Left ventricular outflow tract obstruction in patients with Ebstein anomaly

Defne Gunes Ergi, MD,[a] Hartzell V. Schaff, MD,[a] Heidi M. Connolly, MD,[b] William R. Miranda, MD,[b] David S. Majdalany, MD,[c] and Joseph M. Dearani, MD[a]

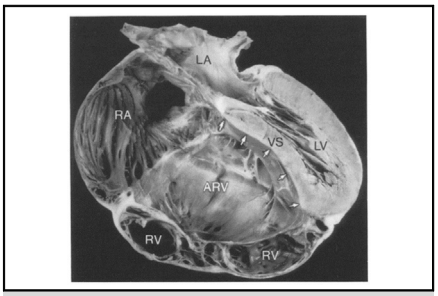
ABSTRACT

Objective: In this study, we investigated the clinical characteristics of patients with Ebstein anomaly and left ventricular outflow tract (LVOT) obstruction as well as possible mechanisms of obstruction as assessed by 2-dimensional echocardiography.

Methods: We queried our institutional echocardiography and surgical databases for patients with the diagnosis of Ebstein anomaly seen from 1985 through 2022. Fourteen patients had the additional diagnosis of LVOT obstruction identified from transthoracic echocardiography.

Results: The mean age of the 14 patients at the time that LVOT obstruction was identified was 51.9 ± 9.9 years, and 11 (78%) were female. LVOT obstruction (mean gradient 61.0 ± 25.7 mm Hg) was documented at the time of initial diagnosis of Ebstein anomaly for 8, and in the remaining, was recognized on follow-up imaging. Dynamic LVOT obstruction with systolic anterior motion (SAM) was the most common mechanism and was mostly accompanied by leftward septal movement and septal hypertrophy. Seven of the 9 patients with SAM had the diagnosis of hypertrophic cardiomyopathy. Leftward bowing of the septum appeared to be the sole cause of LVOT obstruction in 3 and a contributing factor to SAM in 4. Among the 13 patients who underwent an operation for Ebstein anomaly, 7 had concomitant septal myectomy and 3 had a subsequent procedure.

Conclusions: There are multiple mechanisms of LVOT obstruction in patients with Ebstein anomaly, including SAM and leftward bowing of the interventricular septum, which may exist alone or in combination. Septal myectomy at the time of tricuspid valvuloplasty is safe and effectively reduces gradients in the outflow tract and may prevent the need for subsequent reintervention. (JTCVS Open 2023;16:641-7)



Atrialized portion of the right ventricle compressing and the left ventricular cavity.

CENTRAL MESSAGE

There are multiple mechanisms involved in LVOT obstruction in Ebstein anomaly. Septal myectomy at the time of Ebstein repair surgery is safe and effectively reduces gradients in the outflow tract.

PERSPECTIVE

We investigated the clinical characteristics of patients with Ebstein anomaly and LVOT obstruction as well as possible mechanisms of obstruction. Dynamic LVOT obstruction with SAM was the most common mechanism and was often accompanied by leftward septal movement and septal hypertrophy. Seven of the 9 patients with SAM had septal-to-free wall ratios >1.3, consistent with the diagnosis of HCM.

Wilhelm Ebstein's description of the tricuspid valve abnormality associated with his name was published in 1866,[1] and the phrase "bilateral Ebstein's malformation" was first suggested by Gerlis and colleagues[2] in 1998 to describe left heart involvement in the disease. Compression of the left ventricular (LV) cavity by the leftward septal shift due to an enlarged right ventricle as well as coexisting mitral leaflet abnormalities have been suggested as mechanisms of left ventricular outflow tract (LVOT) obstruction in this population. In this study, we investigated the clinical characteristics of patients with Ebstein anomaly and LVOT obstruction as well as possible mechanisms of obstruction as assessed by Doppler echocardiography.

From the Departments of [a]Cardiovascular Surgery and [b]Cardiovascular Medicine, Mayo Clinic, Rochester, Minn; and [c]Department of Cardiovascular Medicine, Mayo Clinic, Phoenix, Ariz.

Received for publication Sept 7, 2023; revisions received Oct 4, 2023; accepted for publication Oct 10, 2023; available ahead of print Nov 24, 2023.

Address for reprints: Hartzell V. Schaff, MD, Department of Cardiovascular Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (E-mail: schaff@mayo.edu).

2666-2736

https://doi.org/10.1016/j.xjon.2023.10.024

Abbreviations and Acronyms
HCM = hypertrophic cardiomyopathy
LV = left ventricular
LVOT = left ventricular outflow tract
RV = right ventricular
SAM = systolic anterior motion
TR = tricuspid valve regurgitation

METHODS

To identify patients with Ebstein anomaly and LVOT obstruction, we queried institutional echocardiography and surgical databases for all patients with the diagnosis of Ebstein anomaly seen at the Mayo Clinic from 1985 through 2022. From this list, we identified 14 patients with the additional diagnosis of LVOT obstruction. Clinical and echocardiographic data were collected from the patients' electronic medical records; further information was obtained from a review of operative notes of patients who underwent corrective surgery as well as transthoracic and transesophageal echocardiographic images. All patients gave consent for publication, and this study was approved by the Mayo Clinic institutional review board (no. 22-012937, January 10, 2023).

LVOT obstruction in the transesophageal echocardiogram was defined as maximum instantaneous LVOT gradient greater than 30 mm Hg. Calculation of the displacement index was done according to the description by Edwards and William,[3] which involves the measurement of the distance from the insertion of the septal and posterior tricuspid leaflets relative to the insertion of the anterior mitral leaflet (normal <8.0 mm/m^2).

RESULTS

Clinical Characteristics

The mean age of the 14 patients at the time that LVOT obstruction was identified was 51.9 ± 9.9 years, and 11 (78%) were female (Table 1). LVOT obstruction was documented at the initial diagnosis of Ebstein anomaly in 8 patients, and in the remaining patients, LVOT obstruction was recognized on follow-up imaging.

Hypertension was observed in 11 patients (78.5%) at the time that LVOT obstruction was identified. Among the study patients, 5 (35.7%) were using diuretics, and 6 patients (42.8%) were prescribed beta-blockers; one was taking disopyramide in combination with a beta-blocker. In addition, 2 patients (14.2%) were on calcium channel blockers.

In the entire cohort, 9 patients were classified as having New York Heart Association functional class III due to exertional dyspnea when LVOT obstruction was identified. Among the other 5 patients, 2 presented with arrhythmias (Wolff–Parkinson–White syndrome in 1), and 3 were asymptomatic. A coexisting atrial septal defect was present in 3 patients, and 4 had a patent foramen ovale. One patient was noted to have cyanosis of her lower extremities with poor capillary filling, although there was no arterial oxygen desaturation during exercise stress echocardiography.

Echocardiographic Findings

Complete 2-dimensional and Doppler echocardiographic measurements were evaluated, and patients exhibited variable degrees of tricuspid valve regurgitation (TR) and right ventricular (RV) enlargement and systolic function (Table 2). The majority (13/14) of the patients had moderately severe or severe TR; 1 patient was considered to have "atypical" Ebstein anomaly with mild TR, mild RV enlargement, and normal RV systolic function. Eight patients had normal 29.3 ± 2.9 mm RV systolic pressure averaging, and 6 patients had elevated RV systolic pressure averaging 43.5 ± 4.8 mm Hg.

The LV systolic function was normal in all patients, and LV ejection fraction averaged 69 ± 2%. The average LV

TABLE 1. Clinical characteristics of patients with Ebstein anomaly and LVOT obstruction

Patient	Sex	Age, y	Mechanism of LVOT obstruction
1	Female	65	Leftward septal bowing
2	Female	43	SAM
3	Female	52	Leftward septal bowing
4	Female	53	HCM, SAM
5	Male	41	Leftward septal bowing
6	Male	65	Leftward septal bowing, SAM
7	Female	39	HCM, SAM, leftward septal bowing
8	Female	54	Subaortic membrane
9	Female	68	HCM, SAM
10	Female	59	HCM, SAM
11	Female	36	Subaortic membrane
12	Female	56	HCM, SAM, leftward septal bowing
13	Male	42	HCM, SAM
14	Female	53	HCM, SAM, leftward septal bowing

LVOT, Left ventricular outflow tract; *SAM*, systolic anterior motion; *HCM*, hypertrophic cardiomyopathy.

end-systolic and end-diastolic dimensions were 22.6 ± 4.6 mm and 39.2 ± 6.4 mm, respectively, across all 13 patients. One patient with severe hypertrophic cardiomyopathy (HCM) and severe dynamic LVOT obstruction had small end-systolic and end-diastolic LV dimensions. LV mass averaged 114 ± 9 g, and LV mass index averaged 59 ± 6 g/m^2 in all patients. Septal and free wall thicknesses averaged as 13.2 ± 2.5 mm and 10.7 ± 1.5 mm in all patients, and the ratio averaged 1.2 ± 0.7 (Table 2).

The mean LVOT gradient in the cohort was 61.0 ± 25.7 mm Hg, and as seen in Table 2, the mechanism of obstruction differed among the patients. Systolic anterior motion (SAM) of the mitral valve leaflets was seen in 9 patients, and 7 of these had a septal-to-free wall thickness ratio >1.3, suggesting underlying HCM. Moderate mitral valve regurgitation was seen in 2 patients with SAM, and 7 had mild mitral valve regurgitation. Bileaflet mitral valve prolapse was identified in 1 patient who also had SAM. Seven of 14 patients had leftward bowing of interventricular septum, which was considered to contribute to LVOT obstruction; 3 were described as having sigmoid-shaped septum.

Among the 8 patients concurrently diagnosed with Ebstein anomaly and LVOT obstruction, we calculated the tricuspid valve displacement index for 6 patients who had available digital transthoracic echocardiogram or magnetic resonance imaging assessments for the calculations. The mean displacement index measured 16.4 ± 4.2 mm/m^2. Of these patients, 4 exhibited SAM. Among the 2 patients without SAM, one presented with a subaortic membrane, and the other displayed leftward septal bowing.

Of the remaining 6 patients in whom LVOT obstruction was identified during their follow-up, only 2 had available digital transthoracic echocardiogram or magnetic resonance imaging assessments for the displacement index measurements (Table 3). One demonstrated a combination of HCM, SAM, and leftward septal bowing, whereas the other showed only leftward septal bowing as contributors to the LVOT obstruction.

Operative Procedures and Outcomes

During corrective surgery, 6 patients had tricuspid valve replacement with a bioprosthetic valve, and 6 had tricuspid valvuloplasty. One patient with the diagnosis of both Ebstein and LVOT obstruction did not undergo an operation, and another patient had atrial septal defect closure in early childhood and was later found to have features of Ebstein anomaly and LVOT obstruction. Among the patient cohort, 4 patients underwent a second operation for tricuspid valve re-replacement, and 1 of these had a third tricuspid valve replacement. Operative data are represented in Table 4.

Ten patients underwent transaortic septal myectomy to address obstruction in the LVOT. In 1 patient, anomalous attachments of papillary muscles to the ventricular septum were divided at the time of myectomy, and in another, abnormally fused papillary muscles were divided. Seven of the 10 patients who underwent myectomy had the diagnosis of HCM with a septal-to-free wall thickness ratio of over 1.3. Among the remaining 3 patients, 2 had subaortic membranes; one patient with normal left ventricular wall thickness had severe dynamic LVOT obstruction due to SAM of the mitral valve.

TABLE 2. Echocardiographic data of patients with Ebstein anomaly and LVOT obstruction

Patient	TR	RV enlargement	Right ventricle systolic function	RSVP, mm Hg	LVEF, %	LVESD, mm	LVEDD, mm	Septal-to-free wall ratio	Maximum LVOT gradient, mm Hg
1	Moderately Severe	Severe	Mildly reduced	33.0	71	23.0	43.0	1.1	31.0
2	Severe	Severe	Severely reduced	28.0	61	23.0	37.0	1.1	75.0
3	Severe	Severe	Moderately reduced	30.0	66	24.0	41.0	1.1	36.0
4	Severe	Moderate	Normal	51.0	76	23.0	47.0	1.9	100.0
5	Severe	Severe	Moderately reduced	27.0	63	25.0	39.0	1.0	66.0
6	Moderately Severe	Severe	Moderately reduced	28.0	47	33.0	43.0	1.1	65.0
7	Severe	Severe	Moderately reduced	24.0	67	20.0	35.0	1.4	64.0
8	Moderately Severe	Severe	Moderately reduced	33.0	75	25.0	50.0	1.0	42.0
9	Severe	Moderate	Normal	36.0	65	14.0	23.0	1.4	80.0
10	Severe	Moderate	Moderately reduced	44.0	61	13.0	31.0	1.3	120.0
11	Mild	Mild	Normal	46.0	64	24.0	38.0	1.0	39.0
12	Severe	Severe	Mildly reduced	45.0	75	22.0	37.0	1.3	64.0
13	Severe	Severe	Mildly reduced	39.0	69	24.0	43.0	1.8	30.0
14	Severe	Severe	Mildly reduced	32.0	67	24.0	42.0	2.5	43.0

TR, Tricuspid regurgitation; *RV*, right ventricle; *RVSP*, right ventricular systolic pressure; *LVEF*, left ventricular ejection fraction; *LVESD*, left ventricular end-systolic volume; *LVEDD*, left ventricular end-diastolic volume; *LVOT*, left ventricular outflow tract.

TABLE 3. Displacement index measurements

Patient	Displacement index, mm/m^2	Mechanism of LVOT obstruction	Maximum LVOT gradient, mm
Simultaneous identification of Ebstein anomaly and LVOT obstruction			
4	22.1	SAM	100.0
5	20.7	Leftward septal bowing	66.0
6	15.6	SAM	65.0
11	15.1	Subaortic membrane	39.0
12	18.1	SAM	64.0
13	18.7	SAM	30.0
Late identification of LVOT obstruction			
3	11.5	Leftward septal bowing	36.0
14	9.8	HCM, SAM, leftward septal bowing	43.0

LVOT, Left ventricular outflow tract; *SAM*, systolic anterior motion; *HCM*, hypertrophic cardiomyopathy.

A second intervention on the tricuspid valve was required in 4 patients during follow-up. Three had their previous bioprosthesis replaced and one underwent valve replacement with bioprosthesis following initial tricuspid valve repair. Two patients required a third operation; one underwent re-replacement of the previous tricuspid bioprosthesis, and the other underwent transaortic septal myectomy.

There were no perioperative deaths during the initial or subsequent operations, and there have been no deaths during follow-up. Of the patients who had septal myectomy, none of them had evidence of residual LVOT obstruction in their postoperative echocardiography during the follow-up period (mean postoperative gradient was 1.0 $\pm$ 3.7 mm Hg).

DISCUSSION

Patients with Ebstein anomaly may have left ventricular systolic dysfunction or hyperdynamic left ventricular function with dynamic outflow tract obstruction. Jost and colleagues[4] reported that 39% of patients with Ebstein anomaly had left heart abnormalities involving the myocardium or valves, and 2 patients in their report

TABLE 4. Surgical history of the patients with Ebstein anomaly and left ventricular outflow tract obstruction

Patient	First operation	Second operation	Third operation
1	TVR, RRA, maze, PFO closure	TV re-replacement	–
2	TVR-replacement, ASD closure	TV re-replacement, ASD closure (residual), myectomy	–
3	TVR, RRA, maze, PFO closure	–	–
4	TV-ring, RRA, myectomy	–	–
5	ASD closure	–	–
6	–	–	–
7	TVR, RRA, myectomy, ASD closure	–	–
8	TVR, RRA	TV re-replacement, AVR	AV re-replacement, myectomy
9	TV-ring, RRA, myectomy	–	–
10	TVR, RRA, myectomy, ASD closure	–	–
11	TV-ring, RRA, myectomy, PFO closure	–	–
12	TV-ring, RRA, maze, myectomy	–	–
13	TV-ring, RRA, myectomy, Maze		
14	TV-repair	TV re-replacement	TV re-replacement, myectomy

TVR, Tricuspid valve replacement; *RRA*, right reduction annuloplasty; *PFO*, patent foramen ovale; *TV*, tricuspid valve; *ASD*, atrial septal defect; *TV-ring*, tricuspid ring annuloplasty; *AVR*, aortic valve replacement; *AV*, aortic valve.

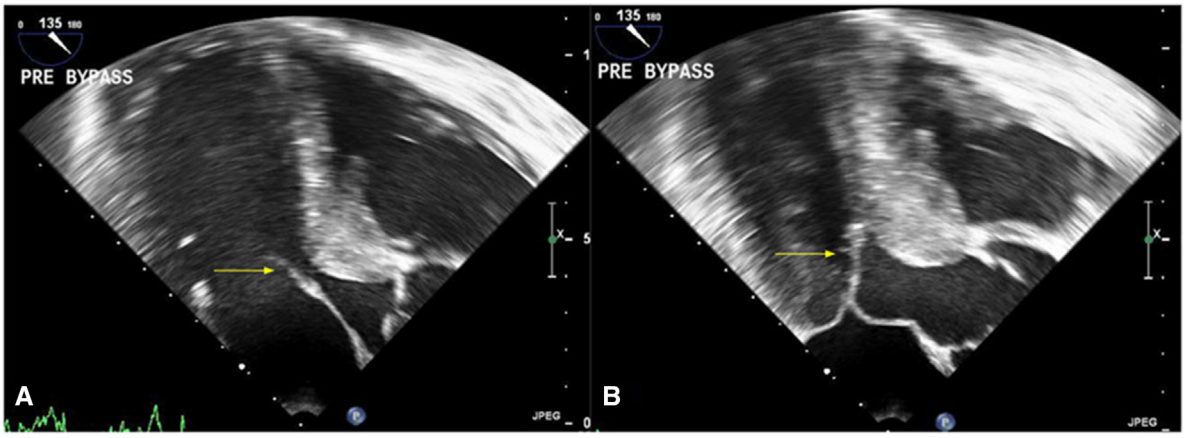


FIGURE 1. Diastolic (A) and systolic (B) frames of the patient who had Ebstein anomaly repair and septal myectomy, with the diagnosis of hypertrophic cardiomyopathy and systolic anterior motion of the mitral valve (*arrow*).

underwent septal myectomy for obstructive HCM. In another review, Brown and colleagues[5] found that 10% of patients with Ebstein malformation had moderate or severe LV systolic dysfunction before surgery for Ebstein anomaly. Obstruction in the LVOT can develop late following surgical correction for Ebstein, or LVOT obstruction may be present when right-sided pathology is identified. In this study, we investigated the characteristics of patients with Ebstein anomaly and LVOT obstruction to better understand the pathophysiologic mechanisms as well as the outcomes of management.

Systemic hypertension is a well-known contributor to the hypertrophy of the left ventricle and is highly prevalent in patients with HCM.[6] Although hypertension is more common in male patients, it has been shown that female patients experience a sharper increase in blood pressure from the third decade of life, and the prevalence of hypertension accelerates with age.[7] In the present study, hypertension was present in the majority of the patients (78.5%), with a high percentage of female patients who were mostly middle-aged. Further, elevated LVOT gradients were associated with a greater displacement index, suggesting a diminished functional capacity of the right ventricle and a more severe manifestation of Ebstein anomaly.

Dynamic LVOT obstruction with SAM was the most common mechanism, but in most patients was accompanied by leftward septal movement and septal hypertrophy. It is notable that patients with SAM had greater LVOT gradients compared with the patients without SAM (Table 2). Seven of the 9 patients with SAM had septal to free wall ratios >1.3, consistent with the diagnosis of HCM. Figure 1 demonstrates preoperative echocardiographic frames of a patient with SAM and probable HCM.

Coexisting obstructive HCM in patients with Ebstein anomaly has been reported in only 2 previous publications. Lee and colleagues[8] described a symptomatic 42-year-old female patient who was diagnosed with HCM and Ebstein anomaly after transthoracic echocardiography demonstrated a thickened interventricular septum and LV posterior wall as well as typical right atrial and tricuspid valvular anomalies of Ebstein anomaly. She was managed medically. Agustín and colleagues[9] described an asymptomatic 72-year-old man with severe asymmetric septal hypertrophy and findings of Ebstein anomaly. Of 7 patients with HCM with dynamic LVOT obstruction in the present series, 6 were symptomatic, and 1 patient did not have overt symptomatology. All 7 underwent septal myectomy in addition to tricuspid valve repair or replacement.

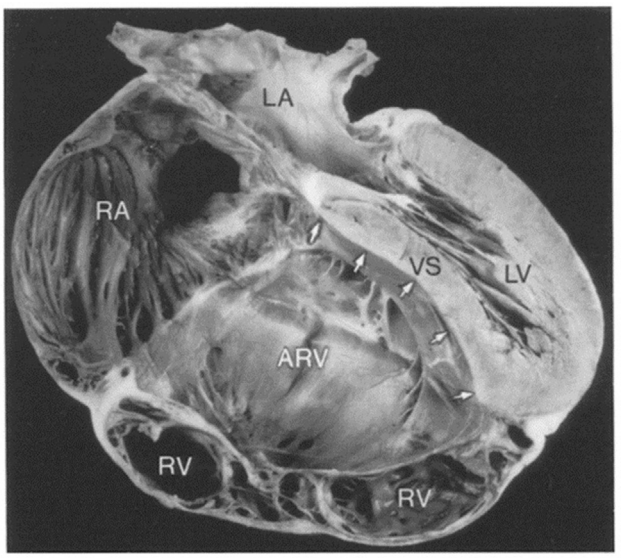


FIGURE 2. Enlarged atrialized portion of the right ventricle compressing and the left ventricular cavity and with leftward bowing of interventricular septum (*arrows*).[3] *LA*, Left atrium; *RA*, right atrium; *VS*, ventricular septum; *LV*, left ventricle; *ARV*, atrialized right ventricle; *RV*, right ventricle.

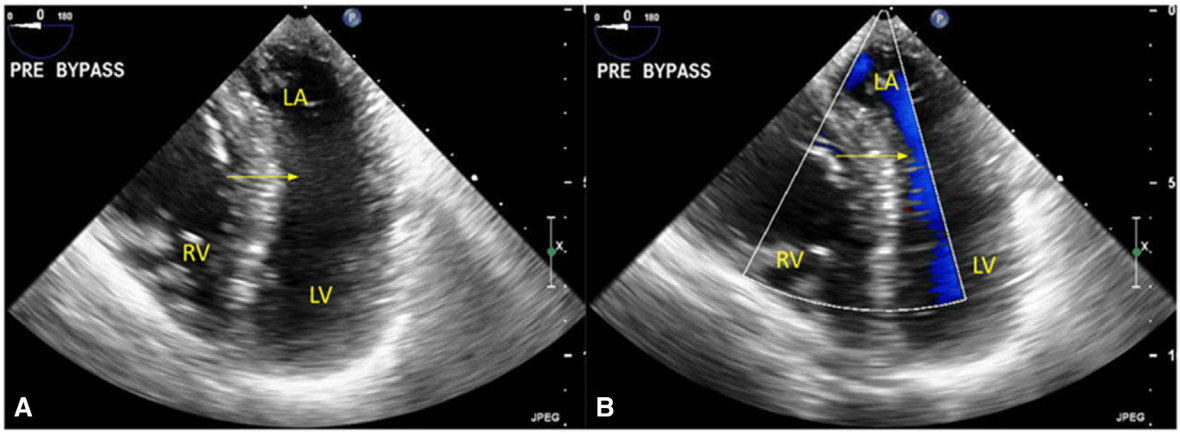


FIGURE 3. Transthoracic echocardiography (A) with color Doppler mode (B) of a patient who underwent Ebstein anomaly repair and septal myectomy. The *arrow* points to the narrowed left ventricular outflow tract caused by the abnormal leftward bowing of the interventricular septum. *LA*, Left atrium; *RV*, right ventricle; *LV*, left ventricle.

The second most common mechanism of LVOT obstruction in our patients with Ebstein anomaly was leftward bowing of the septum into the outflow tract due to right heart enlargement. This phenomenon was described in an autopsy study by Edwards and William[3]; Figure 2 from that report illustrates the enlarged atrialized portion of the RV compressing and deforming the LV cavity. In another study, Daliento and colleagues[10] emphasized the exaggerated leftward movement of the interventricular septum in 24 of 26 patients with Ebstein anomaly. In the present series, leftward bowing of the septum appeared to be the sole cause of LVOT obstruction in three patients and a contributing factor to SAM in four patients. Figure 3 demonstrates a narrowed LVOT by the leftward septal motion in a patient who underwent tricuspid valvuloplasty and septal myectomy.

An important finding in this review was the late development of LVOT obstruction in Ebstein anomaly. One patient who had 2 previous bioprosthetic tricuspid valve

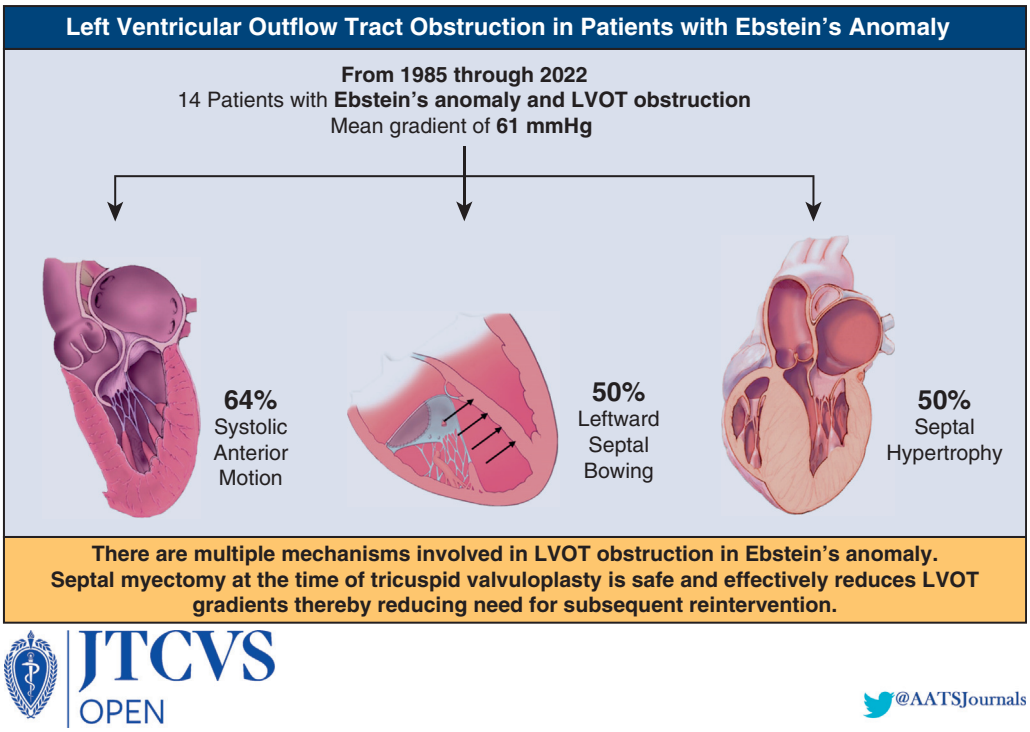


FIGURE 4. Left ventricular outflow tract obstruction in patients with Ebstein anomaly. *LVOT*, Left ventricular outflow tract.

replacements and aortic valve replacement developed prosthetic aortic valve dysfunction 8 years postoperatively. She had the additional finding of subvalvular LVOT obstruction, with a peak outflow tract velocity of 4.5 m/s related to the leftward shift of the septum and a muscular ridge. She underwent aortic valve re-replacement with aortic root enlargement and myectomy. A second patient underwent septal myectomy for dynamic LVOT obstruction 16 years following tricuspid valve replacement. A third patient experienced deterioration in her exercise capacity and lightheadedness due to dynamic LVOT 21 years following tricuspid valve replacement and underwent a successful septal myectomy.

CONCLUSIONS

This experience demonstrates that there are multiple mechanisms of LVOT obstruction in patients with Ebstein anomaly, including SAM and leftward motion of the interventricular septum, which may exist alone or in combination (Figure 4). Septal myectomy at the time of tricuspid valve repair or replacement is a safe option that effectively reduces gradients in the outflow tract and may prevent the need for subsequent reintervention. The late development of LVOT obstruction emphasizes the importance of continuing follow-up of these patients.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: left ventricular outflow tract, obstruction, Ebstein anomaly