



# Diagnostic accuracy of two-dimensional and three-dimensional transesophageal echocardiography in detecting pannus and thrombus in left mechanical valve obstruction

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**Aims:** The aim of this study was to determine the accuracy of two-dimensional and three-dimensional transesophageal echocardiography (TEE) in the detection of pannus and thrombus in left mechanical valve obstruction (LMVO) compared with surgical and histopathology findings.

**Materials and methods:** Patients with suspected LMVO on transthoracic echocardiography were enrolled consecutively. All patients underwent two-dimensional and three-dimensional TEE, and open-heart surgery to replace obstructed valves. Macroscopic and microscopic analysis of the excised masses was used as the gold standard for the diagnosis of thrombus and/or pannus.

**Results:** Forty-eight patients [34 women (70.8%), age  $49 \pm 13$  years, New York Heart Association II: 68.8%, New York Heart Association III: 31.2%] were enrolled. In the diagnosis of thrombus, the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of three-dimensional TEE were 89.2, 72.7, 85.4, 91.7, and 66.7%, respectively, compared with those of two-dimensional TEE (42.2, 66.7, 43.8, 95, and 7.1%, respectively). In the diagnosis of pannus, the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of three-dimensional TEE were 53.3, 100, 85.4, 100, and 82.5%, respectively; compared with those of two-dimensional TEE (7.4, 90.5, 43.8, 50, and 43.2%, respectively). Receiver operating characteristic curves depict that the area under the curves of three-dimensional TEE was higher than the area under the curves of two-dimensional TEE in both diagnoses of thrombus and pannus (0.8560 vs. 0.7330,  $P = 0.0427$  and 0.8077 vs. 0.5484,  $P = 0.005$ , respectively).

**Conclusions:** This study indicated that three-dimensional TEE had a higher diagnostic value than two-dimensional TEE in the detection of thrombus and pannus in patients with LMVO, and can be a reliable imaging modality to identify the causes of LMVO.

**Keywords:** left mechanical valve obstruction, pannus, prosthetic valve complication, three-dimensional transesophageal echocardiography, thrombus

## Introduction

Valvular heart disease is a global health problem. The use of prosthetic heart valves continues to increase. Valve obstruction is a life-threatening complication of mechanical valves with significant morbidity and mortality<sup>[1]</sup>. The most common causes are

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## HIGHLIGHTS

- Prosthetic valve obstruction is a severe complication of mechanical valve replacement; the most common causes are thrombosis or pannus formation; differentiating pannus and thrombus is essential for the selection of proper treatment.
- Detecting thrombus or pannus by either two-dimensional transthoracic echocardiography (TTE) or two-dimensional transesophageal echocardiography (TEE) is often challenging.
- Three-dimensional TEE is a helpful and valuable diagnostic modality to identify the cause of valve obstruction when compared with surgical and histopathological findings and should be performed in patients with suspected left mechanical valve obstruction (LMVO).

thrombus and pannus<sup>[2,3]</sup>. Differentiating between thrombus and pannus in LMVO is important, even in patients not indicated for thrombolytic therapy due to severe symptoms and large masses.

Specifically, thrombus debridement might be favored over replacement, especially in a patient with high surgical risk to reduce the cardiopulmonary bypass time, and debridement might have a lower mortality rate<sup>[4]</sup>. In regards to patients with pannus, valve replacement is preferred because the fibrotic tissues can continue growing over mechanical valve surfaces<sup>[5]</sup>. The decision to replace or debride the obstructive prosthesis is often made at the time of surgery; nevertheless, the diagnosis of the cause of LMVO in advance of surgery facilitates preoperative management. TTE is a first-line imaging modality to detect LMVO<sup>[6]</sup> as well as the standard for evaluation of the hemodynamic performance of valves; an increase in transvalvular gradient and a decrease in orifice area can signal the development of prosthetic dysfunction. The quality of images varies according to patients' conditions, echocardiographers' experience, and acoustic shadowing of mechanical valves. Thus, differentiating between thrombus and pannus by TTE is challenging. Fluoroscopy can help recognize leaflet motion abnormalities but cannot provide precise information regarding the identification of thrombus or pannus. TEE provides a better assessment of the prosthesis<sup>[7]</sup> and is recommended as a next step to differentiate thrombus from pannus<sup>[6]</sup>. Despite better images of prostheses provided, two-dimensional TEE is limited by problems of acoustic shadowing. Real-time three-dimensional TEE yields full dimension images of masses are valuable to distinguish thrombus from pannus formation. Recent studies demonstrated that multidetector-row computed tomography (MDCT) is another effective tool for cardiac valve imaging<sup>[8,9]</sup>, but MDCT is expensive, involves radiation, and puts patients at risk from effects caused by contrast agents.

Data on the accuracy of two-dimensional TEE and three-dimensional TEE in the differentiation of thrombus from pannus formation are scarce<sup>[10-13]</sup>. This study was conducted to investigate the value of two-dimensional TEE and three-dimensional TEE to differentiate thrombus from pannus in LMVO patients, with a diagnosis confirmed by cardiac surgery and histopathology.

## Methods

### *Patient population and study design*

The study recruited patients with obstruction of mechanical prosthetic valves detected by two-dimensional TTE from January 2019 to June 2022, who underwent a two-dimensional TEE and three-dimensional TEE before redo valve replacement. Patients with contraindications to or cautions regarding TEE (including esophageal diseases, cervical spine disease, hiatal hernia, coagulopathy, prior chest radiation, or facial or airway trauma), were excluded. All patients had surgical and histopathologic confirmation of pannus and/or thrombus as the underlying cause of LMVO. Data of patient characteristics including age, sex, medical history, physical and laboratory examination, and surgical records were collected. Patients were considered as having inadequate anticoagulation if the international normalized ratio (INR) < 2 with only aortic mechanical valve replacement, and if INR < 2.5 with only mitral mechanical valve replacement or both mitral and aortic mechanical valve replacement on 2 or more INR measurements. If two INR levels were both subtherapeutic or therapeutic, we reported the first INR value. In cases in which the two INR values were inconsistent, the third INR value was taken and reported<sup>[6]</sup>.

### *Transthoracic echocardiography*

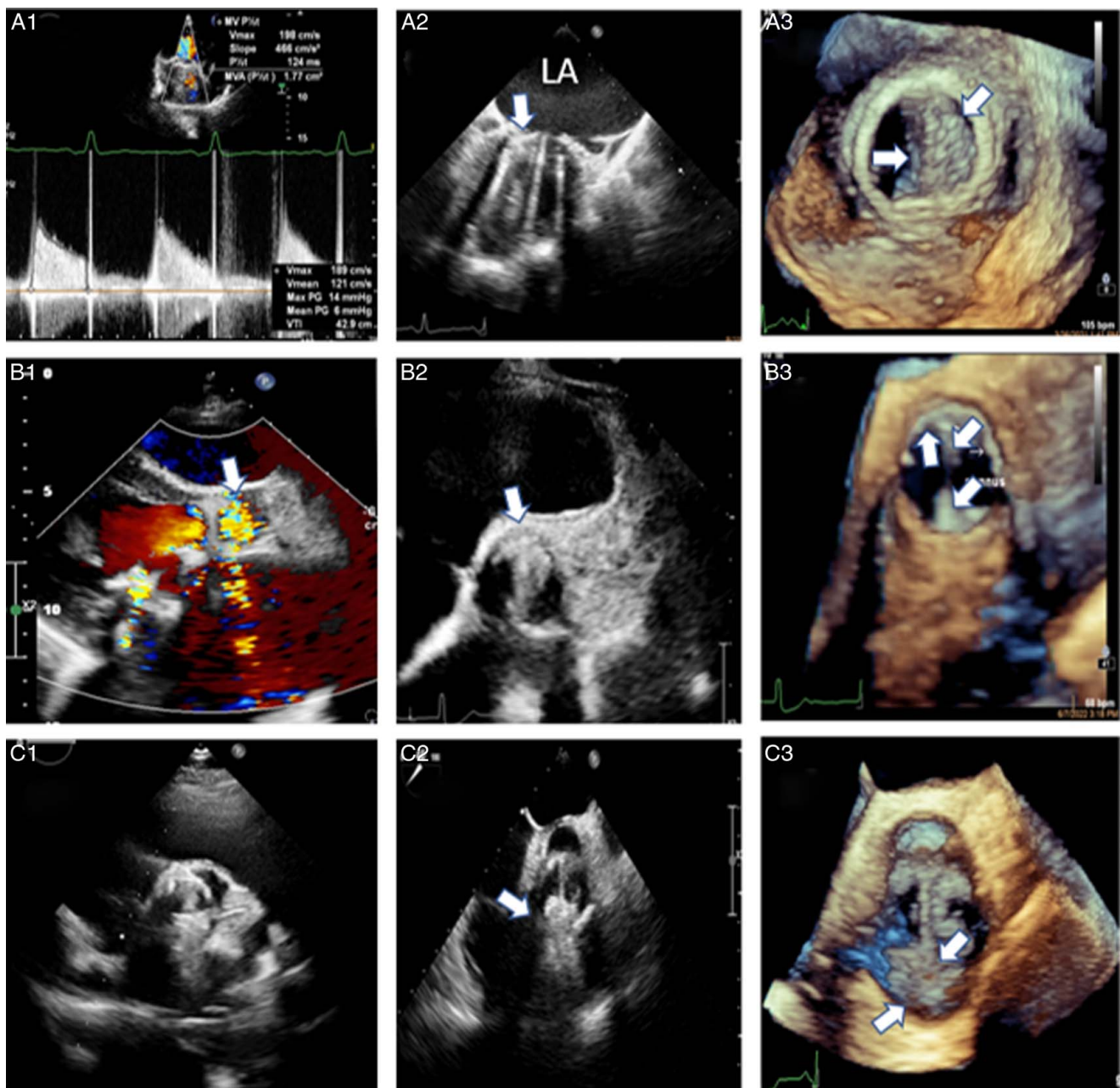
TTE was performed with a 3 MHz transducer (Fig. 1: A1, B1, C1). For aortic mechanical valves, peak velocity (m/s) and mean gradients (mmHg) were calculated as well as effective aortic valve area (cm<sup>2</sup>). For mitral mechanical valves, peak velocity (m/s), mean gradient (mmHg), pressure half-time (ms) as well as mitral valve area by pressure half-time (cm<sup>2</sup>) were calculated. The criteria defining possible valve obstruction were a valve area  $\leq 2$  cm<sup>2</sup>, mean gradient  $\geq 6$  mmHg, and peak velocity  $> 1.9$  m/s for mechanical mitral valves and an effective orifice area  $< 1.1$  cm<sup>2</sup>, mean gradient  $\geq 20$  mmHg, and peak velocity  $\geq 3$  m/s for mechanical aortic valve<sup>[14]</sup>.

### *Transesophageal echocardiography*

TEE was performed using systems with a 5 MHz multiplane two-dimensional probe (Fig. 1: A2, B2, C2) and a three-dimensional probe (Fig. 1: A3, B3, C3). Two-dimensional images were interpreted before the three-dimensional images were analyzed. Live three-dimensional (narrowed-angle), three-dimensional zoom, and full-volume modes were used to image the prosthetic valves with optimized gain settings. Masses seen on the prostheses were diagnosed as thrombus based on mobility, shape (globular), echo density (similar to that of the myocardium), and location (attached to the valve occluder or sewing ring or both). Masses were identified as pannus if firmly fixed, demonstrating echo density brighter than the myocardium and similar to the valve housing, and involving attachment to the valve apparatus (valve housing and pivot guards)<sup>[14]</sup>. The largest diameter and the length of the mass, if present, were measured on three-dimensional TEE. The size of the masses was not quantified on two-dimensional TEE. TTE and TEE imaging were performed and were interpreted by two experienced cardiologists. The cardiologists were unaware of the surgical and pathologic findings.

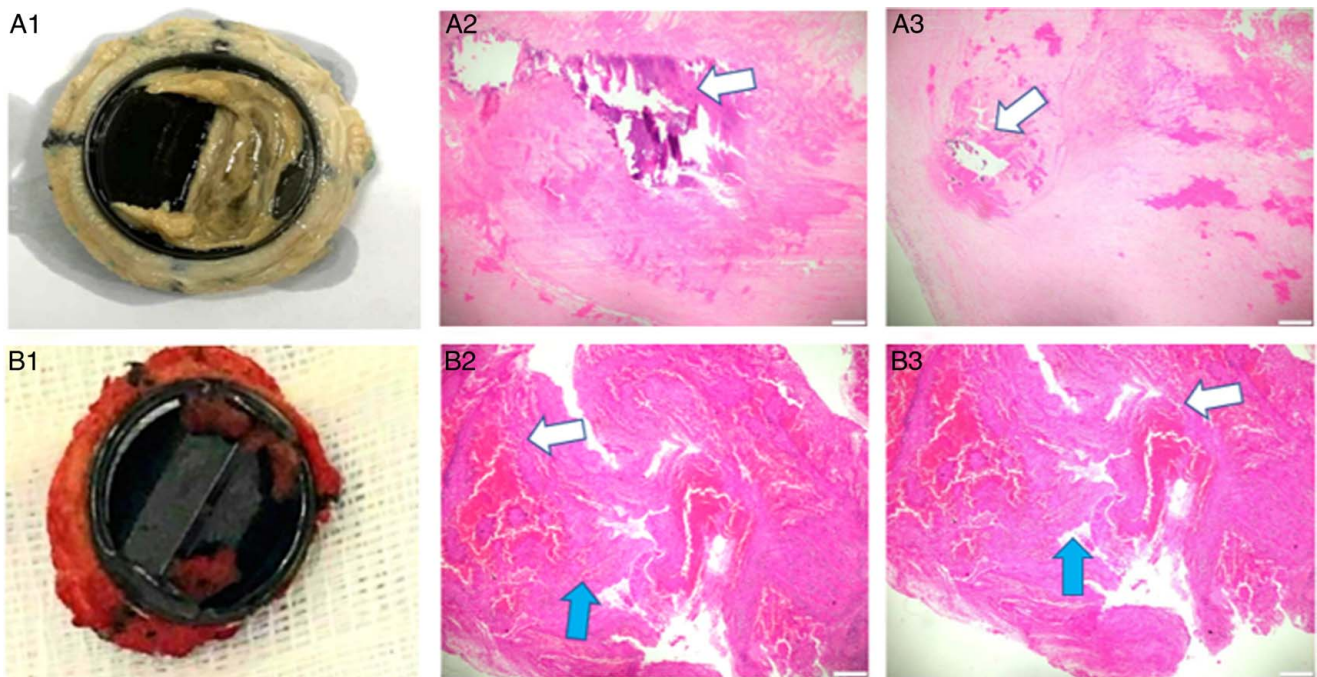
### *Surgery and histopathology*

Cardiac surgery was performed using cardiopulmonary bypass by experienced cardiovascular surgeons. All reoperations were done under moderate hypothermic cardiopulmonary bypass with cold potassium cardioplegia, and they were performed via a repeat median sternotomy. The surgeons examined the mechanical valves before and after removal from the tissue bed to confirm the obstruction of the leaflets as well as the location (left ventricular, left atrium, aortic) and shapes of masses (Fig. 2: A1, B1). The histologic examination was carried out by the pathologist to confirm the surgical findings (Fig. 2: A2, A3, B2, B3). The specimens were fixed in 10% buffered formalin, embedded in paraffin, and then sectioned into slides of 4  $\mu$ m. Slides were stained by hematoxylin-eosin. The association of thrombus with pannus and their positions on the prosthetic surfaces were also assessed, and surgeons decided the main cause of obstruction when there was both thrombus and pannus. Microscopic features of pannus are characterized by the excessive overgrowth of granulation tissue composed of mesenchyme-derived and bone marrow-derived cells, whereas thrombus is composed of fibrin in which erythrocytes, platelets, and leukocytes are enmeshed, with blood vessels walls involved<sup>[15]</sup>. The histopathologists were unaware of the results of three-dimensional TEE and reviewed characteristics of excised masses independently.



**Figure 1.** Two-dimensional TTE, two-dimensional TEE, and three-dimensional TEE static images of three cases with mechanical valve obstruction. (A) Thrombus on the bi-leaflet mechanical mitral valve was confirmed by surgical pathology. (A1) Two-dimensional TTE apical four-chamber view: Elevated transmitral Doppler gradients (14 mmHg) and decreased valve area ( $1.4 \text{ cm}^2$ ) (smaller than previous TTE examination), aberration of opening spikes was seen on continuous wave Doppler. (A2) Two-dimensional TEE midesophageal  $60^\circ$  view: the motion of one disk was normal; the other disk was immobilized (white arrow). (A3) Three-dimensional TEE en-face view of a mitral prosthesis from the left atrial (LA) perspective showed a large, irregular mass attached to the obstructed disk. (B) Pannus on mechanical aortic valve was confirmed by surgical pathology. (B1) Two-dimensional TTE parasternal long axis view: High-velocity turbulent flow suggested an aortic prosthetic obstruction (white arrow). (B2) Two-dimensional TEE midesophageal  $70^\circ$  view showed suspected pannus visualized as a dense mass on a tilting-disk (white arrow). (B3) En-face three-dimensional TEE view of aortic prosthesis revealed small, centripetal masses identified as pannus. (C) A mass which was not precisely-characterized on two-dimensional TTE, two-dimensional TEE, and three-dimensional TEE then was identified as pannus at surgical pathology. (C1) Two-dimensional TTE parasternal short-axis view of the aortic valve: The shape and the echo density of the mass was not adequately visualized due to the distance from the transducer and the oblique angle of the ultrasound beam. (C2) Two-dimensional TEE midesophageal  $70^\circ$  image of the aortic valve showed a mass on the prosthetic ring. The shape and the echo density were not well depicted. (C3) Three-dimensional TEE en-face view of the prosthesis from the aortic perspective showed several masses that were consistent with thrombus (white arrow). TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.





**Figure 2.** (A1) Annular pannus on the excised mechanical aortic valve. (A2, A3): The histological findings of pannus with calcification (white arrow). (B1) Thrombus on the excised mitral mechanical valve. (B2, B3): The histological findings of thrombus: red blood cells (white arrow) surrounded by fibrin accumulation (blue arrow) (hematoxylin-eosin staining, magnification  $\times 40$ ).

### Statistics

Statistical analysis was performed with SPSS 19.0 (IBM SPSS Inc.). Descriptive statistics were reported as mean, SD for continuous variables as the frequency with percentages for the categorical variables. The variables were investigated whether they were approximately normally distributed with the use of the Shapiro–Wilk test. Comparison between two groups for continuous variables with normal distribution used Student *t*-test, while with continuous variables with non-normal distribution used Mann–Whitney *U*-test. The proportions were compared between groups using Fisher’s exact test or the chi-square test. The sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive values (NPV) were assessed in the standard manner. To assess the predictive ability of the two-dimensional TEE and three-dimensional TEE, logistic regression was performed. Associated receiver operating characteristic curves for predicted probabilities were drawn for a diagnostic model with the results of two-dimensional TEE, three-dimensional TEE, and histopathology. The corresponding areas under the curve along with their 95% CIs were calculated. The significance level was accepted as *P*-value less than 0.05.

### Ethical approval

Informed consent was obtained from each patient, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the ethical committee.

### Reproducibility

The qualitative and quantitative parameters on both TTE and TEE of masses were reviewed in 12 randomly selected patients to assess reproducibility. These data were analyzed by two independent cardiologists.

### Results

#### Patient characteristics

Fifty patients were prospectively enrolled in the study. Of those, two patients were excluded since they were in urgent conditions, and underwent reoperation without TEE. Hence, 48 patients with LMVO were included. There were no any adverse events from performing two-dimensional TTE, two-dimensional TEE, and three-dimensional TEE. There were 34 women (70.8%) and 14 men (29.2%), with a mean age of  $49 \pm 13$  years, 100% of patients were Asian. In all cases, there were not any missing data. The dysfunctional mechanical valves included 13 aortic and 35 mitral valves. Compared with patients with aortic prostheses, patients with mitral prostheses had a higher prevalence of atrial fibrillation (60 vs. 23.1%,  $P = 0.02$ ) and a higher LAV index (82 vs. 56 ml/m<sup>2</sup>,  $P = 0.02$ ).

The clinical variables of patients are described in Table 1. All patients were symptomatic. The prevalence of poor functional capacity (New York Heart Association class III) was 31.2%. Histopathological results confirmed 35 cases with thrombus and 13 cases with pannus. Thrombus accounted for 91.4% of obstructed mechanical mitral valves; pannus accounted for 76.9% of obstructed mechanical

**Table 1**  
**Patient clinical characteristics**

Variables	n (%)/ Mean ± SD
Patient demographics	
Women	34 (70.8)
Age (years)	49 ± 13
BMI (kg/m <sup>2</sup> )	21.6 ± 2.2
BSA (m <sup>2</sup> )	1.6 ± 0.1
Time from valve replacement to reoperation (months)	57 ± 38.5
Time from 3-dimensional TEE to reoperation (days)	3.7 ± 1.4
LMVO site	
Mitral	35 (72.9)
Aortic	13 (27.1)
Type of obstructed valve	
Mitral valve	
Sorin carbon (BL)	3 (8.6)
Medtronic (BL)	5 (14.3)
St-Jude (BL)	6 (17.1)
Carbomedics (BL)	12 (32.3)
On-X (BL)	9 (25.7)
Aortic valve	
Medtronic	4 (30.8)
Carbomedics	6 (46.2)
On-X	3 (23.1)
Atrial fibrillation	
NYHA	24 (50)
I	0 (0)
II	33 (68.8)
III	15 (31.2)
History of rheumatic valvular disease	37 (77.1)
Pregnancy	2 (4.2)
Hypertension	8 (16.7)
Diabetes mellitus	5 (10.4)
Hyperlipidemia	11 (22.9)
Coronary artery diseases	3 (6.3)
INR	2.2 ± 1.0
Echocardiography variables	
Mean transvalvular gradients (mmHg)	24.3 ± 17.2
Maximum transvalvular gradients (mmHg)	40.2 ± 29.0
Valve areas (cm <sup>2</sup> )	1.0 ± 0.5
LVEF (%)	58.5 ± 9.6
Diameter long axis of RV (mm)	23.2 ± 5.8
FAC (%)	38.3 ± 5.1
PASP (mmHg)	49.0 ± 14.2
LAVi (ml/m <sup>2</sup> )	75.2 ± 35.9
Surgical and histopathological data	
Cause of LMVO	
Thrombus	33 (68.8)
Pannus	13 (27.1)
Both	2 (4.1.7)
Mitral valve: thrombus/pannus	32/3 (91.4/8.6)
Aortic valve: thrombus/pannus	3/10 (23.1/76.9)
Other valve injuries	
Mitral valve	4 (11.4)
Severe tricuspid valve regurgitation	1 (7.7)
Aortic valve	6 (46.2)
Severe mitral valve regurgitation	
Severe tricuspid valve regurgitation	
Valve replacement type	
Mechanical valve	14 (29.2)
Bioprosthetic valve	34 (70.8)

BL, bi-leaflet; BSA, body surface area; FAC, fractional area change; LAVi, left atrial volume index; LMVO, left mechanical valve obstruction; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PASP, pulmonary arterial systolic pressure; RV, right ventricle.

**Table 2**  
**Comparison of clinical characteristics and transthoracic echocardiography Doppler results between patients with pannus and patients with thrombus**

	Mean ± SD/n (%)		
	Thrombus (n=35)	Pannus (n=13)	P
Age (years)	46 ± 12	56 ± 11	0.021
Time from valve replacement to reoperation (months)	46 ± 33	86 ± 38	0.001
NYHA III	13 (37.1)	2 (15.4)	0.002
INR	2.2 ± 1.2	2.0 ± 0.6	0.514
Suboptimal INR	25 (71.4)	10 (76.9)	0.712
Atrial fibrillation	23 (65.7)	1 (7.7)	0.000
Mitral/aortic	32 (91.4)/3 (8.6)	3 (23.1)/10 (76.9)	0.000
LAVi (ml/m <sup>2</sup> )	83.5 ± 6.3	52.8 ± 5.3	0.007
Mitral valve (n)	32	3	
Maximum velocity (m/s)	2.5 ± 1.6	2.5 ± 1.5	0.812
Mean gradient (mmHg)	15 ± 8.3	14 ± 3.6	0.782
Valve area (cm <sup>2</sup> )	1.1 ± 0.5	1.1 ± 0.6	0.981
Mass visualized on mechanical valve	10 (31.3)	0	
Aortic valve (n)	3	10	
Maximum velocity (m/s)	4.9 ± 1.1	4.4 ± 2.2	0.156
Mean gradient (mmHg)	52.3 ± 2.1	47.4 ± 11.5	0.482
Valve area (cm <sup>2</sup> )	0.8 ± 0.1	0.9 ± 0.2	0.502
Mass visualized on mechanical valve	0	2 (20)	

INR, international normalized ratio; LAVi, left atrial volume index; NYHA, New York Heart Association.

aortic valves. The median time from performing three-dimensional TEE to reoperation was 3.7 ± 1.4 days.

#### **Clinical characteristics of patients with pannus versus thrombus formation**

Clinical data of patients with LMVO due to thrombus or pannus formation are shown in Table 2. Patients with thrombus and patients with pannus had similar INR levels, and the proportion of inadequate anticoagulation was similar. Time from valve replacement to reoperation in patients with pannus was longer than that of patients with thrombus (86 ± 38 vs. 46 ± 33 months,  $P=0.001$ ). The average age of patients with thrombus was significantly lower than the average age of patients with pannus (46 ± 12 vs. 56 ± 11,  $P=0.021$ ). The percentage of patients with the severe symptom (New York Heart Association III) in thrombus groups was higher than that in pannus group (37.1 vs. 15.5%,  $P=0.002$ ).

#### **Transthoracic echocardiographic findings: pannus versus thrombus formation**

Results of valve hemodynamics by transthoracic Doppler are shown in Table 2. In both mitral and aortic obstructed valves, the peak velocity, mean transvalvular gradients and valve area were similar between the thrombus and pannus groups. Imaging with TTE detected thrombus on obstructed mitral valves in 31.3% of cases and pannus on obstructed aortic valves in 20% of cases.

**Table 3**  
**Description of mechanical valve by two-dimensional TEE and three-dimensional TEE in left mechanical valve obstruction caused by thrombus or pannus formation**

	2-dimensional TEE		3-dimensional TEE	
	Thrombus	Pannus	Thrombus	Pannus
Detection of abnormalities	<i>n</i> = 35	<i>n</i> = 13	<i>n</i> = 35	<i>n</i> = 13
Abnormal valve motion [ <i>n</i> (%)]	35 (100)	13 (100)	35 (100)	13 (100)
Mass visualized on mechanical valve [ <i>n</i> (%)]	22 (62.8)	6 (46.2)	33 (94.2)	9 (69.2)

TEE, transesophageal echocardiography.

### Transesophageal echocardiography findings: pannus versus thrombus formation

Parameters by TEE in valves with thrombus formation or pannus are shown in Table 3. Leaflet motion abnormality was seen in all forty-eight cases on two-dimensional TEE. Regarding the detection of mass on the mechanical valve, two-dimensional TEE visualized a mass in 28/48 patients (58.3%), while three-dimensional TEE visualized a mass in 42/48 patients (87.5%). In the cases where a mass was detected by three-dimensional TEE, the length of the pannus was significantly longer than that of the thrombi; however, the area of the pannus did not significantly differ from the area of the thrombus.

### Diagnostic value of two-dimensional transesophageal echocardiography and three-dimensional transesophageal echocardiography

The true positive, false positive, true negative, and false negative were calculated and presented in Table 4. Compared with two-dimensional TEE in the diagnosis of thrombus, three-dimensional TEE demonstrated higher sensitivity [33/37 (89.2%) vs. 19/45 (42.2%)], specificity [8/11 (72.7%) vs. 2/3 (66.7%)], accuracy [41/48 (85.4%) vs. 21/48 (43.8%)], PPV (91.7 vs. 95%), and NPV (66.7 vs. 7.1%). Compared with two-dimensional TEE in pannus diagnosis, three-dimensional TEE demonstrated higher sensitivity [8/15 (53.3%) vs. 2/27 (7.4%)], specificity [33/33 (100%) vs. 19/21 (90.5%)], accuracy [41/48 (85.4%) vs. 21/48 (43.8%)], PPV (100 vs. 50%), and NPV (82.5 vs. 43.2%) (Table 4). A receiver operating characteristic curve analysis was used to estimate the diagnostic performances of two-dimensional TEE and three-dimensional TEE in the diagnosis of thrombus and pannus. In the diagnosis of thrombus, the area under the curve of three-dimensional TEE was significantly higher than the area under the curve of two-dimensional TEE (0.8560 vs. 0.7330,

$P=0.0427$ ). In the diagnosis of pannus, significance testing showed better performance of three-dimensional TEE than two-dimensional TEE (0.8077 vs. 0.5484,  $P=0.005$ ) (Fig. 3).

### Discussion

This study sought to evaluate the role of two-dimensional TTE, two-dimensional TEE, and three-dimensional TEE in the detection of left heart valve dysfunction and in the differentiation between thrombus and pannus formation. Patients with pannus formation had longer duration from heart valve replacement to the time of reoperation (Table 2). The results of previous studies suggest that pannus formation takes at least 6 months; however, a shorter time interval to reoperation has been reported<sup>[16]</sup>. Histological and immunohistological studies of pannus tissue revealed that pannus formation is a chronic inflammatory response with the proliferation of myofibroblasts and extracellular matrix<sup>[17]</sup>.

In this study, inadequate anticoagulation occurred in 71.4% patients with thrombus and 76.9% patients with pannus. In previous studies, thrombus formation was seen more often in patients with inadequate anticoagulation. In our study, 90% of the cases of thrombus formation were seen in patients with mechanical mitral prostheses, which can be explained by the slow blood flow that induced thrombosis by activating clotting factors<sup>[15,18]</sup>. In addition, regional turbulent flow disrupted laminar flow and promoted platelet adhesion to the valve surface which resulted in endothelialization inhibition and pro-thrombotic phenotype induction<sup>[15]</sup>. The proportion of atrial fibrillation and the left atrium size in patients with mechanical mitral valves were higher than in patients with mechanical aortic valves, as expected, and likely also play a role. In contrast, 76.9% pannus formation was in mechanical aortic valves, which can be explained by the surgical technology and wall shear stress in the vicinity of aortic valve prostheses. Particularly, one of the pivot guards of mechanical aortic valves is placed in the native annulus and may be a nidus of pannus formation<sup>[19,20]</sup>.

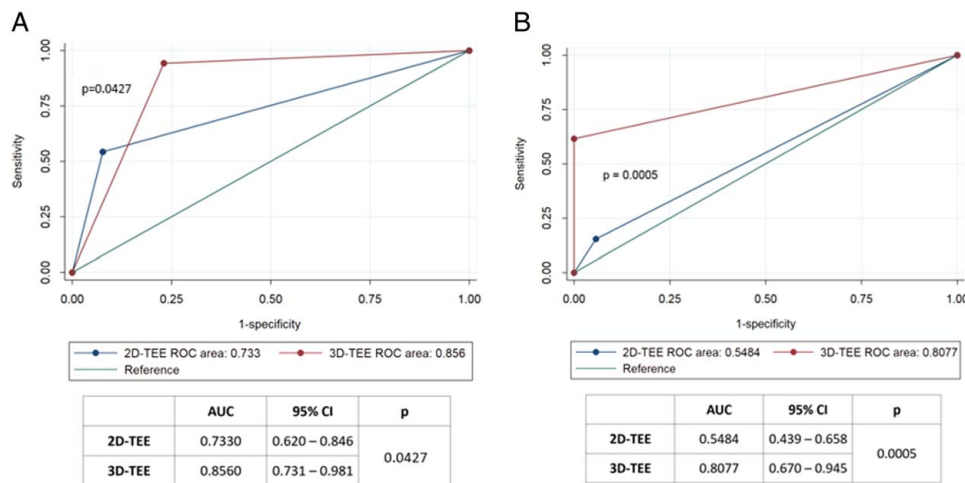
### Differentiating thrombus from pannus formation

Two-dimensional TTE could not distinguish between thrombus and pannus. Two-dimensional TTE provided direct visualization of left-sided mechanical valves and valuable hemodynamic parameters. However, the hemodynamic parameters on two-dimensional TTE were similar between thrombus and pannus groups. Due to attenuation and acoustic shadowing, TTE is limited in detecting valvular masses, much less characterizing them, and thus is limited in differentiating the cause of LMVO<sup>[21]</sup>. This was the reason why TTE visualized only nine of 48 cases

**Table 4**  
**Accuracy of two-dimensional TEE and three-dimensional TEE diagnosis of thrombus and pannus on left mechanical valve obstruction**

Diagnosis methods	True positive ( <i>n</i> )	True negative ( <i>n</i> )	False positive ( <i>n</i> )	False negative ( <i>n</i> )	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Diagnosis of thrombus									
2-dimensional TEE	19	2	1	26	42.2	66.7	43.8	95.0	7.1
3-dimensional TEE	33	8	3	4	89.2	72.7	85.4	91.7	66.7
Diagnosis of pannus									
2-dimensional TEE	2	19	2	25	7.4	90.5	43.8	50	43.2
3-dimensional TEE	8	33	0	7	53.3	100	85.4	100	82.5

NPV, negative predictive value; PPV, positive predictive value; TEE, transesophageal echocardiography.



**Figure 3.** (A) ROC curve of two-dimensional TEE and three-dimensional TEE in the diagnosis of thrombus. (B) ROC curve of two-dimensional TEE and three-dimensional TEE in the diagnosis of pannus. AUC, area under the curve; ROC, receiver operating characteristic; TEE, transesophageal echocardiography.

(18.8%) with thrombotic masses. Two-dimensional TEE visualized 62.4% of thrombus and 41.5% of pannus formation cases, while three-dimensional TEE visualized 94.2% of thrombus and 69.2% of pannus formation cases.

TEE with the probe placed in the esophagus near left atrium removes the interference of the lungs, providing a superior assessment of LMVO mechanisms. Fluoroscopy provides better assessment of prosthesis' disk movement and its angle, but the information does not influence the selection of treatment strategy, while patients are exposed to radiation.

According to the 2020 American Heart Association/American College of Cardiology Guidelines for the Management of Valvular Heart, fibrinolysis is recommended when LMVO is caused by thrombi less than 0.8 cm<sup>2</sup>[6]. Hence, the accuracy and reproducibility of mass measurements are particularly vital in the choice between surgery and thrombolytic therapy, and in follow-up. Two-dimensional TEE could underestimate thrombus size due to limitation in selecting the maximum diameter when masses have irregular shapes. This problem may be solved by analysis of three-dimensional TEE images. Our study found that three-dimensional TEE was superior in discriminating between thrombus and pannus, likely because three-dimensional TEE allows better detailed anatomical visualization, though it can be subject to over-gaining creating artifacts leading to over-measurement of thrombus or pannus sizes.

ECG-synchronized MDCT provides excellent anatomic assessment and temporal resolution and may be superior in the assessment of size and shape of thrombus and pannus, but only when the heart rate is adequately low. High resting heart rate is common among our patients because of heart failure due to delayed presentation. Most patients who had thrombus were farmers who lived in rural areas and had rheumatic valvular disease and atrial fibrillation. There were two women (4.7%) who were pregnant and had mechanical mitral valve thrombosis. In many low- and middle-income countries, MDCT is considerably more expensive than TEE and involves exposure to radiation and iodinated contrast agents.

### Limitations

In this study, TEE was not compared with MDCT, and our sample size was somewhat small. Further studies should be performed with larger sample sizes and across multiple institutions to have more precise evidence-based for the potential advantages of three-dimensional TEE.

### Conclusions

Three-dimensional TEE is helpful and valuable in differentiation between thrombus and pannus. The result of this study suggested that three-dimensional TEE should be considered as a routine imaging tool in patients with suspected LMVO obstruction.

### Ethical approval

The study received the permission of the Ethical and Scientific Committee of Bach Mai Hospital, Hanoi, Vietnam (approval number 2347/QD-BM).

### Consent

Written informed consent was obtained from all patients for publication of this study and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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### Author contribution

H.T.T.N.: the corresponding author, supervisor, conceptualization, methodology, investigation, writing – original draft preparation and editing, visualization. T.T.T.P.: the first author, methodology,



investigation, formal analysis, writing – original draft preparation and editing, visualization. J.N.K.: conceptualization, methodology, writing – reviewing, and editing. H.D.D.: investigation, writing – reviewing. H.M.P.: investigation, writing – reviewing. T.T.V.: formal analysis, writing – original draft preparation and editing. N.T.M.G.: investigation, writing – reviewing. H.V.T.: investigation, writing – reviewing. Y.T.H.N.: investigation. M.T.N.H.: investigation.

### Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

### Research registration unique identifying number (UIN)

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