Regression of Systolic Anterior Motion in Progressive Hypertrophic Cardiomyopathy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

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Patient:	**Female, 78-year-old**
Final Diagnosis:	**Hypertrophic cardiomyopathy**
Symptoms:	**Chest discomfort • dyspnea**
Medication:	**—**
Clinical Procedure:	**Mitral valve repair • transesophageal echocardiogram**
Specialty:	**Cardiology**

Objective: Unusual clinical course

Background: Systolic anterior motion (SAM) is the dynamic anteriorly directed movement of the anterior mitral valve leaflet during systole toward the left ventricular outflow tract (LVOT). The history of SAM in progressive hypertrophic cardiomyopathy (HCM) is unclear. It is believed that SAM is an irreversible process that progresses as the gradient over the LVOT increases. We present a case where SAM regressed after extensive left atrial (LA) and left ventricle (LV) remodeling in a patient with progressive HCM.

Case Report: A 78-year-old woman presented with effort dyspnea. Echocardiogram revealed HCM with an interventricular septal (IVS) thickness of 20 mm, significant pressure gradient over LVOT, and prominent SAM. The LV chamber dimensions were within normal range. The patient was prescribed medications against heart failure and discharged. Six years later, she was admitted with an acute respiratory infection. She underwent transthoracic and transesophageal echocardiograms, which showed no systolic function change. The IVS thickness was lower, LV and LA were significantly enlarged, and there was a significant mitral regurgitation with an anteriorly directed jet and no SAM. The transesophageal echocardiogram revealed a posterior leaflet's prolapse with a flail P2 segment, which required percutaneous edge-to-edge mitral repair.

Conclusions: Our case highlights the multiple theories behind the mechanism of SAM in HCM. The long-standing pressure gradient over the LVOT lead to extensive left side remodeling, which then altered the geometric, kinetic, and structural forces and, consequently, the Venturi effect. At the end stage of HCM, IVS lost its thickness, pressure gradient declined, and SAM regressed.

Keywords: Cardiomyopathy, Hypertrophic • Mitral Valve Insufficiency • Ventricular Remodeling

Abbreviations: **SAM** – systolic anterior motion; **TTE** – transthoracic echocardiogram; **TEE** – transesophageal echocardiogram; **LVOT** – left ventricular obstructive tract; **LVH** – left ventricular hypertrophy; **LVOTPG** – left ventricular outflow tract pressure gradient; **MR** – mitral regurgitation; **LA** – left atrium; **LV** – left ventricle; **ER** – emergency room; **LAVI** – left atrium volume index; **mPAP** – mean pulmonary artery pressure; **PCR** – polymerase chain reaction; **ICRBBB** – incomplete right bundle branch block

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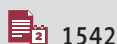
Background

Systolic anterior motion (SAM) describes the dynamic movement of the anterior mitral valve leaflet during systole anteriorly toward the left ventricular outflow tract (LVOT) [1]. SAM was first reported as a potential complication of mitral valve repair in 1977 by Termini et al [2] and was long thought to be due to hypertrophic cardiomyopathy (HCM), specifically. However, it is currently understood that SAM can arise secondary to other etiologies, including HCM, following cardiac surgery, and can be due to medical causes such as diabetes mellitus [3].

We report a case in which a long-standing SAM led to extensive left-sided remodeling, which subsequently led to the regression of SAM. We further elaborate on various mechanisms of action, multifactorial etiologies, and possible theories.

Case Report

We describe a 78-year-old woman who presented to the emergency department (ED) in 2014 with symptoms of effort angina and dyspnea. Her past medical history included long-standing controlled hypertension, adult-onset diabetes mellitus, and hyperthyroidism. In 2006, she underwent a coronary catheterization owing to stable angina pectoris, which showed patent coronary arteries. Her medications included a non-dihydropyridine calcium channel blocker (verapamil), angiotensin receptor blocker (ARB, losartan), hydrochlorothiazide, metformin, levothyroxine, and a statin. On arrival, an electrocardiogram (ECG) showed signs of left ventricular hypertrophy with no ischemic changes. She underwent an echocardiogram (**Figures 1-3**), which demonstrated good global systolic function, with an LV ejection fraction of 60%. Mild diastolic dysfunction due to abnormal relaxation and no regional wall motion abnormality, significant interventricular septal (IVS) hypertrophy of 20 mm, and a posterior wall thickness of 18 mm (1.3: 1 ratio) were noted. There was SAM with moderate anteriorly directed mitral regurgitation (**Videos 1, 2**) and a pressure gradient over the LV outflow tract (LVOT) of 100 mmHg. The LV end-diastolic diameter was 49 mm and the LV end-systolic diameter was 23 mm. The left atrial (LA) size was 39 mm, LA volume was 20 mL, and LA volume index was 32 mL/m². The patient's mean pulmonary artery pressure was normal. We assumed that her symptoms
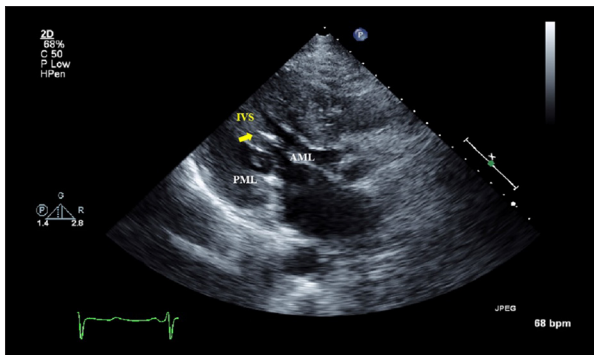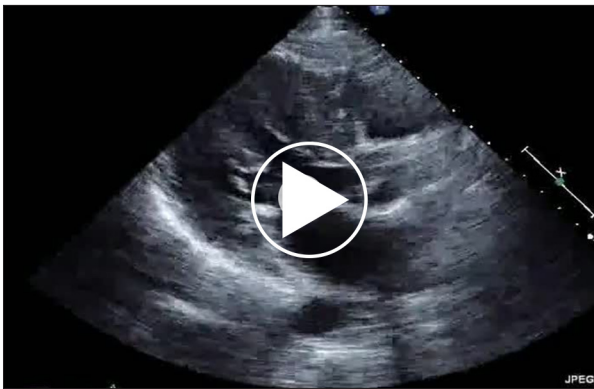

Figure 1. Transthoracic echocardiogram at admission (2014). Parasternal long-axis view. The motion of the anterior mitral leaflet toward the interventricular septum during systole (yellow arrow).
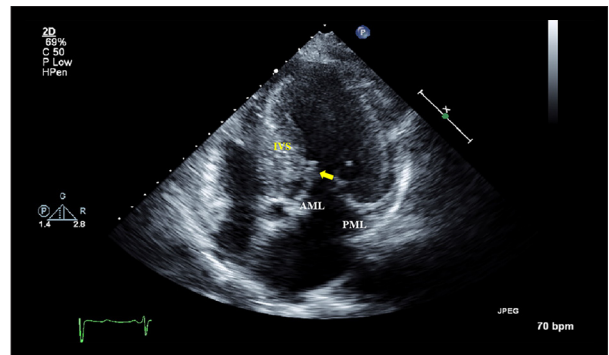
Figure 2. Transthoracic echocardiogram at admission (2014). 4-chambers view. The motion of the anterior mitral leaflet toward the interventricular septum during systole (yellow arrow).
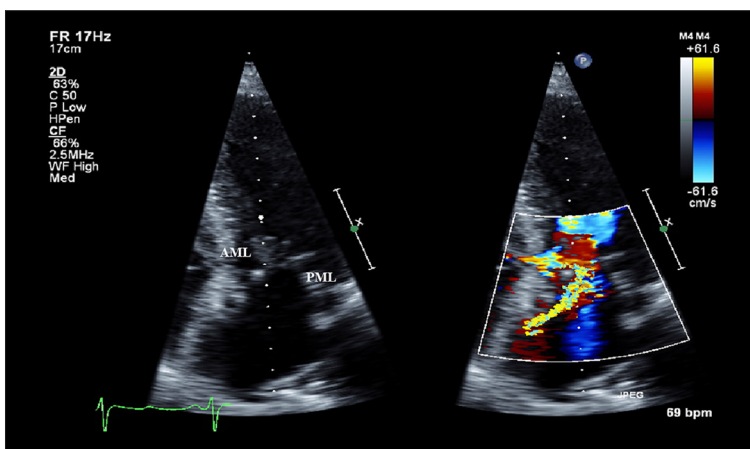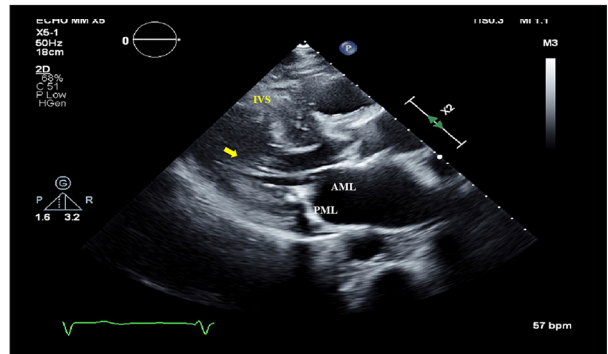

Figure 3. Transthoracic echocardiogram at admission (2014). 4-chambers view. The anteriorly directed jet of mitral regurgitation (**right figure**).

Video 1. Transthoracic echocardiogram at admission (2014). The systolic motion of the anterior mitral leaflet toward the interventricular septum in parasternal long-axis view.
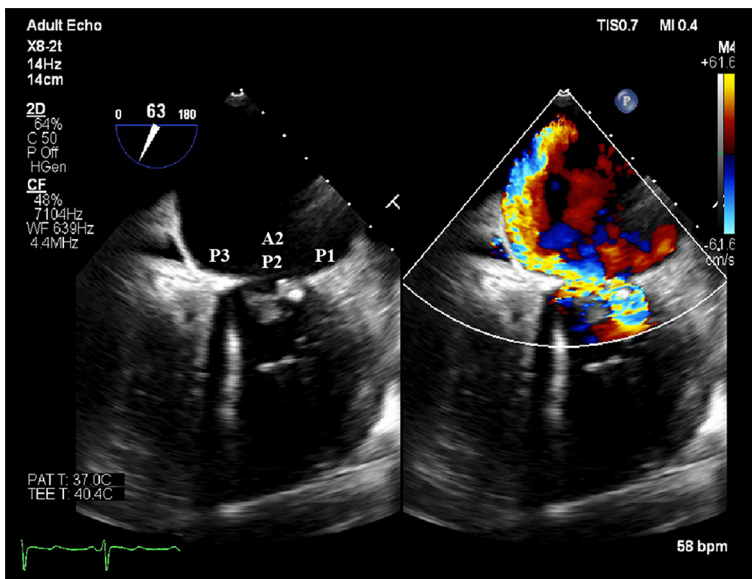

Video 2. Transthoracic echocardiogram at admission (2014). The systolic motion of the anterior mitral leaflet toward the interventricular septum in 4-chambers view.

Figure 4. Transthoracic echocardiogram in 2020. Parasternal long-axis view. No evidence of systolic anterior motion.

were related to the structural changes since there was no evidence of cardiac injury or ischemia. Bisoprolol, a beta-blocker, was added to her daily medication regimen.

Six years later (2020), the patient was admitted to the hospital owing to significant dyspnea at rest, cough, and fever. She denied having effort-related chest pain from 2014 until her presentation in 2020 but reported having progressive dyspnea to the point that her daily activity was significantly limited. She was not hospitalized or followed up by a cardiologist. In the ED, her blood pressure was 136/72 mmHg and she had a regular heart rate of 78 beats/min. Heart auscultation revealed a grade IV holosystolic murmur at the apex, radiating to the axilla. Lung auscultation indicated bilaterally diffuse coarse crackles. An ECG showed a sinus rhythm with an incomplete right bundle branch block pattern and signs of left ventricular hypertrophy. On the chest X-ray, the heart silhouette was enlarged, with evidence of congestion and a new lung infiltration. A respiratory tract swab was taken and sent for viral
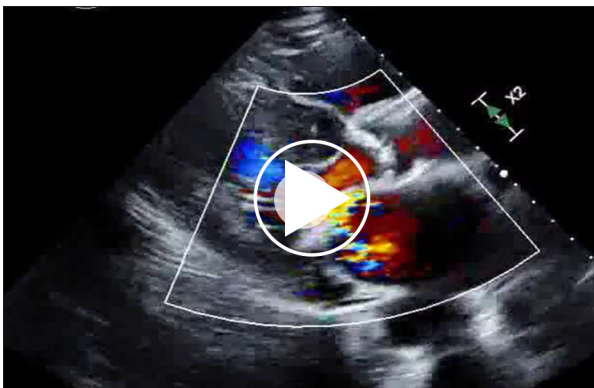
Figure 5. Transthoracic echocardiogram in 2020. Mid-esophageal commissural view. The anteriorly directed jet of mitral regurgitation.
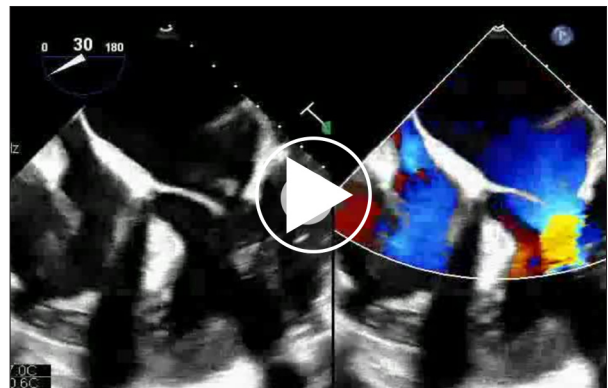
Video 3. Transthoracic echocardiogram in 2020. Parasternal long-axis view. No evidence of systolic anterior motion.
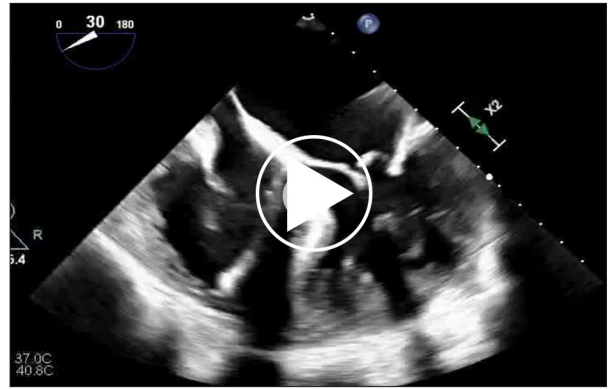
Video 5. Transthoracic echocardiogram in 2020. Mid-esophageal commissural view. Prolapse of the posterior wall with flail P2 segment.

Video 4. Transthoracic echocardiogram in 2020. Color-flow mapping. Parasternal long-axis view. Significant mitral regurgitation with posteriorly directed jet with no evidence of an enlarged left atrium.

Video 6. Transthoracic echocardiogram in 2020. Mid-esophageal commissural view. The anteriorly directed jet of mitral regurgitation.

polymerase chain reaction testing, and the results were positive for influenza virus. The patient was treated with oseltamivir. During hospitalization, levofloxacin was added to her medication regimen to cover hospital-acquired pneumonia.

While the patient was hospitalized, she underwent transthoracic (TTE) and transesophageal (TEE) echocardiograms. The TTE (**Figures 4, 5**) showed good global systolic function with an LV ejection fraction of 60%. The IVS thickness measured 15 mm, and the posterior wall thickness was 15 mm (1: 1 ratio). The pressure gradient over the LVOT was 49 mmHg. We noticed a significant mitral regurgitation with an anteriorly directed jet and no SAM (**Videos 3, 4**). The LA was significantly enlarged with an LA volume index of 69 mL/m^2. The LV chamber was enlarged, the LV end-diastolic was 52 mm, and the LV end-systolic diameter was 29 mm. The mean pulmonary artery pressure was 60 mmHg. The TEE revealed the prolapse of the posterior leaflet with the flail P2 segment (**Videos 5, 6**). The patient underwent a successful percutaneous edge-to-edge mitral repair.

Discussion

The mechanism behind SAM was long thought to be related to the Venturi effect, where fluid flowing through a stenotic tube reduces the pressure on the tube walls to gain flow velocity, maintaining the mass continuity principle. Recent studies have suggested that the Venturi effect could account for the presence of SAM in cases of an aorto-mitral angle <15°. Nonetheless, some patients with SAM presented with an aorto-mitral angle of 21°, suggesting that other factors are involved in the pathogenesis of SAM [1-3].

Drag forces are thought to be at least one of these other factors mentioned above, contributing to the development of SAM. Charles et al [4] proposed that SAM emerges by the synergistic effect of the Venturi effect, where the flow jet elevates the mitral valve, and drag forces move the mitral valve anteriorly toward the LVOT. Naturally, SAM develops only in a predisposed heart, where many structural, geometric, or kinetic factors permit the forces to be manifested. Ventricular

morphological changes also play a role in SAM. Acquired hypertrophy and HCM can lead to SAM. HCM is unique among heart diseases because it can present clinically at any age [5].

Olivotto et al described the progression patterns and stages of HCM. End-stage HCM, known as stage IV, represents about 5% of HCM patients [6]. At this advanced stage, there are 2 morpho-functional manifestations. The hypokinetic-dilated form is characterized by volume increase and spherical remodeling of the LV. Mitral regurgitation can be observed in variable degrees; conversely, LV outflow obstruction is almost always absent, and atrial dilatation is typically severe and bilateral [7,8].

Maron and Spirito reported that during the progression to end-stage HCM, LV wall thickness regresses by about 25% (from 20 mm to 15 mm, on average). The LV end-diastolic cavity dimension increases by about 20%, accompanied by an increase in end-systolic dimension. Ejection fraction can decrease substantially from supranormal values of >70% to <45%, but often only to slightly below the lower limits of the normal range. The other form, known as hypokinetic-restrictive, is characterized by a small and stiff LV with extreme diastolic dysfunction, resembling primary restrictive cardiomyopathy [9,10].

Many other factors were found to be associated with the development of SAM. The condition of the mitral leaflets is believed to play a prominent role in the contribution to SAM, whereby excessive anterior or posterior leaflet tissue provides a larger surface area on which drag forces act. This redundant tissue can also cause the coaptation point to move anteriorly toward the LVOT [11]. An elongated anterior mitral leaflet can also be the cause of SAM. A study by Shah et al [12] supports this notion, showing that anterior mitral leaflet length by itself is an important predictor of SAM. The relationship between the mitral leaflets is also important, where an anterior mitral leaflet to posterior mitral leaflet ratio <1.3 is considered a risk factor for SAM [13,14].

Moreover, the mitral annulus status is critical, as shown in both animal and clinical studies, where the insertion of rigid or semirigid mitral rings is associated with disruption of mitral annulus dynamics, leading to SAM. The subvalvular apparatus can alter the coaptation point's position in regards to the septum, thus resulting in SAM [15-17].

There is growing evidence that elongation and buckling of the chordae may be associated with SAM. Papillary muscles play a special role in asymmetric ventricular hypertrophy, where the anterior and medial displacement of the papillary muscle significantly influences SAM. Mitral valve repair with leaflet resection and a mitral valve rigid ring independent of leaflet size can be a primary cause of SAM [18]. This is supported by a large series of patients who underwent mitral valve annuloplasty with major efforts to fit the appropriate ring size, and as a result, demonstrated successful postoperative mitral dynamics. The functionality of the papillary muscles in the present study seems to have played an additional role in SAM development, where the pacing of the papillary muscles resulted in the disappearance of SAM [19]. The mechanisms of systolic anterior motion in HCM can be different from non-HCM. Anterior displacement of the papillary muscles in HCM creates diastolic downward vortex forces, which pull the mitral valve into the LVOT [20]. The IVS hypertrophy, which is characteristic of HCM, increases the drag forces and promotes the Venturi effect, moving the mitral valve anteriorly, resulting in SAM [21].

Our case presents a unique observation of the chronological progression of SAM in a patient with HCM. The alteration of the preload, afterload, and contractility of the LV, seen in the advanced remodeling stage of HCM, led to a shift in the flow forces to the LA right-sided chambers and resulted in accelerating LA dilatation and extensive mitral regurgitation progression. We believe that the geometrical changes and the hemodynamical flow alteration directly affected the basic elements of the Venturi effect and finally led to its regression.

Conclusions

We report a case of regression of systolic anterior motion of the anterior mitral leaflet in end-stage HCM, which is caused by various etiologic factors and mechanisms. We attempted to understand the consequences of HCM within these pathophysiologic mechanisms in regards to the Venturi effect.

Conflicts of Interest

None.

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