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CASE REPORT
Other

Transcatheter mitral valve repair for the treatment of severe mitral regurgitation and exertional pre-syncope in a patient with non-obstructive hypertrophic cardiomyopathy: a case report

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Background Hypertrophic cardiomyopathy (HCM) has a complex pathophysiology and heterogeneous phenotypic expression. In obstructive HCM with significant mitral regurgitation (MR), MitraClip device implantation reduces MR severity and symptoms. There are no data regarding MitraClip implantation in patients with non-obstructive HCM and significant MR.

Case summary A 78-year-old woman with non-obstructive HCM and significant functional MR (3+) was admitted to our centre for dyspnoea and episodes of pre-syncope under light stress. Transthoracic and transoesophageal echocardiography showed a normal left ventricular ejection fraction and normal right heart pressures, an inverted mitral filling pattern, and a central prevalent jet (A2-P2 origin) of MR. Exercise echocardiography performed to verify exercise tolerance was interrupted at the 50-W stage due to severe hypotension and pre-syncope. After transcatheter edge-to-edge repair using the MitraClip system, the patient exhibited a reduction in MR Grade from 3+ to 1+. Follow-up up to 1-year post-procedure revealed noticeable improvements in exercise tolerance and symptoms. There were no further episodes of pre-syncope.

Discussion In non-obstructive HCM, the pathophysiological role of MR in symptom generation is unknown. In this patient, we speculated that significant MR contributed to the mechanisms responsible for severe hypotension and pre-syncope during exercise. A reduction in MR after MitraClip implantation was associated with symptomatic improvements. Our findings further highlight the potential utility of the exercise stress test in therapeutic decision-making for patients with non-obstructive HCM and MR.

Keywords MitraClip • Mitral regurgitation • Non-obstructive hypertrophic cardiomyopathy • Pre-syncope • Case report

ESC Curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 4.3 Mitral regurgitation • 6.5 Cardiomyopathy

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Learning points

- In non-obstructive hypertrophic cardiomyopathy (HCM), moderate to severe mitral regurgitation (MR) may contribute to anomalous blood pressure responses and pre-syncope onset during exercise.
- The exercise stress test may be useful for therapeutic decision-making in patients with symptomatic non-obstructive HCM and moderate to severe MR.
- Percutaneous correction of moderate to severe MR with transcatheter edge-to-edge repair may improve symptoms and quality of life among patients with non-obstructive HCM.

Introduction

Hypertrophic cardiomyopathy (HCM) is the most common monogenic cardiovascular disorder with a prevalence of 1 per 500 persons in the general population.[1] Hypertrophic cardiomyopathy is characterized by a complex pathophysiology and heterogeneous phenotypic expression.[2] Symptoms of HCM include exertional dyspnoea, reduced exercise capacity, chest pain, and pre-syncope or syncope. Affected patients have an increased risk of progressive heart failure, supraventricular and ventricular arrhythmias, and sudden cardiac death.[1]

Obstructive HCM is typified by obstruction of the left ventricle outflow tract (LVOT) related to septal hypertrophy as well as systolic anterior motion (SAM) of the mitral valve. SAM together with abnormalities of the mitral valve and subvalvular apparatus are potentially associated with mitral regurgitation (MR), a component of HCM that likely contributes to the genesis of symptoms.

In recent years, the MitraClip device (Abbott Laboratories, Abbott Park, IL, USA) has been utilized in several small studies of patients with obstructive HCM and significant MR who were ineligible for standard surgical treatment.[3–5] In these studies, transcatheter edge-to-edge repair (TEER) decreased the severity of MR and eliminated SAM-septal contact, improving the LVOT gradient and patient symptoms.

To date, there are no published data regarding TEER with MitraClip in patients with non-obstructive HCM and significant MR. Here, we present the case of an elderly woman with non-obstructive HCM and MR who was treated with MitraClip implantation.

Timeline

Date	Event
2004	First diagnosis of non-obstructive hypertrophic cardiomyopathy and mitral regurgitation (MR). Pharmacological treatment with low dose of furosemide and bisoprolol.
June 2019	Onset of significant dyspnoea and pre-syncope episodes under light stress.
September 2019 (Hospital inpatient)	Significant MR detected on transoesophageal echocardiography. Exercise echocardiography interrupted due to severe hypotension and pre-syncope.
November 2019 (Hospital inpatient)	Percutaneous edge-to-edge mitral repair with MitraClip implantation.
February 2020 (3 months follow-up)	Symptoms notably improved and no further episodes of pre-syncope. Improvements in quality of life score and 6-minute walking test performance. Significant reduction in left atrium volume; mild residual MR.
May 2020 (6 months follow-up)	Normal blood pressure response and successful completion of the exercise protocol for stress testing.
November 2020 (12 months follow-up)	Improvements sustained and confirmed.

Case presentation

A 78-year-old Caucasian woman who had been routinely followed at our centre for non-obstructive HCM and paroxysmal atrial fibrillation presented with functional MR lasting more than 10 years. The patient also had chronic obstructive pulmonary disease and chronic renal insufficiency. Her main symptom related to HCM and MR was exertional dyspnoea; when atrial fibrillation occurred, she experienced orthopnoea and dyspnoea at rest. She had never been hospitalized for heart failure, but sometimes reported pedal oedema. Pharmacological management included furosemide 25 mg, apixaban 2.5 mg (twice daily), bisoprolol 1.25 mg, and amiodarone 100 mg.

In June of 2019, the patient experienced a worsening of symptoms including frequent breathlessness and pre-syncope episodes under light stress (e.g. while climbing stairs). In September of 2019, the patient was admitted to our centre to evaluate her global status. Upon physical examination, her blood pressure was 105/70 mmHg and she had normal oxygen saturation, a pulse rate of 70 b.p.m., and a pansystolic murmur over the apex. Intravenous furosemide (40 mg) was administered to treat minor lower leg congestion. The patient did not experience any arrhythmias during hospitalization. Transthoracic echocardiography (*Figure 1*) revealed symmetrical thickening of the LV wall (20 mm at the basal anteroseptal wall) with a small cavity, a LVOT gradient of 3 mmHg, a normal LV ejection fraction (62%), and an inverted mitral filling pattern. Right heart sections were not dilated. Pulmonary artery systolic pressure (PAPs) was 23 mmHg at rest. The degree of MR appeared to have worsened compared to previous echocardiographic findings; transoesophageal echocardiography is shown in *Figure 2*. Mitral regurgitation was

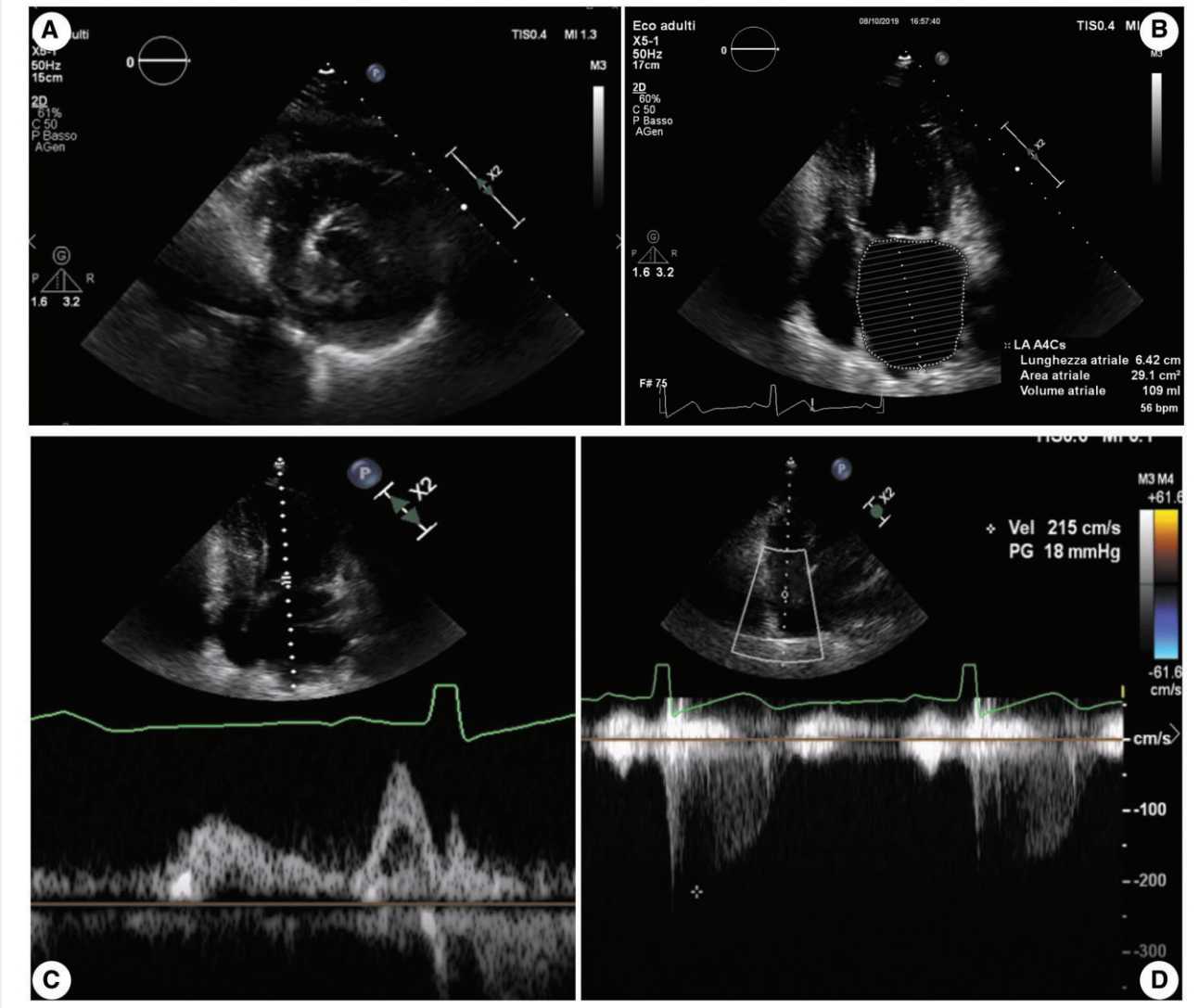

Figure 1 Transthoracic echocardiogram showing a symmetrical increase in left ventricle wall thickness (*A*), left atrium volume of 109 mL and normal thickness of right heart sections (*B*), an inverted mitral filling pattern (*C*), and normal pulmonary artery systolic pressure at rest (*D*).

moderate-to-severe (3+), width of the vena contracta was 7 mm and regurgitant volume was 51 mL. The prevalent jet was central (A2-P2 origin) caused by leaflet tethering secondary to papillary muscle displacement. Moreover, mitral findings (length of the posterior leaflet, 10 mm; mitral valve area, 4.64 cm^2; mean gradient across the valve, 1 mmHg; no calcification) were compatible with percutaneous edge-to-edge repair. Angiography revealed no coronary disease and spirometry showed a slight obstructive deficit. During the 6-minute walking test (6MWT), the patient walked 170 m without oxygen desaturation. The patient had no chest pain during an exercise stress test with echocardiography using a bicycle ergometer and a symptom-limited Bruce protocol. Echocardiography during the stress test indicated the absence of an exercise-induced LVOT gradient and an inverted mitral filling pattern. At peak stress, MR grade evolved from moderate-severe to severe and PAPs increased from 20 mmHg to 40 mmHg (*Figure 3*). Exercise was interrupted at the 50-W stage due to severe hypotension (systolic blood pressure, 70 mmHg) and pre-syncope.

Priorities during the Heart Team discussion included improving patient quality of life [Minnesota Living with Heart Failure Questionnaire (MLHFQ) score, 65] and addressing pre-syncope and exercise-induced hypotension. The patient had already rejected any open surgical intervention; therefore, the Heart Team proposed percutaneous mitral valve repair using the MitraClip system.

In November of 2019, the patient underwent placement of a single MitraClip NTr centrally over the A2-P2 scallops, which produced a reduction in MR grade from moderate-to-severe to mild (*Figure 4*). Residual MR was located at the A1 segment (antero-lateral) and the

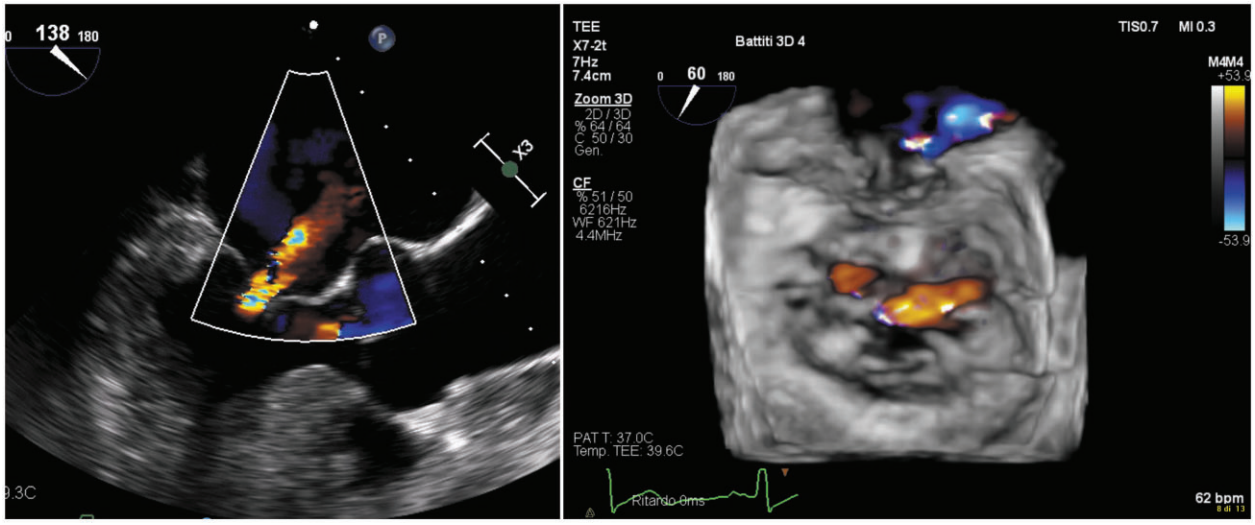

Figure 2 Mitral regurgitation investigated on transoesophageal echocardiography. Findings included a central prevalent jet (A2-P2 origin) and antero-lateral secondary jet.

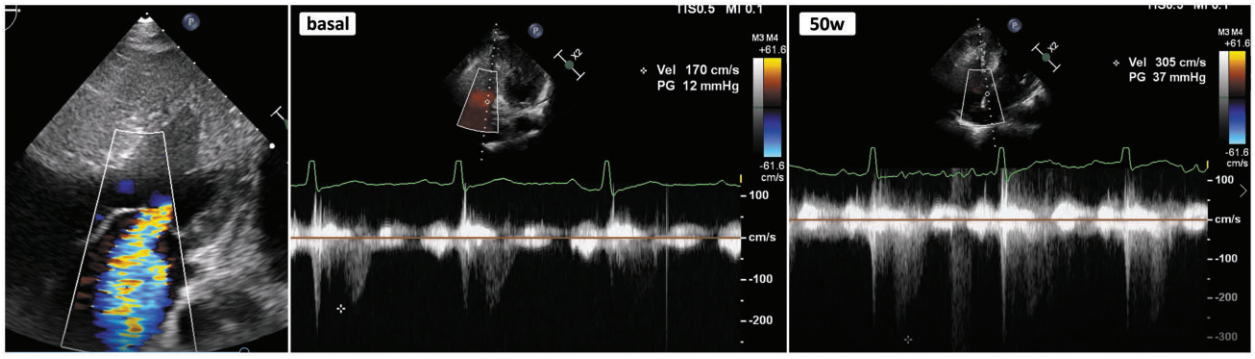

Figure 3 Echocardiographic findings during the pre-procedural stress test including mitral regurgitation severity and pulmonary artery systolic pressure at rest and during peak stress (50-W stage).

final mean gradient across the valve was 2 mmHg. There were no intra-operative or post-operative complications during hospitalization and the patient was discharged in good condition. Medical therapy was unchanged except for the addition of clopidogrel 75 mg daily in the first months after the procedure.

Follow-up was performed at 3, 6, and 12 months post-procedure (*Figure 5*). At each follow-up visit, the patient was in sinus rhythm and exhibited noticeable improvements in exercise tolerance and symptoms; she did not report further episodes of pre-syncope. At 3 months, the patient's MLHFQ score had increased to 20 and she walked 374 m during the 6MWT. Transthoracic echocardiography showed a significant reduction in left atrium volume (from 109 mL to 76 mL) and no change in residual mild MR. At 6 months, the patient successfully completed the exercise echocardiography protocol (up to the 75-W stage) without pre-syncope; during peak stress, MR remained mild, the mitral filling pattern evolved from inverted to pseudonormal, systolic blood pressure was 165 mmHg, and the increase in PAPs was well-tolerated. Improvements were sustained at 12 months follow-up.

Discussion

The present case of non-obstructive HCM and MR was successfully treated with percutaneous edge-to-edge repair using the MitraClip device. The best treatment for this patient was thoroughly debated by Heart Team since the pathophysiological role of MR in generating symptoms in non-obstructive HCM is unknown. Literature findings

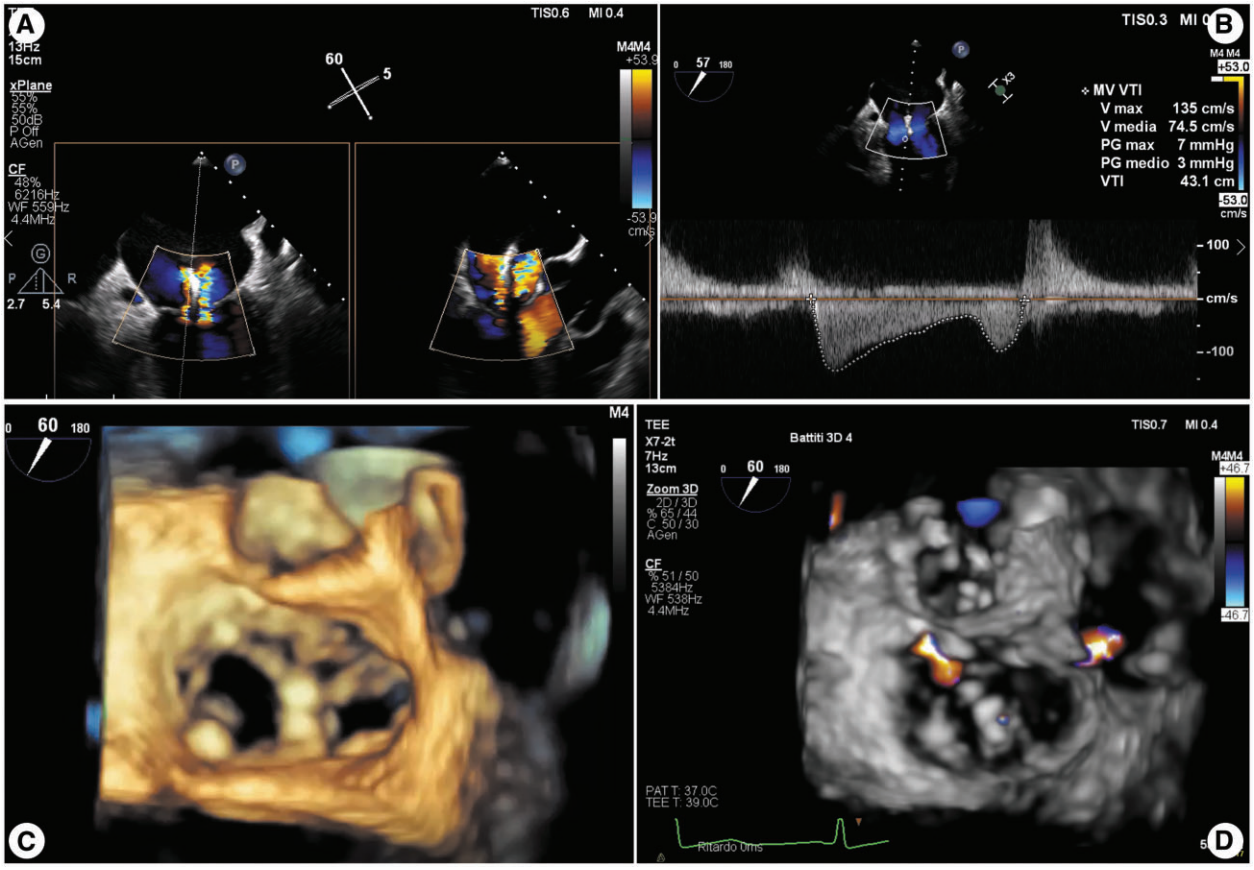

Figure 4 Echocardiographic views of MitraClip implantation: MitraClip NTr positioning (*A*) and the final mitral gradient (*B*); 3D mitral reconstruction after MitraClip deployment (*C*); and residual mitral regurgitation (*D*).

suggest that, in the context of HCM, hypotension during exercise is driven by an inappropriate decrease in systemic vascular resistance, subendocardial ischaemia, and a decrease in stroke volume.[6] Decreased stroke volume may be the result of systolic dysfunction during exercise[7] or impaired LV filling secondary to LV hypertrophy and tachycardia. In our case, we hypothesized that MR contributed to a reduction in stroke volume during exercise leading to hypotension. Additionally, we speculated that, during systole, MR produced a decrease in LV volume during prolonged and vigorous LV contraction, resulting in the activation of LV mechanoreceptors responsible for reflex hypotension.[8] It is likely that an exacerbation of pre-existing MR during June of 2019 contributed to the patient's worsening of symptoms and pre-syncope onset.

Transcatheter edge-to-edge repair with MitraClip implantation is an emerging structural therapy for HCM in cases with co-existing significant MR;[9,10] yet, few successful cases of MitraClip treatment have been reported for obstructive HCM and significant MR[3–5] and no cases have been reported for non-obstructive HCM, as standard care for this condition is only supportive. No specific disease-modifying therapies in non-oHCM are known so far,[10] and we have no definite indication on remarkable therapeutic options in patients with non-obstructive HCM and severe MR.

Exercise echocardiography is useful for defining the optimal management strategy in patients with symptomatic HCM refractory to treatment without LVOT obstruction at rest.[11] For patients with a non-inducible LVOT gradient, a cardiac transplant is the recommended treatment option.[11] Our patient did not develop an exercise-induced LVOT gradient during testing and was also ineligible for heart transplant given advanced age; therefore, the only feasible therapy was MR correction. Transcatheter edge-to-edge repair with MitraClip is also a valid alternative as a bridge to heart transplant or LV assist device.[12] Therefore, structural repair with the MitraClip may be suitable in patients with non-obstructive HCM who are ineligible for transplant or awaiting transplant.

Based on the findings of our case, stress echocardiography may also be useful for identifying patients with HCM and MR who can benefit from percutaneous mitral valve repair.[13] In our case, the exercise stress test replicated the patient's most serious symptom and thus influenced therapeutic decision-making. The stress test also demonstrated that even non-severe MR can be haemodynamically significant under stress conditions in a patient with reduced cardiac functional reserve. Conversely, hypotensive response during exercise has been proposed as a risk factor for sudden cardiac death in patients with HCM.[6,14] Both of these factors substantiated our

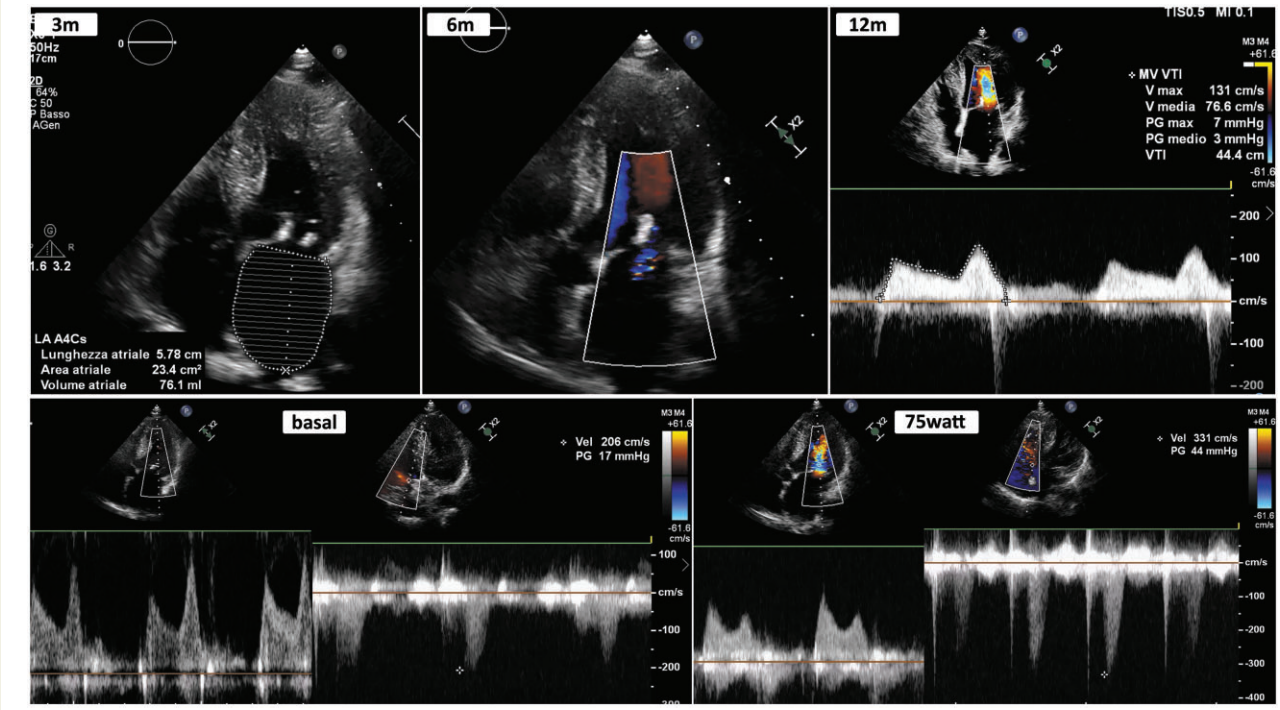

Figure 5. Upper panel: Echocardiographic follow-up findings: left atrium volume at 3 months, mild residual mitral regurgitation at 6 months, and trans-mitral gradient at 12 months. Lower panel: Echocardiographic findings during stress testing at 6 months follow-up including mitral filling pattern and pulmonary artery systolic pressure at rest and during peak stress (75-W stage).

decision to explore and treat the pathophysiological mechanisms responsible for pre-syncope in this patient.

While the long-term effect of the MitraClip intervention on our patient's prognosis is unknown, structural treatment significantly reduced symptoms and substantially improved her quality of life. Transcatheter edge-to-edge repair with MitraClip should be carefully considered as a possible option for treating patients with non-obstructive HCM as well as obstructive HCM with significant MR.

Lead author biography

Dr Katya Lucarelli is an interventional cardiologist at the General Hospital 'F. Miulli' in Acquaviva delle Fonti, Italy. Her areas of interest include interventions for coronary and structural heart diseases as well as ventricular assist device implantation and right cardiac catheterization. She has proficiency in transoesophageal echocardiography and stress echocardiography.

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 these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that the patient involved in this case provided written informed consent for publication of this case report, including image(s) and associated text, in line with COPE guidance.

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