MitraClip and Transcatheter Aortic Valve Replacement in a Patient With Recurrent Heart Failure

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Case Presentation

An 85-year-old man presented to the emergency department with a 3-week history of progressive dyspnea, orthopnea, and mild ankle edema without chest discomfort. His past medical history was significant for coronary artery disease with a non–ST-segment–elevation myocardial infarction 8 years prior with percutaneous coronary intervention to the distal right coronary artery, with mild residual nonobstructive disease in the left anterior descending artery and circumflex artery. Cardiovascular risk factors included hypertension, dyslipidemia, and chronic kidney disease stage 3. His remaining medical history was significant for cecal adenocarcinoma with a right hemicolectomy 20 years prior, and pulmonary sarcoidosis that was quiescent without any history of steroid use or immunosuppression. The most recent pulmonary function tests revealed normal spirometry and diffusion capacity. He was a nonsmoker, and before the onset of symptoms he was functionally independent only using a cane for mobility.

Initial vital signs revealed a regular heart rate of 81 bpm, and blood pressure of 121/78 mm Hg. He was afebrile, and his oxygen saturation was 95% on 2-L nasal prongs. Jugular venous pressure was elevated at 7 cm above the sternal angle with a normal waveform; the hepatojugular reflex was positive. The carotid pulse was of decreased volume but normal contour, without audible bruits. Auscultation revealed a normal S1 and S2, a holosystolic murmur at the apex, and a grade 2 midpeaking systolic ejection murmur at the base, with radiation to the carotids. Respiratory examination revealed clear and equal breath sounds bilaterally with the presence of bibasilar crackles at the lung bases. Peripheral pulses were present, with bilateral pitting edema at the ankles. Abdominal examination was unremarkable. Initial investigations revealed hemoglobin of 103 g/dL, and electrolytes within the normal range with a creatinine of 121 mmol/L (estimated glomerular filtration rate 50 mL/min). Troponin I (high sensitivity) was elevated with peak of 684 down to 674 ng/L (upper limit of normal <30 ng/L). Twelve-lead ECG showed normal sinus rhythm, normal intervals, and evidence of left ventricular hypertrophy by voltage criteria. Chest x-ray showed pulmonary vascular redistribution with a small right pleural effusion, consistent with pulmonary edema.

The patient was admitted to the hospital and started on intravenous furosemide for acute decompensated heart failure. An echocardiogram showed the left ventricle was severely dilated (left ventricular end-diastolic diameter, 6.6 cm; left ventricular end-systolic diameter, 5.5 cm) with severe eccentric left ventricular hypertrophy. The calculated left ventricular ejection fraction was 51% (stroke volume 57 mL/m^2), there was moderate diastolic dysfunction with elevated left atrial pressure, and the basal inferior and inferolateral walls were akinetic with scar. The right ventricle was normal in size and function. The aortic valve was moderately calcified with moderate aortic stenosis (peak/mean pressure gradient of 34/23 mm Hg, aortic valve area, 0.96 cm^2, dimensionless valve index, 0.32), and mild aortic regurgitation. There was moderate mitral regurgitation (effective regurgitant orifice area, 0.22 cm^2, regurgitant volume 44.2 mL), and mild pulmonary hypertension with right ventricular systolic pressure of 42 mm Hg (Figures 1 and 2). Cardiac catheterization and coronary angiography revealed a peak-to-peak gradient of 34 mm Hg on pullback, the right coronary artery stents were patent, the circumflex artery had mild disease, and there was a calcified 80% to 90% stenosis in the proximal left anterior descending artery; the patient underwent percutaneous coronary intervention with 1 drug-eluting stent to the proximal left anterior descending artery. His clinical course was unremarkable in hospital. He was transitioned to oral furosemide and remained on dual-antiplatelet therapy. On discharge, he was ambulating, with minimal assistance without oxygen.

Two weeks after hospital discharge, he presented to his outpatient cardiologist's office with severe dyspnea unable to climb one flight of stairs, orthopnea, and paroxysmal nocturnal dyspnea indicative of New York Heart Association functional class III symptoms. His clinical examination was consistent with mild congestion, his ECG did not show any further acute ischemic changes, and his high sensitivity troponin was not elevated.

Dr Gandhi: Our patient presents with recurrent episodes of acute decompensated heart failure with evidence of both

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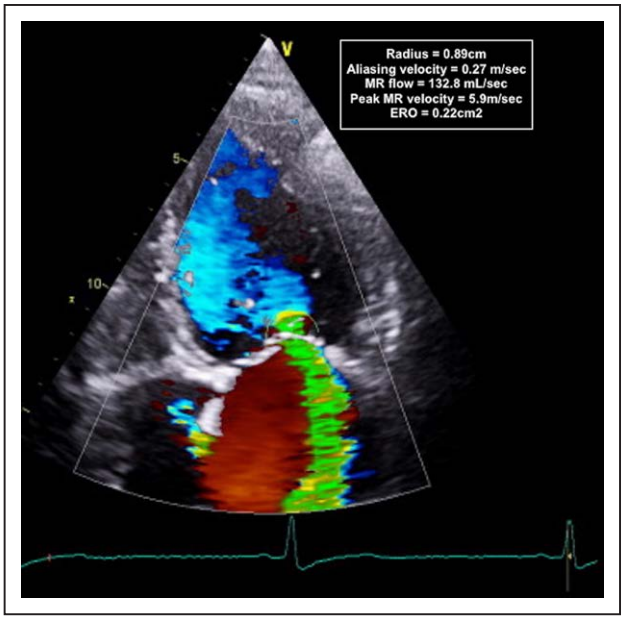

Figure 1. Transthoracic echocardiogram: moderate mitral regurgitation (MR). ERO indicates effective regurgitant orifice.

aortic and mitral valve disease, with patency of his drug-eluting stent. What is the next step in management?

Dr Velianou: The concern is that our patient has a dilated left ventricle without a clear cause and mild left ventricular dysfunction. With the history of severe exercise-induced symptoms, the transthoracic echocardiogram may underestimate the severity of mitral regurgitation. Transesophageal echocardiography (TEE) often provides key information including further delineation of the mitral valve anatomy, mechanism of the mitral regurgitation, and confirmation of secondary findings such as left atrial enlargement, pulmonary vein systolic flow reversal, and pulmonary hypertension. The aortic valve may also be further assessed with visualization of aortic valve opening and the degree of calcification.

Dr Gandhi: TEE was performed without complications. The aortic valve was moderately calcified with mild aortic insufficiency. The mitral valve leaflets were mildly thickened, with moderate mitral regurgitation. The cause of the mitral valve disease was secondary to both left ventricular and left atrial dilatation classified as functional, with no organic problem identified with the mitral valve leaflets. There was normal pulmonary vein flow with the absence of flow reversal; there was no left atrial appendage thrombus (Figures 3 and 4).

Dr Dokainish: The findings of secondary or *functional* mitral regurgitation have both important diagnostic and prognostic implications. The cause of secondary mitral regurgitation is multifactorial; mitral valve closing forces in systole are reliant on synchronous contraction of the left ventricular walls and mitral annulus to prevent the mitral valve from opening during systole. Tethering forces are applied by the leaflets, chordae, and papillary muscle to prevent prolapse of the mitral valve leaflets into the left atrium.[1] The alteration in this balance with left ventricular dilatation and severe atrial/annular dilation alters this tethering area and coaptation depth. Our patient has scar in the inferior/inferolateral wall resulting in tethering of the mitral valve, severe left ventricular dilatation with papillary muscle displacement, and severe left atrial dilatation with annular stretch resulting in malcoaptation. At this time, our patient would be classified as American College of Cardiology/American Heart Association stage D secondary mitral regurgitation (Table).[2,3] With his exercise-induced symptoms, an exercise stress echocardiogram may be helpful to assess dynamic mitral regurgitation and provide correlation with symptoms. Previous American College of Cardiology/American Heart Association guidelines recommend that exercise Doppler echocardiography may be reasonable in patients with chronic primary mitral regurgitation when there is a discrepancy between symptoms and the severity of mitral regurgitation at rest (Class IIa, Level of Evidence B).[3]

Dr Gandhi: How can we correlate exercise hemodynamics to echocardiographic findings?

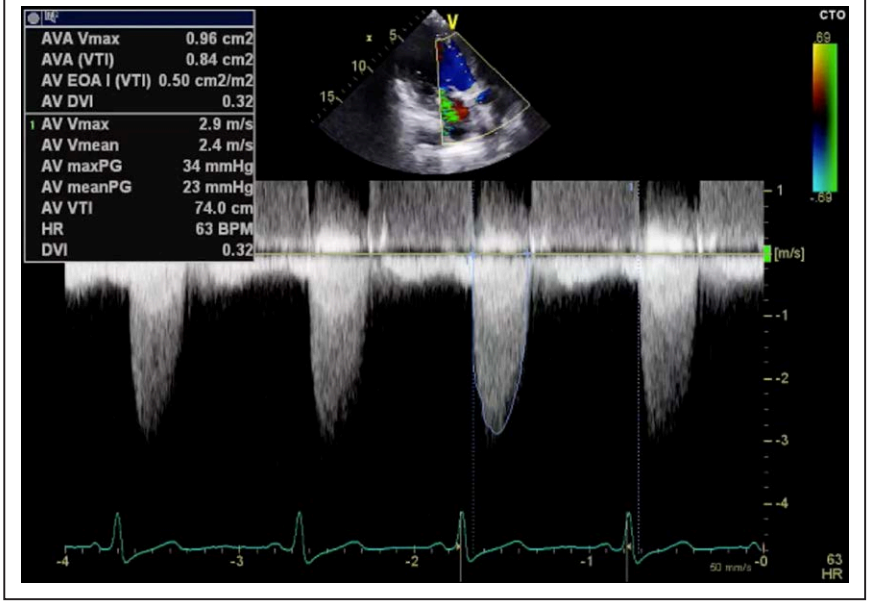

Figure 2. Transthoracic echocardiogram: moderate aortic stenosis.

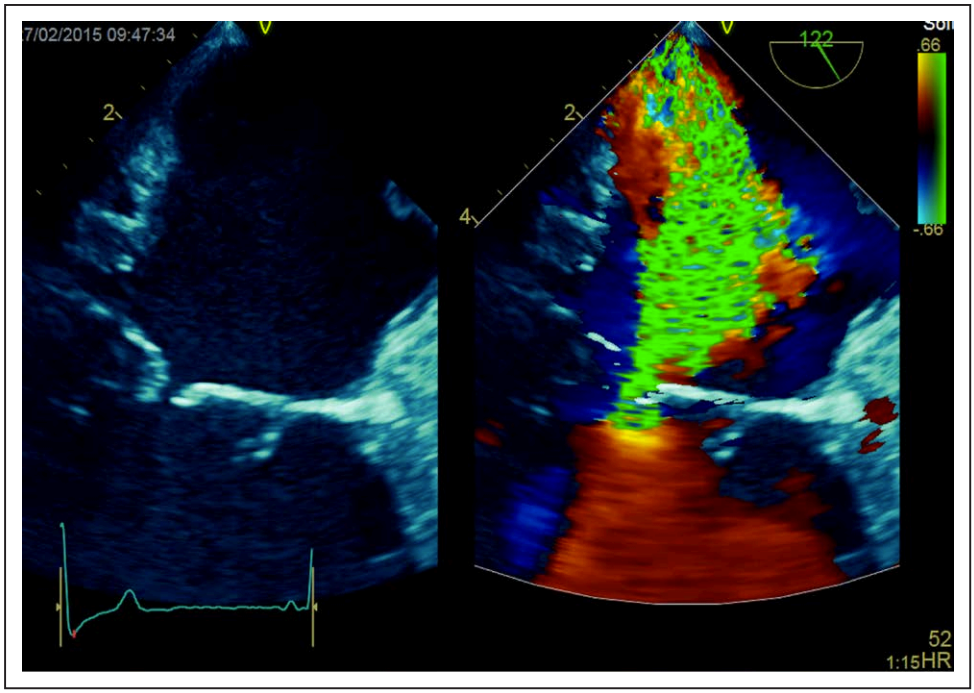

Figure 3. Transesophageal echocardiogram: mid-esophageal long-axis view showing malcoaptation of the mitral valve leaflets.

Dr Dokainish: Exercise will increase venous return, preload, contractility, with peripheral vasodilation and afterload reduction. The increase in preload may lead to an increase in left ventricular systolic and diastolic dimensions further exacerbating malcoaptation, which may increase the severity of mitral regurgitation seen on echocardiography color Doppler.

Table. Stages of Secondary Mitral Regurgitation

Grade and Definition	Mitral valve Anatomy	Mitral valve Hemodynamics	Associated Cardiac Findings	Symptoms
A, at risk of MR	Normal valve leaflets, chords, and annulus in a patient with coronary artery disease or cardiomyopathy	No MR jet or small central jet area <20% LA on Doppler	Normal or mildly dilated LV size with fixed (infarction) or inducible (ischemia) regional wall motion abnormalities	Symptoms caused by coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
		Small vena contracta <0.3 cm	Primary myocardial disease with LV dilation and systolic dysfunction	
B, Progressive MR	Regional wall motion abnormalities with mild tethering of mitral leaflet	ERO <0.40 cm^{2}*	Regional wall motion abnormalities with reduced LV systolic function	Symptoms caused by coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
	Annular dilation with mild loss of central coaptation of the mitral leaflets	Regurgitant volume <60 mL	LV dilation and systolic dysfunction caused by the primary myocardial disease	
		Regurgitant fraction <50%		
C, Asymptomatic severe MR	Regional wall motion abnormalities and LV dilation with severe tethering of mitral leaflet	ERO ≥0.40 cm^{2}*	Regional wall motion abnormalities with reduced LV systolic function	Symptoms caused by coronary ischemia or HF may be present that respond to revascularization and appropriate medical therapy
	Annular dilation with severe loss of central coaptation of the mitral leaflets	Regurgitant volume ≥ 60 mL	LV dilation and systolic dysfunction caused by the primary myocardial disease	
		Regurgitant fraction ≥50%		
D, Symptomatic severe MR	Regional wall motion abnormalities and LV dilation with severe tethering of mitral leaflet	ERO ≥0.40 cm^{2}*	Regional wall motion abnormalities with reduced LV systolic function	HF symptoms due to MR persist even after revascularization and optimization of medical therapy
	Annular dilation with severe loss of central coaptation of the mitral leaflets	Regurgitant volume ≥ 60 mL	LV dilation and systolic dysfunction caused by primary myocardial disease	Decreased exercise tolerance
		Regurgitant fraction ≥50%		Exertional dyspnea

Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence. ERO indicates effective regurgitant orifice; HF, heart failure; LA, left atrial; LV, left ventricle; and MR, mitral regurgitation.

*The measurement of the proximal isovelocity surface area by 2-dimensional transthoracic echocardiogram in patients with secondary MR underestimates the true ERO because of the crescentic shape of the proximal convergence.

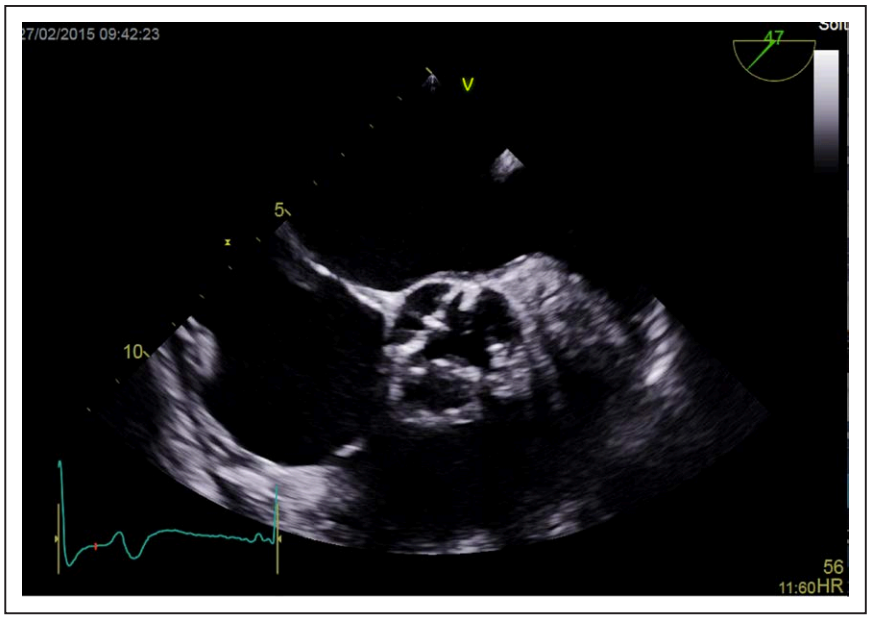

Figure 4. Transesophageal echocardiogram: mid-esophageal short-axis view of the aortic valve opening consistent with moderate aortic stenosis.

Furthermore, the increased contractility in the normal myocardial segments will result in dyssynchrony within the area of scar/akinetic segments, resulting in further malcoaptation and tethering of the mitral valve apparatus exacerbating the mitral regurgitation.

Dr Gandhi: Our patient achieved 85% of the maximum predicted heart rate with an appropriate blood pressure response to exercise. The test was stopped because of shortness of breath and fatigue. There were no diagnostic ECG changes of ischemia or significant arrhythmia. At rest, echocardiographic findings showed moderate posteriorly directed mitral regurgitation (effective regurgitant orifice, 0.23 cm^2, regurgitant volume 51 mL) with resting right ventricular systolic pressure of 36 mm Hg. At peak exercise, there were no new regional wall motion abnormalities; however, there was severe, posteriorly directed mitral regurgitation with visual flow reversal into the pulmonary veins with the right ventricular systolic pressure increased to 50 mm Hg (Figure 5). In summary, our patient has dynamic exercise-induced pulmonary hypertension as a consequence of severe mitral regurgitation, which is likely causing his symptoms, as well as concomitant moderate aortic stenosis. What would be the next best step in management?

Dr Chu: In patients with left ventricular dysfunction, secondary mitral regurgitation (effective regurgitant orifice area ≥20 mm2) and exercise-induced increase in effective regurgitant orifice area >13 mm^2 are independent markers of poor prognosis with increased cardiac mortality.[4] This was a difficult case and required discussion with the Heart Team including experts in echocardiography, interventional cardiology, and cardiac surgery. Our focus was to improve symptoms and decrease hospitalizations for heart failure. For treatment of the mitral regurgitation, cardiac surgery would include insertion of a restrictive mitral valve annuloplasty ring to improve coaptation with concomitant mitral valve repair if needed or bioprosthetic mitral valve replacement. His aortic stenosis is moderate and he would also need bioprosthetic aortic valve replacement. Current recommendations for intervention are limited to those undergoing concomitant coronary artery bypass graft surgery or aortic valve replacement for the primary aortic valve disease.[3,4] His risk for cardiac surgery because of his age and comorbidities would be high with Society of Thoracic Surgeons score >10% for mortality and >50% for morbidity and mortality.

Dr Gandhi: Is there any consideration for percutaneous mitral valve repair?

Dr Mehta: The Mitral Valve Clip (MitraClip) is an emerging therapy for percutaneous mitral valve repair of primary and secondary mitral regurgitation in symptomatic patients who are at high risk for cardiac surgery. The MitraClip is a cobalt chromium clip that, under transesophageal guidance, is delivered through a steerable guide catheter using femoral vein access and a trans-septal route. By grasping both the anterior

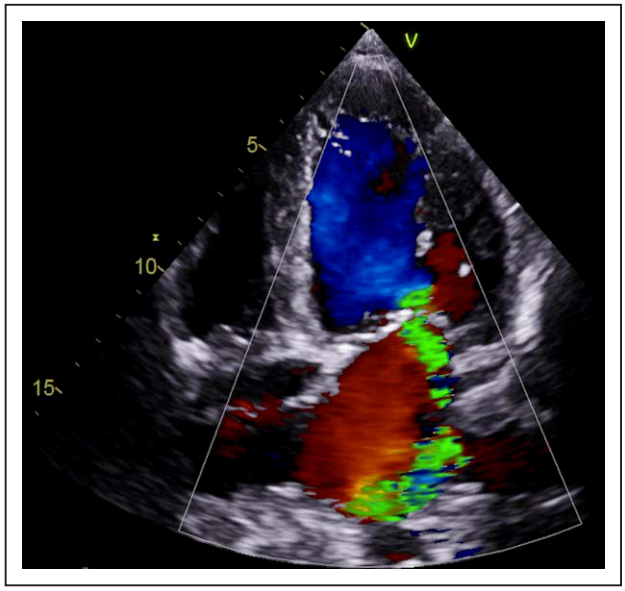

Figure 5. Post-stress severe mitral regurgitation (with visual flow reversal in the right upper pulmonary vein).

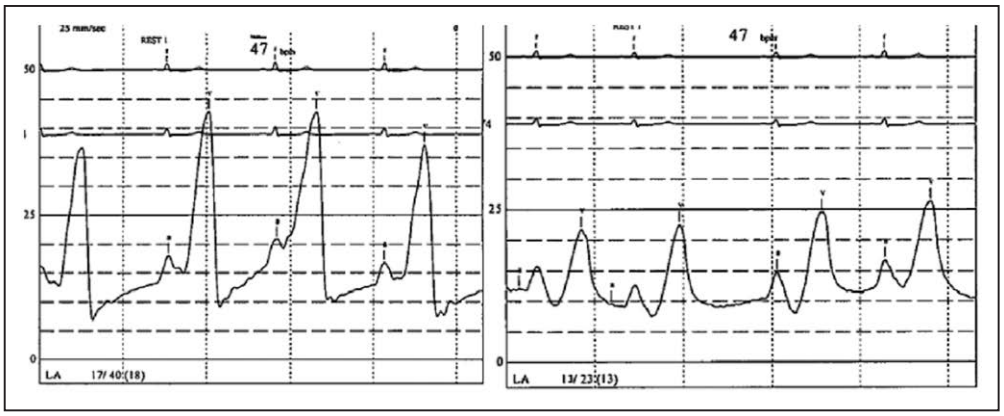

Figure 6. Intraoperative hemodynamic tracing of the left atrium pre- and post-MitraClip insertion.

and posterior leaflets with the clip leads, there is coaptation of the leaflets thereby reducing the degree of mitral regurgitation. The EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) High Risk Registry enrolled patients with grade 3 to !4+ mitral regurgitation who were eligible for both surgical and percutaneous therapy; 27% of patients enrolled in this trial had functional mitral regurgitation. The MitraClip met safety end points and patients experienced a significant reduction in New York Heart Association functional class, improvement in quality of life, a reduction in hospitalization and improvement in ventricular geometry.[5] We discussed the case extensively and decided with our patient that MitraClip insertion would be the best option for his exercise-induced severe mitral regurgitation and pulmonary hypertension.

Three months after his initial presentation, our patient was brought to the cardiac catheterization laboratory and with induction by general anesthesia, TEE guidance was performed throughout. Venous access was obtained, a transeptal puncture was performed, and the delivery sheath was advanced across the septum into the left atrium. The initial left atrial pressure was 18 mm Hg with a v wave of 40 mm Hg confirming severe mitral regurgitation (Figure 6). Using TEE guidance, the clip was advanced into the left ventricle with excellent grasping of both the anterior and posterior leaflets, with the first successful detachment. The mitral regurgitation was reduced from 4+ to 2+, however, still a very small medial jet. A second clip was placed medial to the first clip reducing the mitral regurgitation to <1+. Post-procedure hemodynamics saw a significant decrease in left atrial pressure to 13 mm Hg with a v wave of 23 mm Hg. He was transferred to the coronary care unit in stable condition.

Dr Gandhi: Post-procedure transthoracic echocardiogram showed well-seated mitral clips and mild mitral regurgitation with a mean diastolic gradient across the mitral valve of 5 mm Hg. However, the aortic stenosis was now severe with peak/mean pressure gradient of 76/48 mm Hg and aortic valve area 0.82 cm^2. His post-procedure care was uneventful; he was restarted on oral diuretics and was discharged home within 4 days. Unfortunately, our patient represented to the hospital on multiple occasions with further heart failure, and ongoing New York Heart Association class III–IV symptoms with repeated echocardiograms showing severe aortic stenosis. Was the increase to severe aortic stenosis expected?

Dr Natarajan: This case shows the complexities of multivalvular disease, it is suspected that repair of one valvular lesion has allowed us to visualize the impact of a downstream lesion.[6] A contributing factor to the increase in gradients across the aortic valve after MitraClip is likely because of the significant under measurement of aortic valve gradients in the pre-procedure echocardiogram. Figure 2 shows that the aortic valve spectral Doppler trace is not optimal with poor sample volume alignment. Further scrutiny and interrogation should be undertaken with the use of alternative echocardiographic imaging windows such as the right parasternal window; the pencil or pulse echo Doppler flow velocity, or PEDOF probe, provides additional benefit with higher signal/noise ratio and allowance of optimal transducer positioning and angulation.[7] Furthermore, mitral regurgitation results in a low-flow state with low stroke volume, resulting in lower transaortic gradients. Low-dose dobutamine stress echocardiography or invasive measurements

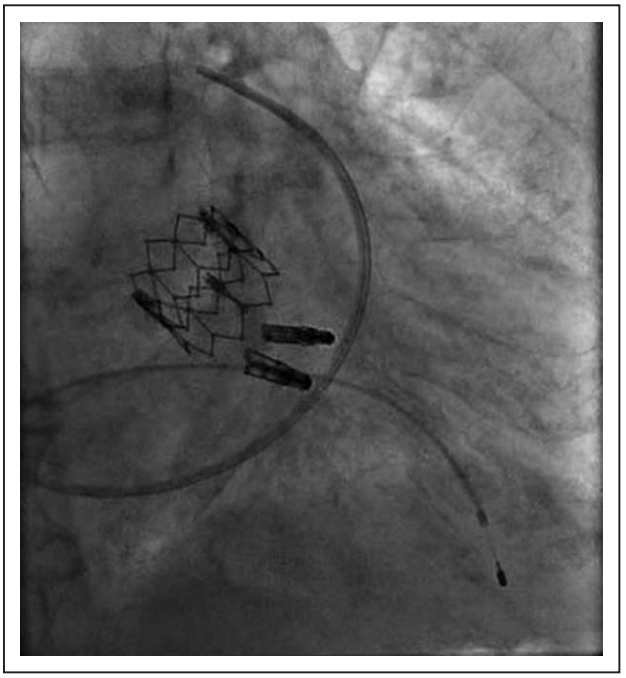

Figure 7. Fluoroscopy post–transcatheter aortic valve replacement with MitraClip.

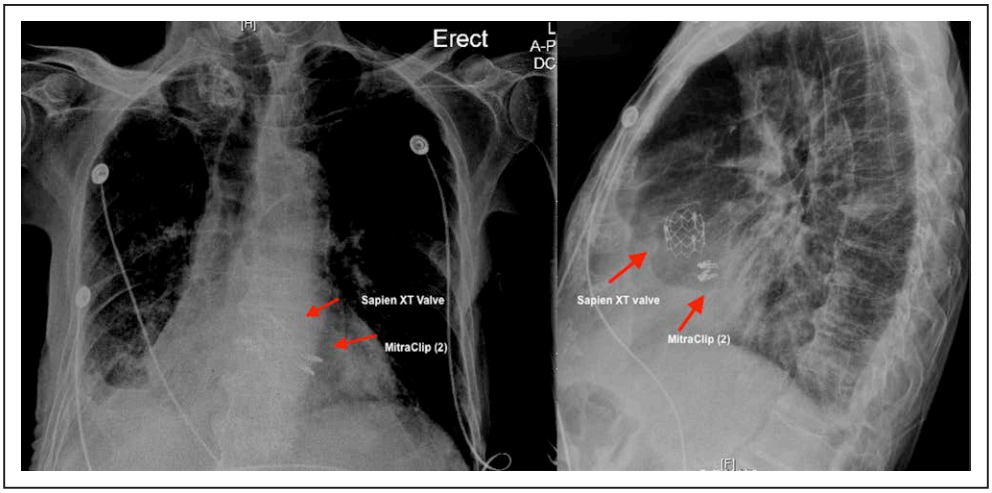

Figure 8. Chest x-ray post-MitraClip and transcatheter aortic valve replacement.

with cardiac catheterization is an alternative modality for assessment of the severity of aortic stenosis when clinical and echocardiographic discrepancies are seen. This includes patients with a calculated aortic valve area ≤1 cm2 and aortic velocity <4 m/sec (or mean pressure gradient <40 mm Hg) with visualization of a calcified aortic valve with reduced opening and left ventricular ejection fraction <50%. Mitral regurgitation also provides afterload reduction to the left ventricle and after MitraClip implantation, the increase in stroke volume likely resulted in an increase an transaortic gradients, which increased the classification of aortic stenosis from the moderate to severe. Our patient had persistent symptoms of heart failure and required intervention on his aortic valve in the form of transcatheter aortic valve replacement (TAVR). In situations where patients present with both primary aortic stenosis and severe functional mitral regurgitation, relief of the aortic stenosis has shown to be effective in reducing the severity of functional mitral regurgitation. In patients with continued severe mitral regurgitation after TAVR, MitraClip implantation is safe and effective; however, there is limited experience for TAVR in patients with concomitant MitraClip.[8]

Dr Gandhi: TAVR in patients with MitraClip is rare. Were there any special periprocedural considerations for this case?

Dr Natarajan: The patient underwent standard pre-TAVR assessment including a cardiac computerized tomography that demonstrated appropriate annular size, adequate distance to the ostium of the left main coronary artery, absence of significant left ventricular outflow tract, and subannular calcification, with good peripheral vessels for transfemoral access. The MitraClip was clearly visualized without any significant anatomic issues for TAVR implantation. Six months after MitraClip, our patient was brought to the cardiac catheterization laboratory and the procedure was undertaken with general anesthesia and TEE guidance; we deferred conscious sedation and transthoracic echocardiogram guidance as it was important to visualize the mitral valve and MitraClip, as well the aortic valve and left ventricular outflow tract for optimal implantation. Placement of a #26 Sapien XT valve was uncomplicated, with no paravalvular leak or coronary artery compromise. All devices were removed, and the patient was brought to the coronary care unit in stable condition (Figure 7). Postprocedure echocardiogram showed a normal functioning bioprosthetic aortic valve with trivial regurgitation, trace to mild mitral regurgitation with an insignificant diastolic gradient. The patient did not have any further episodes of heart failure, and serial echocardiograms showed reduction in ventricular end-diastolic dimensions (Figure 8).

Dr Gandhi: What are the take-home messages from this case?

Dr Velianou: Patients who present with multivalvular disease have complex hemodynamic findings on transthoracic echocardiography. Exercise stress echocardiography provides key information for the assessment of pulmonary hypertension, dynamic severity of regurgitant and stenotic lesions, contractile reserve in those with left ventricular dysfunction, and correlation with symptoms. The Heart Team is essential to planning percutaneous valve interventions for both patient selection and appropriateness.[3] Our patient underwent serial MitraClip and TAVR implantation, which were both effective and safe. Our case demonstrates the key principal that diagnostic tests for valvular disease require meticulous attention to detail and expertise in cardiac imaging and evaluation of hemodynamics.[3]

Disclosures

None.

References

1. Bertrand PB, Schwammenthal E, Levine RA, Vandervoort PM. Exercise Dynamics in secondary mitral regurgitation: pathophysiology and therapeutic implications. *Circulation*. 2017;135:297–314. doi: 10.1161/CIRCULATIONAHA.116.025260.
2. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. doi: doi.org/10.1161/CIR.0000000000000503.
3. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, Sundt TM 3rd, Thomas JD; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report

of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:e521-e643. doi: 10.1161/CIR.0000000000000031.
4. Lancellotti P, Troisfontaines P, Toussaint AC, Pierard LA. Prognostic importance of exercise-induced changes in mitral regurgitation in patients with chronic ischemic left ventricular dysfunction. *Circulation*. 2003;108:1713–1717. doi: 10.1161/01.CIR.0000087599.49332.05.
5. Glower DD, Kar S, Trento A, Lim DS, Bajwa T, Quesada R, Whitlow PL, Rinaldi MJ, Grayburn P, Mack MJ, Mauri L, McCarthy PM, Feldman T. Percutaneous mitral valve repair for mitral regurgitation in high-risk patients: results of the EVEREST II study. *J Am Coll Cardiol*. 2014;64:172–181. doi: 10.1016/j.jacc.2013.12.062.
6. Unger P, Clavel MA, Lindman BR, Mathieu P, Pibarot P. Pathophysiology and management of multivalvular disease. *Nat Rev Cardiol*. 2016;13:429–440. doi: 10.1038/nrcardio.2016.57.
7. Baumgartner H, Hung J, Bermejo J, Chambers JB, Edvardsen T, Goldstein S, Lancellotti P, LeFevre M, Miller F, Jr, Otto CM. Recommendations on the echocardiographic assessment of aortic valve stenosis: a focused update from the European Association of Cardiovascular Imaging and the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2017;30:372–392. doi: 10.1016/j.echo.2017.02.009.
8. Kische S, D'Ancona G, Paranskaya L, Schubert J, Arsoy N, Hauenstein KH, Alozie A, Jovanovich B, Nienaber C, Ince H. Staged total percutaneous treatment of aortic valve pathology and mitral regurgitation: institutional experience. *Catheter Cardiovasc Interv*. 2013;82:E552–E563. doi: 10.1002/ccd.24809.

KEY WORDS: aortic stenosis ■ MitraClip ■ mitral regurgitation ■ stress echocardiography ■ transcatheter aortic valve implantation ■ transcatheter aortic valve replacement ■ transcatheter mitral valve repair

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