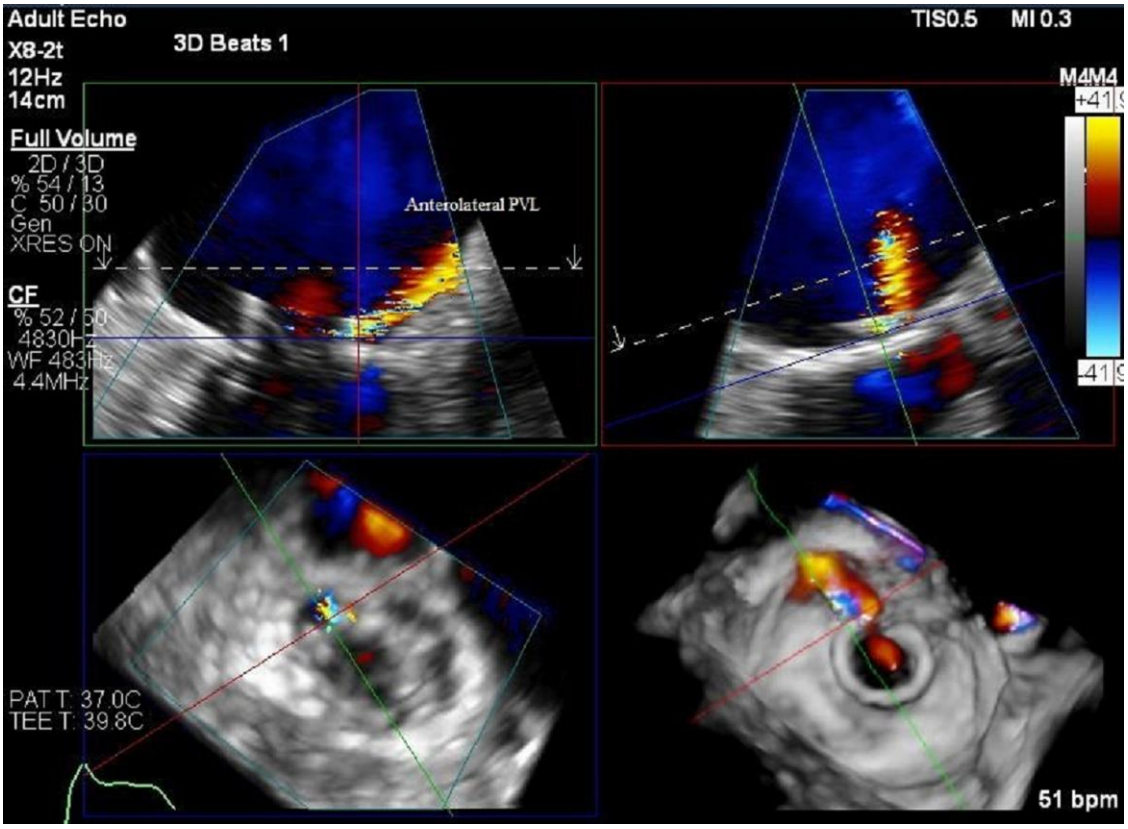
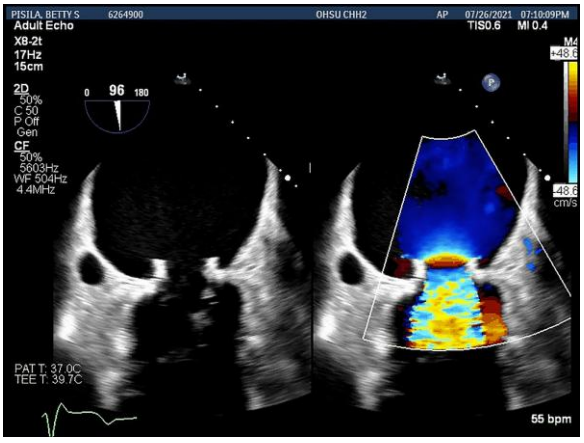
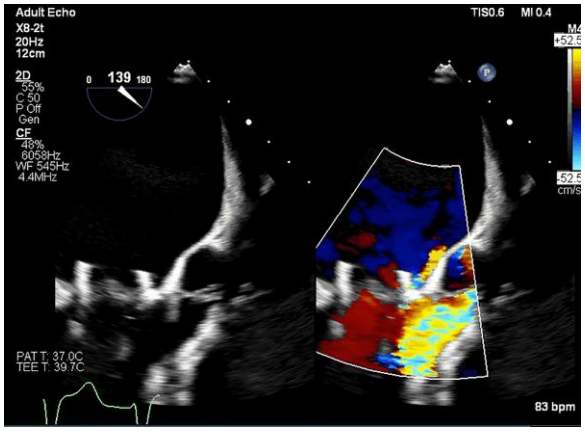


Figure 2 Transesophageal echocardiogram image of the 26 edwards sapien 3 valve within the 30 mm edwards physio II ring with mild anterolateral paravalvular leak.



Video 2 A video of the TEE showing anterolateral paravalvular leak through the 26 S3 valve inside the mitral annuloplasty ring.



Video 3 TEE video of the anterolateral paravalvular leak before the 29 mm balloon valvuloplasty.

ongoing haemolytic anaemia requiring blood transfusions, acute kidney injury from pigment induced acute tubular necrosis and hyponatremia. A detailed work for the haemolytic anaemia at this point was unyielding with a negative Coombs test, peripheral blood smear revealed a small amount of schistocytes and multiple acanthocytes, serum ferritin was elevated to 2 266 ng/mL, serum fibrinogen levels were normal. A repeat TMVR was performed with a 29 mm Edwards S3 prosthesis within the previously placed bioprosthesis to eliminate all flow through the valve frame and avoid any collision of blood flow (*Figure 4* A pre &B post VIV). After the VIV procedure (S3 within an S3) patient's haemolysis

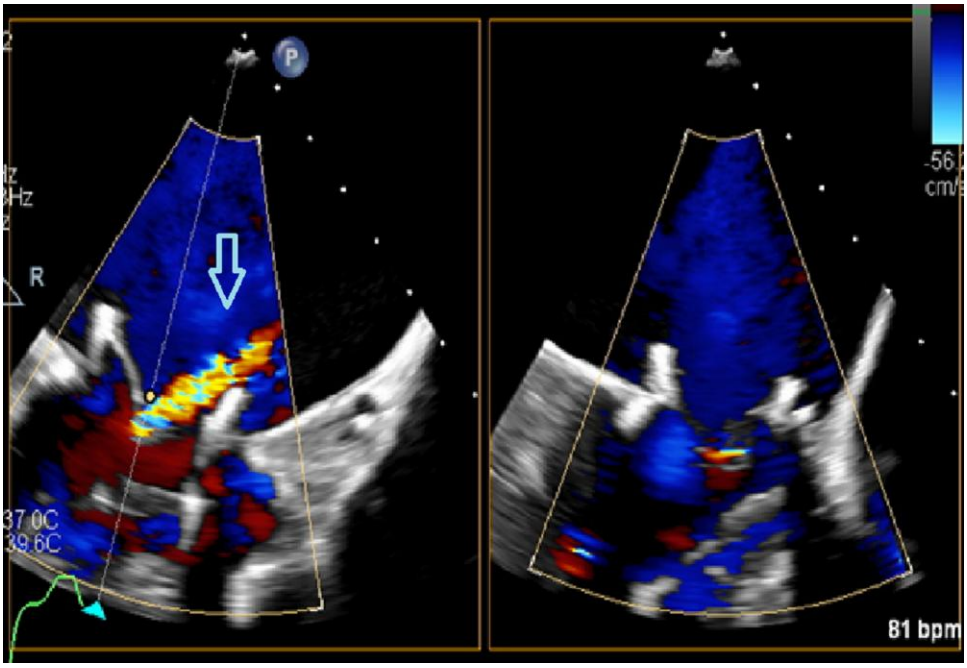
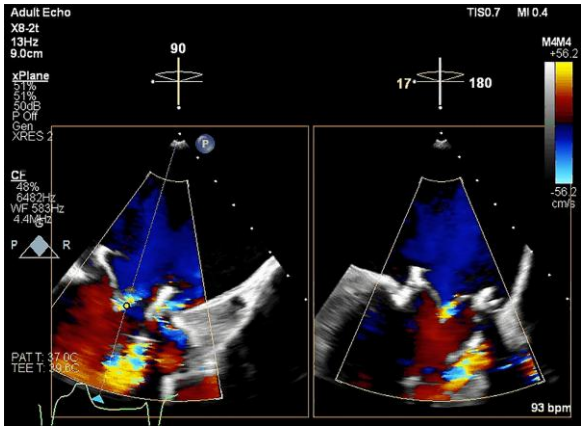


Figure 3 Transesophageal echocardiogram image of the of the 26 edwards sapien 3 valve within the 30 mm edwards physio II ring after the 29 mm balloon dilation showing mild central mitral regurgitation and trace anterolateral paravalvular leak.



Video 4 TEE of the mitral valve in ring with trace paravalvular leak after the 29 mm balloon valvuloplasty.

had resolved. On 30 day follow up the laboratory work showed a serum LDH reducing to 624 units/L, serum creatinine improving to 1.49 mg/dL with stabilization of the haemoglobin (*Figure 5*, *Video 6*).

Discussion

Cardiac prosthesis-related haemolytic anaemias (CPHA) is a rare but well described entity and often, its severity is mild. However, it can lead to life threatening, blood transfusion-dependent anaemia and a need for renal replacement therapy. The incidence of CPHA varies depending on the type and number of prostheses.[1,2] In a prospective study, subclinical prosthesis-related haemolysis was observed in 26% of the patients with bileaflet mechanical valves and only 5% of the bioprosthetic valves.[5] The principal pathophysiology for CPHA is breakdown of the RBCs due to excessive shearing either via PVLs or with collision of the blood flow with structures in the path of blood flow.[3,4]

The most relevant mechanism for haemolysis in this case was blood jet fragmentation and shearing of RBCs by collision between prosthetic valve frame and anterior mitral valve leaflet after the valve in ring (VIR) TMVR. VIR procedures have become a viable option for patients with failed mitral annuloplasty rings at a high risk for redo surgery.[6–8] Prior data from the society of thoracic surgeon transcatheter valvular therapy, TMVR multicenter registry and most recently Mitral Implantation of Transcatheter Valves (MITRAL) trial have reported a 30-day mortality from 6 to 10% after VIR TMVR. Therefore, food and drug administration recently expanded the use of balloon expandable Edwards S3 and S3 Ultra (Edwards life sciences, Irvine, California) for mitral VIR procedures.[9]

Only one case of haemolysis was reported in the MITRAL trial for the VIR arm.[6]

Since the blood flow across the valvular prosthesis colliding with anterior mitral valve leaflet can cause fragmentation of jet and shearing of RBC and subsequently haemolysis; by performing a repeat TMVR within the previously placed valve, the flow through the valve frame was eliminated, thus leading to resolution of haemolytic episodes. A novel technology by Edwards Sapien M3 (Edwards Life Sciences) which utilizes a nitinol-based docking system to encircle both mitral leaflets before the prosthetic valve implantation, can reduce the risk of anterior mitral valve leaflet causing left ventricular outflow tract obstruction

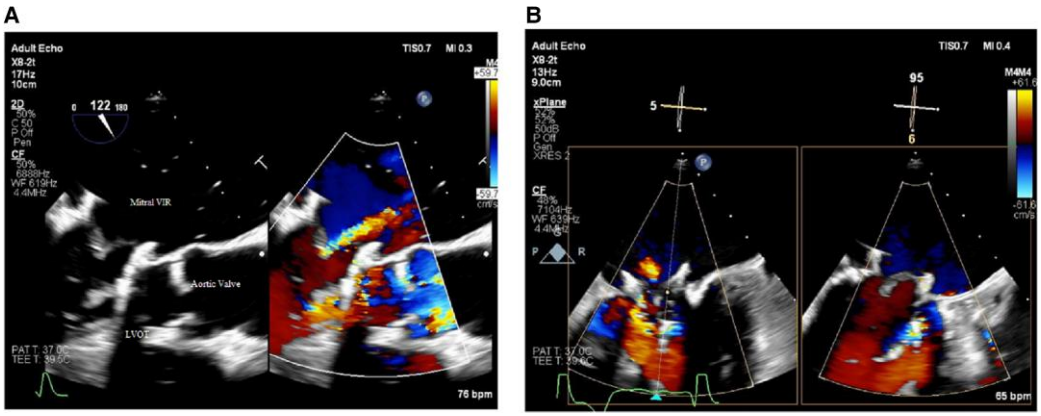


Figure 4 (*A* and *B*): transesophageal echocardiogram images showing the collision of the blood through the valve struts.

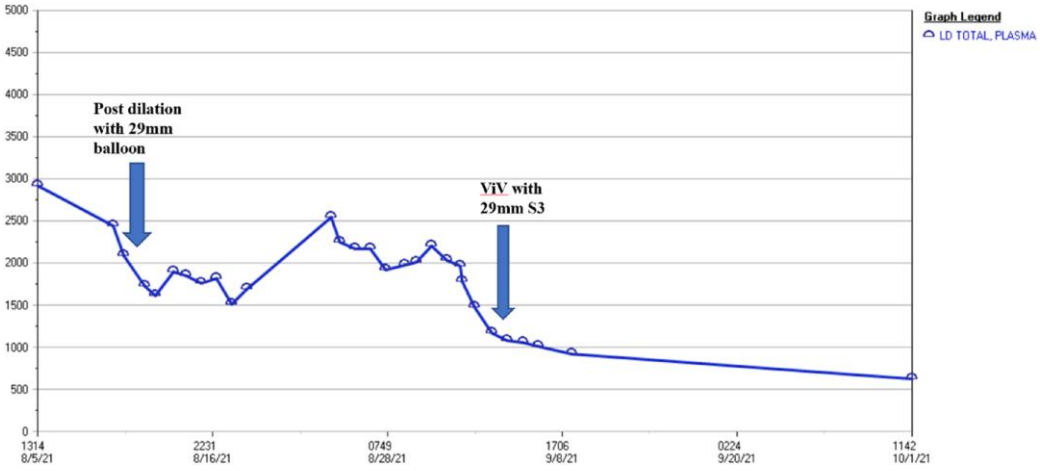
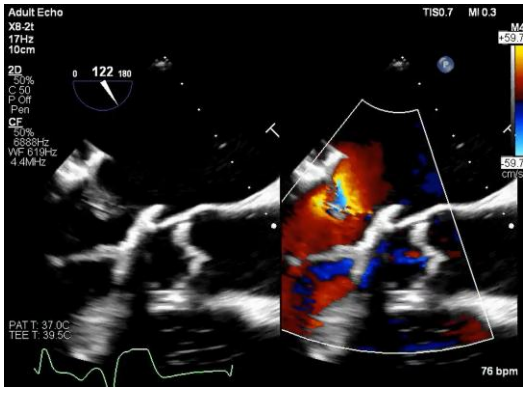


Figure 5 This figure shows the trend of serum lactate dehydrogenase. The major procedures are shown by blue arrow. VIV, valve in valve, LD, lactate dehydrogenase.

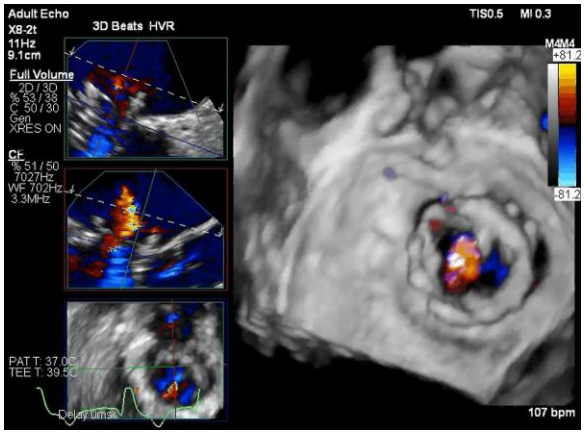


Video 5 A video of the long axis view of the left ventricular outflow tract and mitral valve in ring prosthesis. The area of collision of blood flow through the valve struts is seen.

or collision with the blood flow as seen in our case. The initial data of the Sapien M3 reported 88.6% procedural success and 2.9%, 30- day all-cause mortality.[10] Currently, the ongoing SAPIEN M3 System TransCatheter MItral Valve ReplaCement via TransseptaL AccEss (The ENCIRCLE High-Risk Trial) (NCT04153292) aims to provide further data on this device. Several other devices which are under trial for percutaneous TMVR, including the Medtronic (Medtronic Plc, Minneapolis, MN, USA) Intrepid™ TMVR System in Patients with Severe Symptomatic Mitral Regurgitation (APOLLO) NCT03 242642 and Edwards (Edwards Life Sciences, Irvine, California) EVOQUE Eos MISCEND Study NCT0271800. The incidence of post-procedural haemolysis with the use of these devices is currently unknown.

Conclusion

In conclusion, we report a complex case of transcatheter mitral VIR procedure which was complicated by intravascular haemolysis and acute renal failure. The recurring haemolytic episodes resolved



Video 6 Final 3D multiplanar reconstruction of the valve in valve transcatheter mitral valve replacement within a previously placed bioprosthesis showing no paravalvular leak and no collision of blood flow across the valve frame.

after a repeat VIV procedure by reducing the collision of RBCs with the valve frames and anterior mitral leaflet. This case highlights an atypical pathophysiology of CPHA due to blood jet fragmentation and turbulence due to blood flow through the valve frame and anterior mitral valve leaflet.

Lead author biography

Bhaskar Bhardwaj is currently a Structural Heart disease Fellow at the Oregon Health and Science University, in Portland Oregon, USA. His research interests include outcome research in interventional and structural heart disease.

Supplementary material

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

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 of the case report including images and associated text has been obtained from the patient's family in line with COPE guidance.

Conflict of interest: None declared.

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