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Lessons Learned From Intermittent Dysfunction of Mechanical Heart Valve

ABSTRACT

Background: Intermittent malfunction is a rare but potentially serious complication of prosthetic heart valve replacement. This study aimed to describe the clinical features and etiologic causes of patients with intermittent mechanical prosthetic heart valve dysfunction.

Methods: Between 2010 and 2021, 16 patients who were evaluated in the echocardiography laboratory of Koşuyolu Training and Research Hospital with the diagnosis of intermittent malfunction of prosthetic valves were included in the study.

Results: The evaluated patients consisted of 12 bi-leaflet mitral valve replacements and 2 mono-leaflet mitral valve replacements. The underlying causes of intermittent malfunction were classified as follows: residual chord (n=4), obstructive thrombus (n=2), non-obstructive thrombus (n=2), vegetation (n=2), pannus and obstructive thrombus coexistence (n=1), and solely pannus (n=1). One of the patients with mono-leaflet mitral valve replacements had pannus and obstructive thrombus. In the other patient with mono-leaflet mitral valve replacement, a stuck valve was observed in 1 of 12 beats secondary to arrhythmia. There were also 2 patients with aortic valve replacements. One patient had moderate aortic regurgitation due to prominent calcification and the other had moderate obstruction due to pannus. In the patient with pannus, a stuck leaflet was observed in 1 of 6 beats and moderate aortic regurgitation arose in 1 of 2 beats in the patient with calcification.

Conclusions: The intermittent stuck valve may have catastrophic outcomes. When making a treatment decision in these patients, assessing the degree of regurgitation or stenosis is essential. In particular, the frequency of entrapment should be taken into consideration when deciding the optimal therapy for intermittent prosthetic heart valve dysfunction.

Keywords: Prosthetic, valve disease, dysfunction, echocardiography

INTRODUCTION

Intermittent malfunction is a rare but potentially serious complication of prosthetic heart valve (PHV) replacement.[1-5] It can occur in both mitral and aortic PHVs and may lead to either periodic obstruction or regurgitation of flow, depending on the position of the valve and the phase of the cardiac cycle in which the disc gets trapped.[6,7] The most frequently reported causes of intermittent disk dysfunction include pannus formation, entrapment of the disk by thrombi (nonobstructive or obstructive), subvalvular mitral tissue, suture material, vegetations, ventricular myocardium, and arrhythmia.[4,5,8,9] A multimodality approach that includes transthoracic echocardiography (TTE), 2-dimensional (2D) or real-time 3-dimensional (RT-3D) transesophageal echocardiography (TEE), cardiac computed tomography (CT), and fluoroscopy may help the diagnosis of intermittent malfunction of the PHV.[10] If not treated appropriately, intermittent dysfunction can lead to permanent disc immobilization and have more catastrophic consequences.[1] Hence, prompt diagnosis and treatment are essential. Despite several case reports in the literature,[1-9] there is no clear consensus regarding the pathological process and possible etiological causes associated with intermittent mechanical PHV dysfunction. This study aimed to describe the clinical features and etiologic causes of patients with intermittent mechanical PHV dysfunction.

ORIGINAL INVESTIGATION

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METHODS

Patient Population

A total of 16 patients with intermittent mechanical left-sided PHV dysfunction who were evaluated in Koşuyolu Training and Research Hospital between February 2010 and March 2021 were included in this retrospective study. The intermittent valve disc dysfunction was conclusively proven with multimodality imaging tools, as well as Doppler examination. Patients whose medical records could not be accessed or whose definitive intermittent valve disc dysfunction was not proven by multimodality imaging tools were excluded from the study. This retrospective study was conducted in accordance with the principles of the Helsinki Declaration and approved by the Local Institutional Review Board (2021/22-282).

Definitions

Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg measured with the patient in supine position, or history of antihypertensive medication use.[11] Diabetes mellitus was defined as a fasting serum glucose level ≥ 126 mg/dL, glycated hemoglobin level ≥ 6.5%, or a history of hypoglycemic medication(s).[12] Cigarette smoking was defined as a history of smoking more than 10 cigarettes per day for at least 1 year without any attempt(s) to quit. Coronary artery disease was defined as significant stenosis [>50%] in at least 1 epicardial artery.[13] Chronic kidney disease was defined as the presence of kidney damage or glomerular filtration rate of <60 mL/min/1.73 m^2 for >3 months.[14] Ischemic cerebrovascular accident (CVA) included transient ischemic attack (TIA) and stroke. The TIA was defined as brief episodes of neurological dysfunction resulting from focal cerebral ischemia not associated with permanent cerebral infarction.[15] Besides, ischemic stroke was defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction.[16] These embolic events and the presence of clinical signs were confirmed by imaging modalities (magnetic resonance imaging with or without CT). The 2015 European Society of Cardiology–modified criteria were used to diagnose prosthetic valve endocarditis (PVE).[17]

Imaging, Clinical, and Laboratory Assessment

Echocardiography images were independently assessed by 3 cardiologists with more than 10 years of experience.

HIGHLIGHTS

- This study aimed to describe the clinical features and etiologic causes of patients with intermittent mechanical valve dysfunction.
- Intermittent malfunction is a rare but potentially severe complication of the prosthetic heart valve.
- It requires elaborative examination in symptomatic patients, and transesophageal echocardiography is crucial for differential diagnosis.
- The frequency of entrapment and the degree of regurgitation or stenosis play a fundamental role in making treatment decisions.

All patients underwent TTE using Vivid 7 Dimension® (GE Vingmed Ultrasound AS N-3190, Horten, Norway) or Philips iE33 (Philips Medical Systems, Andover, Mass, USA) echocardiography devices and S5-1 sector array transducer. Following TTE, 2D and RT-3D TEE studies were performed on all patients by using an X7-2t transducer on an iE33 ultrasound machine (Philips Medical Systems). The presence of intermittent malfunction was defined on the basis of Doppler echocardiographic measurements and other imaging modalities.

The diagnosis of thrombus, pannus, vegetation, and residual subvalvular apparatus was determined in accordance with previous publications.[9,10,18-22] Discrimination between obstructive pathologies such as pannus or thrombus was mainly based on 2D and RT-3D TEE studies in the majority of the patient population. In patients with inconclusive findings, multi-detector CT was performed for the assessment and the differential diagnosis between pannus and thrombus.[22] Moreover, cine fluoroscopy (CF) was also performed for the evaluation of stuck valves. In the case of bileaflet valves, the disks were directly visualized, and opening and closing angles were measured using a tangential view.[19]

A complete blood count and chemistry tests were obtained from the hospital database of all patients at the time of admission. Besides, the patient demographic characteristics, medical history, elapsed time since valve surgery, type and position of the prosthetic valve, rhythm disorders, New York Heart Association (NYHA) functional class, and leading symptoms were obtained from the hospital database and telephone interviews.

The Treatment Strategies

The low-dose, slow/ultra-slow infusion of thrombolytic therapy (TT) strategies were performed as appropriate, based on the protocols described in previous reports.[23-25] A TT regimen with 6 hours infusion of 25 mg t-PA (alteplase) without a bolus (repeat up to 6 times if needed, maximum total dose of 150 mg) was administered as a first-line therapy to NYHA functional class III-IV patients with obstructive prosthetic valve thrombosis who had no contraindications for TT. All patients underwent serial TTE and TEE examinations between each TT session. Thrombolytic therapy sessions with low-dose slow-infusion of t-PA were repeated until resolution of the obstruction was maintained. In patients with NYHA functional class I-II, a TT regimen with 25 hours infusion of 25 mg t-PA without a bolus (repeat up to 8 times if needed, maximum total dose of 200 mg) was administered as first-line therapy. Patients underwent serial TTE after each 12 hours, and immediate 2D and RT-3D TEE was performed in patients when a partial or complete resolution of the obstruction was observed.

All patients were operated on under general anesthesia and a median re-sternotomy was utilized. Mediastinal adhesions were opened, and cardiac and great vessels were exposed before systemic heparinization. Surgical intervention was performed using a standard cardiopulmonary bypass technique with central cannulation under moderate degree hypothermia. Myocardial protection was provided with

antegrade intermittent or continuous retrograde isothermic blood cardioplegia solution. Previously implanted valve and sutures were removed, the valvular annulus was clearly exposed, and interrupted pledgeted sutures were used. Subsequently, hot shot cardioplegia was delivered, and aortic cross-clamp was removed once the heart started beating. Once all parameters were satisfactory, cardiopulmonary bypass was weaned off and the sternum was closed.

In cases of PVE, the majority of patients were treated with empiric broad-spectrum antibiotics. If a patient was referred from another hospital, antibiotic treatment was administered according to the previous culture results. Subsequently, the patients were switched over to suitable antibiotics in accordance with their antibiotic susceptibility reports and standard recommendations. These recommendations were based on the European Society of Cardiology guidelines.[17]

RESULTS

A total of 16 patients with intermittent PHV dysfunction were included in the study. The preoperative demographic features, comorbidities, electrocardiographic, and laboratory findings of the patients are listed in Tables 1 and 2, respectively. There were 11 females and 5 males with an average age of 57 years (range, 25-80 years). All patients had left-sided mechanical PHVs. Two patients had aortic valve replacement (AVR), and 14 had mitral valve replacement (MVR); 12 of them had bileaflet and 2 had monoleaflet mitral prosthesis (Table 1). The shortest elapsed time after valve surgery was 15 days; the average time was 42 months. The most common reason for valve replacement was rheumatic mitral stenosis (n=7). The other causes were rheumatic mitral regurgitation (MR) (n=3), MR due to senile degeneration with chordal rupture (n=2), and ischemic MR (n=2), whereas the 2 patients had underwent AVR due to severe aortic stenosis with bicuspid aortic valve (Table 1).

The chief complaints on admission, etiologic causes, and treatment strategies of patients with intermittent PHV dysfunction are summarized in Table 3. The causes of dysfunction in 12 bileaflet mitral prosthesis were classified as follows: residual chordae (n=4), obstructive thrombus (OT) (n=2), non-obstructive thrombus (NOT) (n=2) (Figure 1, Video 1), vegetation (n=2), coexistence of pannus and OT (n=1), and pannus formation (n=1).

Surgical Therapy

Totally 4 of 16 patients required surgical therapy. The main clinical manifestations of surgery group included NYHA class 3 or 4 dyspnea (n=3) and CVA-related confusion (n=1) (Table 3). One of the patients who had residual chordae suffered severe intermittent MR in 1 of every 3-beat and presented with NYHA class 4 symptoms (Figures 2, 3 and Videos 2, 3). This patient also suffered from recurrent hospital admissions. Subsequently, the patient underwent reoperation. Intermittent MS due to OT was detected in 2 patients. One patient presented with ischemic CVA, while the other presented with NYHA class 4 symptoms. Reoperation was performed in both patients. Moreover, 1 patient had intermittent obstructive MS due to pannus formation, and reoperation was performed due to the patient's newly developed and progressive symptoms (NYHA-3). However, the patient (patient #12) died on the ninth day of the operation due to low cardiac output syndrome and acute kidney injury.

Table 1. Preoperative Demographics, Comorbidities, Baseline Clinical Characteristics, and Electrocardiographic Findings

Patient	Gender	Age	DM	HT	CVA	AF	CAD	Valve Type	ETSVS	Surgery Indication
1	M	51	0	1	0	0	0	AVR	26 M	Bicuspid aortic valve-aortic stenosis
2	M	80	1	1	0	1	1	AVR	66 M	Bicuspid aortic valve-aortic stenosis
3	F	64	0	1	1	1	0	MVR	1 M	Senile degeneration chordal rupture-mitral regurgitation
4	F	56	0	1	1	0	0	MVR	15 D	Rheumatic mitral regurgitation
5	F	62	1	1	1	0	0	MVR	212 M	Rheumatic mitral regurgitation
6	F	52	1	1	0	1	0	MVR	1 M	Rheumatic mitral regurgitation
7	M	66	0	1	0	0	0	MVR	47 M	Rheumatic mitral stenosis
8	F	36	0	0	0	0	0	MVR	37 M	Rheumatic mitral stenosis
9	F	53	0	0	0	0	0	MVR	60 M	Rheumatic mitral stenosis
10	F	25	0	0	0	0	0	MVR	21 M	Rheumatic mitral stenosis
11	F	40	0	0	0	0	0	MVR	6 M	Rheumatic mitral stenosis
12	M	60	1	1	0	1	0	MVR	54 M	Senile degeneration-chordal rupture-mitral regurgitation
13	M	54	1	0	0	0	1	MVR	6 M	Severe ischemic mitral regurgitation
14	F	65	0	1	0	0	1	MVR	43 M	Severe ischemic mitral regurgitation
15	F	47	0	0	0	1	0	MVR-MONO	61 M	Rheumatic mitral stenosis
16	F	48	0	1	0	1	0	MVR-MONO	35 M	Rheumatic mitral stenosis

DM, diabetes mellitus; HT, hypertension; CVA, cerebrovascular accident; AF, atrial fibrillation; CVA, coronary artery disease; ETSVS, elapsed time since valve surgery; MVR-MONO, MVR monoleaflet; M, Month; D, day.

Table 2. Patient's Laboratory Values

Patient	HGB (g/dL)	WBC (mm^3)	PLT ($10^3/\mu L$)	INR	CRP (mg/dL)	Creatinine (mg/dL)	BUN (mg/dL)	LDL (mg/dL)	HDL (mg/dL)	TG (mg/dL)	Blood Type
1	14.5	7.4	216	2.36	14	1.14	26	161	37	140	A RH+
2	12.1	5.1	145	2.1	0	0.98	36	126	35	159	0 RH+
3	14.1	6.4	263	1.03	0.4	0.75	14	158	58	215	B RH+
4	13	6	243	1.6	18	0.6	22	101	49	75	AB RH+
5	10.6	4.96	166	2.84	45	0.67	8	169	43	167	B RH+
6	8.6	18.5	181	3.16	3.29	0.92	61	145	48	178	B RH+
7	13.8	7.4	264	2.43	4.47	0.76	38	139	44	89	B RH+
8	8	9	424	1.97	5	0.53	31	70	45	57	A RH+
9	10.6	5.8	213	2.63	2.94	0.67	27.1	121	34	153	A RH–
10	14	8	233	1.4	5	0.58	16	100	62	122	0 RH–
11	10	4	154	1.89	11.9	4.15	84	68	35	62	0 RH+
12	12.7	5.4	150	1.96	0.85	1.08	29	183	35	161	A RH+
13	10.4	29	218	2.01	20.1	1.06	69	110	42	129	A RH–
14	10	12.8	459	4.63	4	1	38	105	66	140	A RH+
15	13.2	6.9	220	2.5	0	0.59	22	168	48	152	B RH+
16	12.1	7	179	1.42	3.11	0.77	19.19	101	44	122	AB RH–

HGB, hemoglobin; WBC, white blood cell; PLT, platelet; CRP, C-reactive protein; BUN, blood urea nitrogen; TG, triglycerides; INR, international normalized ratio.

Non-Surgical Therapy

The treatment modalities of the remaining patients were as follows: fibrinolytic therapy (n=4), antibiotic therapy (n=2), and routine medical monitoring (n=6). The main clinical manifestations of these patients included dyspnea (n=8), fever (n=2), and palpitations (n=2) (Table 3). Two patients with intermittent PHV dysfunction with residual chordae etiology were in stable clinical condition. Hence, the decision of medical follow-up was made. Two patients presented with intermittent moderate MR due to NOT (NYHA classes 2 and 3). Both of these patients received low-dose, ultra-slow infusion of tPA, and complete lysis was achieved. Two patients had intermittent PHV dysfunction due to the combination of pannus and thrombi. The intermittent MS was detected in 1 of them (monoleaflet) due to OT and pannus formation, and intermittent PHV dysfunction completely resolved after low-dose slow infusion of tPA. The other patient had NOT and pannus formation, and intermittent MR completely resolved after low-dose, ultra-slow infusion of TT. Two patients with PVE presented with fever. These patients had severe intermittent MR and were treated with antibiotic therapy for 6-8 weeks. In the other patient with monoleaflet MVR, a stuck valve was observed in 1 of 12 beats secondary to arrhythmia. As obstruction was observed infrequently, the patient was followed up with medical treatment. In the patients with AVR, one had moderate aortic regurgitation due to prominent calcification, and the other had moderate obstruction due to pannus formation. Follow-up under medical treatment was considered for these patients. In the patient with pannus, stuck valve formation occurred in 1 of 6 beats, and moderate aortic regurgitation arose in 1 of 2 beats in the patient with calcification. All non-surgical patients were discharged uneventfully.

Fifteen discharged patients (surgical and non-surgical) are followed up closely at 3-month intervals.

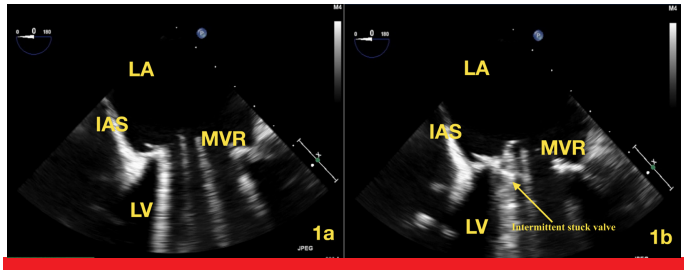

Figure 1. Transesophageal echocardiography images show intermittent entrapment due to thrombus, the arrow reveals stuck leaflet. LA, left atrium; LV, left ventricle; IAS, interatrial septum; MVR, mitral valve replacement.

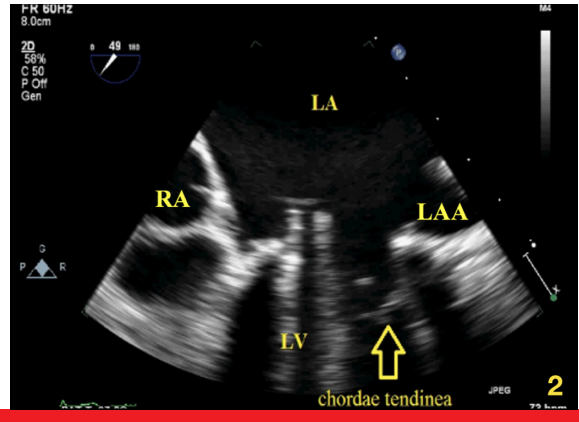

Figure 2. Transesophageal echocardiography images indicate residual chordae causes restraining the closure of mitral valve leaflet. LA, left atrium; LV, left ventricle; RA, right atrium.

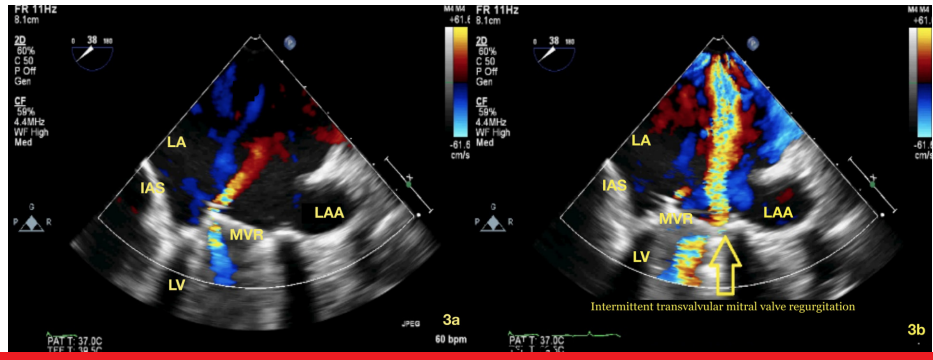

Figure 3. Transesophageal echocardiography image shows intermittent transvalvular mitral valve regurgitation due to entrapment by residual chordae. LA, left atrium; LV, left ventricle; LAA, left atrial appendage; IAS, interatrial septum; MVR, mitral valve replacement.

DISCUSSION

The major finding of the current study is that the entrapment frequency and the severity of dysfunction should be prioritized in making a treatment decision in patients with intermittent dysfunction of mechanical PHVs. Intermittent entrapment leads to suspended disc motion or immobilization in closed or open positions, resulting in obstruction or regurgitation. Consequently, intermittent PHV dysfunction may have catastrophic outcomes and necessitates prompt diagnosis and treatment.

The major underlying etiologies of intermittent prosthetic valve dysfunction are thrombus, pannus, or vegetation.[1-10] Also, Carlson et al[23] previously reported the etiology of intermittent malfunction of PHV due to wearing and technical specialty of valve type. Poppet (tilting disc) valves, well-known in the mid-1970s, had increased wear and reduced poppet substance. These disadvantages caused decreased rotation and irregular stress distribution across the disc. In terms of prosthetic valve thrombosis, bioprosthetic valves are the safest option. Mechanical valves in the mitral and aortic positions may have a thrombosis risk of 0.5%-8%; however, mechanical tricuspid valves have the highest risk ratio (20%).[24,25] The 2020 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines recommend urgent initial treatment with either slow-infusion, low-dose TT, or emergency surgery for symptomatic left-sided prosthetic valve thrombosis.[26] Hence, the low-dose slow or ultra-slow infusion of TT protocol was our treatment approach in patients with intermittent PHV dysfunction due to OT or NOT.[25-28] We observed full recovery without complication in 2 cases with OT and NOT, respectively.

Epidemiology of PVE is changing due to the following several factors. In developing countries, rheumatic disease is the primary IE etiology caused chiefly by *Streptococci* and has a poor prognosis with a low healthcare supply. However, in developed countries, patients are elderly and associated with advanced healthcare facilities. Thus, degenerative valves, prosthetic valves, and intracardiac devices have replaced rheumatic disease as the leading risk factor, with *Staphylococci* being the most frequently isolated pathogens.[29] In patients with left or right-sided endocarditis, specific or empiric antibiotic therapy should be initiated; in case of failure, a therapy modification may be required.[30] A heart valve team should make a decision about the optimal timing of surgical intervention.[31] In the present study, 2 patients responded well to 6 weeks of antibiotherapy.

Pannus formation is a well-known non-structural valvular dysfunction. Extreme overgrowth of fibroblastic tissue due to non-immune reactions is the major underlying pathology. Collagen and elastic fibrous tissue conducted by endothelial cells, chronic inflammatory cells infiltration, and myofibroblasts constitutes the primary structure of pannus overgrowth,[32] which may reduce the effective orifice area of the prosthetic valve and cause obstruction. Tissue overgrowth burden is associated with the degree of obstruction.[33] Nevertheless, surgical treatment of pannus-related obstruction has shown relatively good results.[34] In our series, 3 patients had an intermittent PHV dysfunction due to pannus formation. One of the patients with monoleaflet MVR also had NOT. We determined that the entrapment was due to the presence of NOT. After successful TT, complete clinical recovery was maintained. One patient who underwent bileaflet MVR 5 years ago developed pannus overgrowth. Redo surgery was our traditional treatment approach for this patient. On the other hand, 1 patient who had pannus formation after AVR had a moderate obstruction due to infrequent development of stuck valve. Further pannus growth may result in permanent disc entrapment; thus, a strict and regular follow-up was recommended for this patient.

Except for the cases mentioned above, an arrhythmia-related intermittent stuck valve has not been previously reported. Atrial fibrillation is characteristically followed by irregular ventricular responses, which may not provide effective stroke volume.[35] In such cases, the prosthetic valve may not properly open or close. Underlying heart disease and continuous atrial fibrillation itself have an impact on atrial remodeling. Progressive remodeling results in irreversible structural changes, and AF becomes permanent. Several implications have been well identified in AF management, including rhythm control, rate control, and prevention of thromboembolism.[36] Our approach in the case was rate control, and 1 month later, the follow-up evaluation revealed no trace of an intermittent entrapment.

Table 3. Clinical Terms Associated with Patients Who Suffered Intermittent Entrapment Mechanical Valve.

Patient	Chief Complaint on Admission	Complication (intermittent)	Entrapment Frequency	Gradient (mm Hg)	NYHA Class	Type of Admission-Inspection Criteria	Hospital Readmission (in last 30 days)	Etiology	Follow-Up Time	Treatment	Survival During Follow Up
1	Palpitation	Moderate AR	1 of 2	31-21	1	Routine monitoring	No	Severe calcification	46 months	Medical	Yes
2	Dyspnea	Moderate AS	1 of 6	22-10	1	Routine monitoring	Yes	Pannus	32 months	Medical	Yes
3	Dyspnea	Severe MR	1 of 4	14-7	3	URGENT-CLINICAL SUSPICION	Yes	Not	34 months	TT	Yes
4	Dyspnea	Severe MS	1 of 3	21-13	4	Urgent-clinical suspicion	No	OT	43 months	Surgery	Yes
5	Confusion-CVA	Severe MS	1 of 2	25-14	1	Urgent-clinical suspicion	No	OT	28 months	Surgery	Yes
6	Fever	Severe MR	1 of 5	6-3	2	Urgent-clinical suspision	No	Vegetation	51 months	Antibiotherapy	Yes
7	Dyspnea	Moderate MR	1 of 4	14-6	2	Routine monitoring	Yes	Residual chorda	18 months	Medical	Yes
8	Dyspnea	Mild MR	1 of 5	12-6	2	Routine monitoring	No	Not	34 months	TT	Yes
9	Dyspnea	Severe MS	1 of 3	27-12	3	Urgent-clinical suspicion	Yes	Pannus	41 months	Surgery	Yes
10	Dyspnea	Severe MS	1 of 3	15-6	3	Urgent-clinical suspision	Yes	OT+Pannus	26 months	TT	Yes
11	Palpitation	Severe MR	1 of 7	9-4	1	Routine monitoring	No	Residual chorda	37 months	Medical	Yes
12	Dyspnea	Severe MR	1 of 3	20-8	4	Urgent-clinical suspision	Yes	Residual chorda	2 months	Surgery	No
13	Fever	Severe MR	1 of 3	33-16	1	Urgent-clinical suspision	Yes	Vegetation	28 months	ANTIBIOTHERAPY	Yes
14	Dyspnea	Severe MR	1 of 12	12-5	1	Routine monitoring	No	Residual chorda	24 months	Medical	Yes
15	Dyspnea	Severe MR	1 of 3	21-8	3	Urgent-clinical suspision	Yes	Pannus+not	17 months	TT	Yes
16	Dyspnea	Severe MS	1 of 12	9-3	1	Routine monitoring	No	Arrhythmia	13 months	Medical	Yes

CVA, cerebrovascular accident; AR, aortic regurgitation; MR, mitral regurgitation; AS, aortic stenosis; MS, mitral stenosis; TT, thrombolytic therapy; OT, obstructive thrombosis; NOT, non-obstructive thrombosis; NYHA, New York Heart Association.

Establishing a diagnosis of prosthetic valve malfunction requires various methods. Transthoracic echocardiography is the first step imaging modality for the assessment of prosthetic valves. Moreover, 2D or RT-3D TEE, cardiac CT, or fluoroscopy may be needed when valve dysfunction is suspected. Diagnosing prosthetic valve obstruction can be difficult, but diagnosing an intermittent stuck valve is even more challenging. Multicycle image acquisition is time-consuming and causes device storage shortages. Prolonged and detailed imaging is necessary for patients with very high clinical suspicion. In the current study, all cases were diagnosed by 2D and 3D-RT TEE, whereas 2D TTE and fluoroscopy helped in the diagnosis of 2 patients individually.

The strategy of diagnosis and treatment in prosthetic valve dysfunction is previously well-identified. Nevertheless, planning the strategy in intermittent dysfunction is challenging. We suggest that the fundamental decision for performing an intervention in patients with intermittent stuck valves depends on the patient's clinical status and the degree of obstruction or regurgitation. Two patients with AVR in our series had moderate stenosis and regurgitation with similar intermittent entrapment frequency. Because of the moderate severity of echocardiographic findings and the good clinical status of the patients, we decided to follow up with medical treatment. The frequency of entrapment of the prosthetic valve constitutes the clinical severity. Patient 4 had severe intermittent MR in 1 of 4 cycles due to obstructive thrombus with the NYHA class 3 heart failure. patient 11 had severe intermittent MR due to residual chords but with rare entrapment frequency (1 of 7); the patient was in a mild condition as NYHA class 1. We noticed the same difference on the obstruction side in patients 9 and 16. In comparison to these patients, the essential difference was the frequency of entrapment.

Study Limitations

It is important to emphasize the limitations pertaining to the methods of this study. First, this was a retrospective study and included a relatively small patient population. However, it should be noted that intermittent dysfunction is a very rare complication of PHV replacement. Second, the absence of surgical confirmation of the underlying pathologies was another limitation. Third, long-term outcomes of this patient population are lacking.

CONCLUSION

The intermittent malfunction of the prosthetic valve is rarely defined and may have catastrophic outcomes and necessitates a comprehensive approach. It requires elaborative examination in symptomatic patients with prosthetic valves, and TEE is crucial for differential diagnosis. When making a treatment decision in these patients with native or prosthetic heart valves, the degree of regurgitation or stenosis is essential. In particular, for intermittent PHV dysfunction, the frequency of entrapment plays a fundamental role in making treatment decisions.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of University Health Sciences Erzurum Training and Research Hospital (Approval no: 2021/22-282).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – S.Kalkan; Design – A.G.; Supervision – M.Ö.; Materials – E.B.; Data collection – M.F.K.; Analysis or Interpretation – M.K., M.O.G., S.G.; Literature Review – M.Y.; Writer – S.Kalkan; Critical Review – S.Karakoyun.

Declaration of Interests: The authors declare that they have no competing interest.

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Video 1: Intermittent entrapment due to non-obstructive thrombus is seen in the 2D-TEE image. 2D-TEE, 2-dimensional transesophageal echocardiography.

Video 2: A 2D-TEE image displays intermittent entrapment due to residual chorda tendinea. 2D-TEE, 2-dimensional transesophageal echocardiography.

Video 3: Color Doppler assessment shows intermittent severe mitral regurgitation.

REFERENCES

1. Rajathurai T, Shivu GN, Wheeler R. Episodic circulatory collapse caused by intermittent prosthetic aortic valve dysfunction. *Heart Surg Forum*. 2012;15(1):E9-E11. [CrossRef]
2. Fan D, Makaryus AN, Hamik A, Finn AV, Isselbacher EM. Prosthetic valve dysfunction presenting as intermittent acute aortic regurgitation. *Echocardiography*. 2008;25(8):925-927. [CrossRef]
3. Fadel BM, Alassas K, Dahdouh Z, Pergola V, Galzerano D, Di Salvo G. Intermittent malfunction of a prosthetic valve-A diagnostic challenge. *Echocardiography*. 2016;33(6):916-919. [CrossRef]
4. Moorthy N, Ananthakrishna R, Rao DPV, Manjunath SC, Nanjappa MC. Prosthetic mitral valve thrombosis, malfunction, and paroxysmal mitral regurgitation. *Echocardiography*. 2018;35(3):388-390. [CrossRef]
5. Shah D, Vijaykumar M, Chandrasekhar K, Reddy KN, Girinath MR. Periodic intermittent electromechanical dissociation: hemodynamic correlate of a malfunctioning mechanical prosthetic valve. *Cathet Cardiovasc Diagn*. 1996;38(4):377-378. [CrossRef]
6. Fadel BM, Bakarman H, Bech-Hanssen O, Pergola V, Di Salvo G. Intermittent entrapment of a prosthetic mitral valve disc: what you see is not what you get. *Circulation*. 2014;129(2):e11-e13. [CrossRef]
7. Foukarakis E, Papoutsakis A, Kafarakis P, Rogdakis E, Lazaros G. A case of intermittent, noncyclic prosthetic aortic valve regurgitation. *Hellenic J Cardiol*. 2020;61(4):281-283. [CrossRef]
8. Shahid M, Sutherland G, Hatle L. Diagnosis of intermittent obstruction of mechanical mitral valve prostheses by Doppler echocardiography. *Am J Cardiol*. 1995;76(17):1305-1309. [CrossRef]
9. Güner A, Kalçık M, Yesin M, Özkan M. Intermittent malfunction and regurgitation of a mitral prosthetic valve due to entrapment by a residual subvalvular apparatus. *Echocardiography*. 2018;35(12):2092-2094. [CrossRef]

10. Lancellotti P, Pibarot P, Chambers J, et al. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2016;17(6):589-590. [CrossRef]
11. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39(33):3021-3104. [CrossRef]
12. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37(27):2129-2200. [CrossRef]
13. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J* 2020;41(3):407-477. [CrossRef]
14. Anderson J, Glynn LG. Definition of chronic kidney disease and measurement of kidney function in original research papers: a review of the literature. *Nephrol Dial Transplant*. 2011;26(9):2793-2798. [CrossRef]
15. Easton JD, Saver JL, Albers GW, et al. American Heart Association; American Stroke Association Stroke Council. *Stroke*. 2009;40(6):2276-2293. [CrossRef]
16. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals From the American Heart Association/American Stroke Association. *Stroke*. 2018;49(3):e46-e110. [CrossRef]
17. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European association of nuclear medicine (EANM). *Eur Heart J*. 2015;36(44):3075-3128. [CrossRef]
18. Ozkan M, Gündüz S, Yildiz M, Duran NE. Diagnosis of the prosthetic heart valve pannus formation with real-time three-dimensional transoesophageal echocardiography. *Eur J Echocardiogr*. 2010;11(4):E17. [CrossRef]
19. Gündüz S, Kalçık M, Gürsoy MO, Güner A, Özkan M. Diagnosis, treatment & management of prosthetic valve thrombosis: the key considerations. *Expert Rev Med Devices*. 2020;17(3):209-221. [CrossRef]
20. Ozkan M, Gürsoy OM, Astarcıoğlu MA, et al. Real-time three-dimensional transesophageal echocardiography in the assessment of mechanical prosthetic mitral valve ring thrombosis. *Am J Cardiol*. 2013;112(7):977-983. [CrossRef]
21. Anwar AM, Nosir YF, Alasnag M, Chamsi-Pasha H. Real time three-dimensional transesophageal echocardiography: a novel approach for the assessment of prosthetic heart valves. *Echocardiography*. 2014;31(2):188-196. [CrossRef]
22. Gündüz S, Özkan M, Kalçik M, et al. Sixty-four-section cardiac computed tomography in mechanical prosthetic heart valve dysfunction: thrombus or pannus. *Circ Cardiovasc Imaging*. 2015;8(12):e003246. [CrossRef]
23. Carlson CJ, Collins JJ Jr, Ockene IS, Cohn LH, Dalen JE. Mitral regurgitation due to intermittent prosthetic valvular dysfunction. *Chest*. 1977;71(1):90-93. [CrossRef]
24. Özkan M, Gündüz S, Gürsoy OM, et al. Ultraslow thrombolytic therapy: a novel strategy in the management of PROsthetic MEchanical valve Thrombosis and the prEdictors of outcomE: the Ultra-slow PROMETEE trial. *Am Heart J*. 2015;170(2):409-418. [CrossRef]
25. Özkan M, Gündüz S, Biteker M, et al. Comparison of different TEE-guided thrombolytic regimens for prosthetic valve thrombosis: the TROIA trial. *JACC Cardiovasc Imaging*. 2013;6(2):206-216. [CrossRef]
26. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. *Circulation* 2021;143(5):e72-e227. [CrossRef]
27. Guner A, Kalcik M, Gursoy MO, Gunduz S, Ozkan M. How to perform and manage low-dose and slow/ultra-slow tissue type plasminogen activator infusion regimens in patients with prosthetic valve thrombosis. *J Thromb Thrombolysis*. 2018;46(3):399-402. [CrossRef]
28. Guner A, Gunduz S, Gursoy MO, Bayam E, Kalkan S, Ozkan M. The PROMETEE protocol is safe and efficient in patients with prosthetic valve thrombosis. *Echocardiography*. 2018;35(9):1487. [CrossRef]
29. Ambrosioni J, Hernandez-Meneses M, Téllez A, et al. The changing epidemiology of infective endocarditis in the twenty-first century. *Curr Infect Dis Rep*. 2017;19(5):21. [CrossRef]
30. Gould FK, Denning DW, Elliott TS, et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother*. 2012;67(2):269-289. [CrossRef]
31. Pettersson GB, Hussain ST. Current AATS guidelines on surgical treatment of infective endocarditis. *Ann Cardiothorac Surg*. 2019;8(6):630-644. [CrossRef]
32. Teshima H, Hayashida N, Yano H, et al. Obstruction of St Jude Medical valves in the aortic position: histology and immunohistochemistry of pannus. *J Thorac Cardiovasc Surg*. 2003;126(2):401-407. [CrossRef]
33. Koo HJ, Ha H, Kang JW, et al. Impact of pannus formation on hemodynamic dysfunction of prosthetic aortic valve: pannus extent and its relationship to prosthetic valve motion and degree of stenosis. *Clin Res Cardiol*. 2018;107(7):554-564. [CrossRef]
34. Van den Brink RB. Evaluation of prosthetic heart valves by transesophageal echocardiography: problems, pitfalls, and timing of echocardiography. *Semin Cardiothorac Vasc Anesth*. 2006;10(1):89-100. [CrossRef]
35. Edmands RE, Greenspan K, Fisch C. The role of inotropic variation in ventricular function during atrial fibrillation. *J Clin Invest*. 1970;49(4):738-746. [CrossRef]
36. Iwasaki YK, Nishida K, Kato T, Nattel S. Atrial fibrillation pathophysiology: implications for management. *Circulation*. 2011;124(20):2264-2274. [CrossRef]