Incremental Value of 3D and Contrast Echocardiography in Evaluation of Endocardial Fibroelastosis and Multiple Cardiovascular Thrombi

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Case report

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Abstract

Background: Endocardial fibroelastosis (EFE) is a rare heart disease characterized by the thickening of the endocardium caused by massive proliferation of collagenous and elastic tissue, usually leading to impaired cardiac function. Thrombosis is a complication of EFE that suggests poor prognosis.

Case presentation: The present report describes an EFE patient with multiple cardiovascular thrombi. To the best of our knowledge, this is the first reported case of three-dimensional (3D) and contrast echocardiography use in EFE with multiple ventricular thrombi. The clinical features and outcomes of this rare condition between 1966 and 2019 are also reviewed.

Conclusions: Through the combination of 3D and contrast echocardiography, the thrombus can be displayed more accurately and vividly, including its nature and density and the connection between the base of the thrombus and ventricular wall. EFE prognosis with left ventricular thrombus is generally poor.

Background

Endocardial fibroelastosis (EFE) is a rare heart disease that usually occurs in infants and children. It is characterized by diffuse thickening of the endometrium due to proliferation of collagen and elastic fibers, cardiac enlargement, and myocardial dysfunction and presents as unexplained heart failure. Herein, we report a case of EFE with multiple thrombosis of the left ventricle (LV), abdominal aorta, common iliac artery, and renal artery diagnosed using multimodality cardiovascular imaging. The important role of three-dimensional (3D) and contrast echocardiography (CE) in clinical diagnosis of thrombi is also discussed.

Case Presentation

An 11-year-old girl was admitted to Shengjing hospital with nausea, vomiting, and difficulty with lower limb mobility. Her medical history included EFE diagnosed 10 years ago. She had been undergoing regular examinations and treatments for a decade, and her condition was relatively stable. Physical examination showed that the liver margin was palpable and located 4 cm below the costal margin and 6 cm below the xiphoid process. Bilateral dorsal foot pulse was not detected. Laboratory test results were as follows: erythrocyte 5.0×10^{12}/L, hemoglobin 118 g/L, erythrocyte sedimentation rate 38 mm/h, urine protein quantification 1.41 g/L, 24-h urine protein quantification 1.41 g/d, uric acid 537 μmol/L, total protein 52.8 g/L, albumin 25.4 g/L, serum cystatin C 1.28 mg/L, IL-6 8.70 pg/mL, prothrombin time 17.1 s, prothrombin time activity 55%, activated partial thromboplastin time 38 s, D-dimer 1258 μg/L, and fibrinogen degradation product 12.4 mg/L. Blood gas analysis revealed that partial pressure of oxygen was reduced to 43.5 mmHg. Electrocardiogram (ECG) results showed sinus rhythm, first degree atrioventricular block, downward ST segment, and T wave inversion.

Two-dimensional (2D) echocardiography revealed that the whole heart was significantly enlarged (LV end-diastolic dimension of 67 mm) and LV wall movement was significantly reduced with uncoordinated movement. The endocardium became thicker (about 2.4 mm at its thickest portion) and the echo was enhanced. Multiple mass images were observed in the LV. There was a slightly deformed high-low mixed echo

mass near the apex of the LV lateral wall with a size of about 50 × 33 mm (Fig. 1A). A mixed strong and weak echogenic mass (40 × 15 mm) with obvious activity and deformation was also detected at the LV apex. It had a narrow and thin base of 1–2 mm (Fig. 1B). Another 8 × 10 mm medium-high echo mass with obvious activity was identified at the apex of the heart (Fig. 1B). Multiple trabeculations were detectable at the LV apex. Small amounts of regurgitation were present in the mitral valve. The LV systolic function with an ejection fraction of 28% was significantly reduced at rest. The 3D echocardiography showed that the thrombus protruded from the side wall of the LV and had a wide base and low mobility (Fig. 2A). A mobile component of the thrombus with a thin pedicle was protruding from the LV apex (Fig. 2B). CE results showed that the mass on the LV lateral wall near the apex was relatively fixed with slight activity and deformation. However, contrast agent was entering at a part of the junction between the base of the mass and LV wall. The other part of the base was tightly connected to the LV wall. The inner portion of the mass showed no contrast enhancement (Fig. 3A). Masses in the LV apex had great mobility and deformation and contrast agents were detected in their peripheral regions. Most of the masses were not contrast-enhanced in the central region (Fig. 3B). These masses were considered to be thrombi due to their echocardiographic morphological characteristics and patient's primary disease.

The 3D computerized tomography angiography (3D-CTA) demonstrated thromboembolism between the abdominal aorta (level of the right accessory renal artery) and bilateral common iliac artery (Fig. 4). Thrombosis was also detected in the proximal left renal artery and the opening of the right renal artery, with multiple ischemic foci in both kidneys. Color Doppler ultrasonography revealed ischemic changes in the arterial spectrum of both lower limbs.

In order to prevent further damage to the kidneys, interventional thrombectomy of the renal artery was performed to remove the obstruction. After five days of anticoagulant treatment, the smallest thrombus at the LV apex disappeared and the other one became significantly smaller (from 40 × 15 to 3 × 4.5 mm). The change in the largest thrombus in the LV lateral wall near the apex was not significant (from 50 × 33 × 17 to 50 × 22 × 18 mm). After 12 days of anticoagulation treatment, the active thrombus disappeared and only the thrombus located in the LV lateral wall near the apex was detected, the dimensions of which were 49 × 19 × 13 mm. Despite adequate medical measures, congestive heart failure did not completely improve, and after two months the patient eventually developed cardiogenic shock, respiratory failure, sepsis, and severe pneumonia. Finally, the patient and her parents abandoned treatment and asked to be discharged.

Discussion And Conclusions

EFE is a rare heart disease characterized by thickening of the endocardium, cardiac enlargement, and myocardial dysfunction. The exact etiology of EFE is unknown and may be related to many factors, including infection [1], congenital developmental malformation [2], autoimmune diseases [3], chromosomal abnormalities and gene mutations [4], and myocardial ischemia and hypoxia [5]. It is one of the causes of heart failure in infants and children [6, 7]. Patients with EFE are prone to endocardial thrombosis, which may be due to enlarged cardiac cavity, systolic dysfunction, and altered endothelium lining [8, 9]. Previous studies have also reported that a thrombus can easily form at the sites of akinetic, dyskinetic, or aneurysmal segments that are potentially at risk for thromboembolism [10]. If the embolus is detached from the mural

thrombus, complications arise and other organ changes occur. A series of studies on EFE with thrombosis between 1966 and 2019 were reviewed and its characteristics and outcomes were summarized.

A total of seven patients diagnosed with EFE with thrombosis were identified. A summary of these patients is presented in Table 1 [8, 9, 11–13]. There were one female and six males, with the age at diagnosis ranging from fetal to 68 years old. Thrombus was found in the right ventricle, right auricular appendage, brain, left internal carotid artery, left middle cerebral artery, coronary artery, LV, and right atrium (RA). Patient complications included pulmonary infarct, myocardial infarct, renal infarct, cerebral infarction, aortic valve stenosis, and atrial fibrillation. Diagnosis methods for EFE with thrombosis included echocardiography, cMRI, and autopsy. The prognosis was very poor and treatments were targeted only at symptom relief.

Table 1
Summary of literature on patients presenting with EFE associated with thrombus.

Study	Age	Sex	Diagnose methods	Position of thrombus	Other symptoms	Treatment	Outcome
Branch et al. (1966) [11]	7 y	M	Autopsy	RV	Bilateral pulmonary infarcts	Medical treatment	Died
	16 m	M	Autopsy	LV, RV, RAA	Myocardial infarcts; Pulmonary infarcts; Renal infarcts	Medical treatment	Died
	13 m	F	Autopsy	Brain; LICA; LMCA	Cerebral infarction	Medical treatment	Died
Lane et al. (1991) [9]	18 m	M	TTE; Autopsy	LAD coronary artery	Myocardial infarction	Digitalis, furosemide, captopril, spironolactone, and low- dose aspirin therapy	Died
Revel et al. (1994) [12]	Fetus (24 w, MA)	M	Fetal echocardiography; Autopsy	LV	Aortic valve stenosis	--	Induction of labor
Tannouri et al. (1998) [13]	Fetus (19 w, MA)	M	Fetal echocardiography; Autopsy	LV	--	--	Induction of labor
Ozdemir D et al. (2019) [8]	68y	M	TTE; cMRI	RA	Atrial fibrillation	Warfarin	Follow-up

Right auricular appendage; LICA: Left internal carotid artery; LMCA: Left middle cerebral artery; LAD coronary artery: Left anterior descending coronary artery; RA: Right atrium; ECG: Electrocardiogram; TTE: Transthoracic echocardiogram; cMRI: cardiac Magnetic resonance imaging; --: No information available.

Due to its availability, versatility, and low cost, traditional 2D echocardiography is the most convenient imaging method to evaluate mass morphology and mobility. However, the accuracy of 2D echocardiography is limited because mass calculations are based on geometric assumptions. Real-time 3D echocardiography provides a novel echocardiographic method to measure a mass by directly observing the myocardial boundaries of the entire LV. On the basis of 2D echocardiography diagnosis, 3D echocardiography

comprehensively shows the location, shape, and narrow base of the mass. 3D echocardiography is also an accurate method for quantifying LV mass. It is in better agreement with the reference value for cardiac magnetic resonance imaging (cMRI), which is considered to be the gold standard for quantifying LV mass [14]. It also has advantages over cMRI due to its availability, rapid image acquisition and processing, and in cases where the patient has no access to the cMRI scanner. Through the combination of 3D echocardiography and CE, the mass can be displayed more accurately and vividly. CE was further utilized to detect the mass's nature, density, and connection to the LV wall in order to make an accurate clinical diagnosis. CE is widely used in cardiovascular diseases. It can be used to evaluate LV structure and function to improve image quality, reader confidence, and reproducibility [15]. Compared to computed tomography (CT), MRI, positron emission tomography (PET), and PET-CT, CE is a fast, effective, well-tolerated, and inexpensive technology [16]. The thrombus image needs to be distinguished from the tumors. Previous studies have reported that CE has a high diagnostic accuracy in differentiating thrombi from benign or malignant tumors [17]. A mass with no contrast enhancement has been considered as a thrombus, while incomplete or complete mass enhancement might be considered a benign or malignant tumor [17, 18]. The present study found that CE plays a great role in delineating the thrombus outline, clarifying its loose and dense portions, and determining the tightness of the connection between the base and LV wall. Contrast enhancement was observed in the peripheral part of the two active thrombi. There was no contrast enhancement in their central regions. These results suggested that the peripheral structure of the mass might be loose and gap-like, while the central portion is dense. These thrombi were considered to have a very high risk of emboli shedding based on their activity and deformation. The newly formed thrombus is usually highly mobile and protrudes into the ventricular cavity, while the old thrombus often has a smooth surface and is usually relatively static. This case had both fresh active and old thrombi, which might be the source of multiple celiac artery thrombosis. The peripheral contrast-enhanced thrombi were first dissolved with anticoagulant at the time of reexamination, which was consistent with the presumption of fresh loose thrombi.

LV thrombosis has been identified as a marker of adverse cardiovascular events. Embolism from the heart or aorta can cause transient ischemic attack, stroke, or peripheral arterial occlusion, which often leads to clinically significant morbidity and mortality [19]. In the present case, multiple thrombi were also found in the abdominal aorta, common iliac artery, and renal artery. Despite adequate medical measures, the patient eventually died of cardiogenic shock, respiratory failure, sepsis, and severe pneumonia.

Based on the literature review, outcomes of EFE with thrombosis are considered very poor. Due to the rarity of EFE and limited specific evidence, it is recommended that prevention of thromboembolism risk and thrombosis treatment follow general guidelines. It is necessary to be vigilant about the occurrence of thromboembolic events in EFE patients.

Abbreviations

EFE: Endocardial fibroelastosis; ECG: Electrocardiogram; 2D echocardiography: Two-dimensional echocardiography; 3D echocardiography: Three-dimensional echocardiography; CE: Contrast echocardiography; 3D-CTA: Three-dimensional computerized tomography angiography; CT: Computed tomography; cMRI: cardiac Magnetic resonance imaging; PET: Positron emission tomography; M: Male; F:

Female; MA: Menstrual age; RV: Right ventricle; LV: Left ventricle; RAA: Right auricular appendage; LICA: Left internal carotid artery; LMCA: Left middle cerebral artery; LAD coronary artery: Left anterior descending coronary artery; RA: Right atrium; ECG: Electrocardiogram; TTE: Transthoracic echocardiogram.

Declarations

Ethics approval and consent to participate

The study has been approved by the ethics committee of Shengjing Hospital of China Medical University, Shenyang, China.

Consent for publication

Written informed consent for publication of this report and any accompanying images was obtained from the parents of the patient. A copy of the consent form is available for review by the editor of this journal.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LJS and YL participated in the design of the study. LJS and JHY collected clinical data. WDR, WQ, YL, and XW performed echocardiographic examination and collected the images. LJS wrote the manuscript. All authors read and approved the final manuscript.

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Not applicable.

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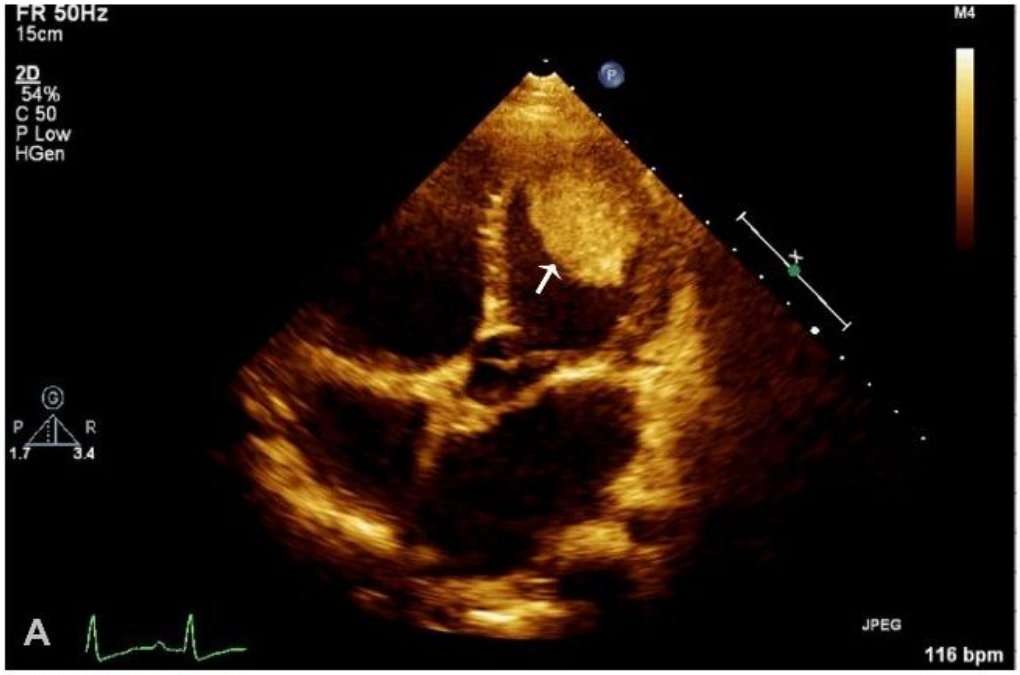
Figures



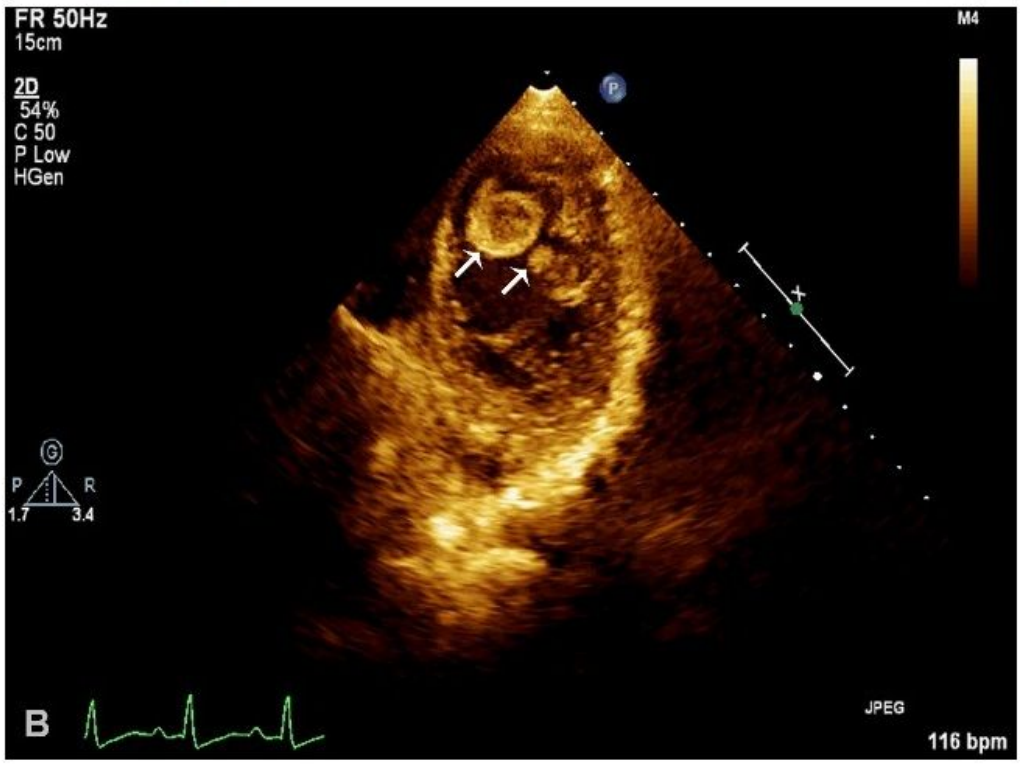


Figure 1

2D echocardiography false color thrombi imaging. A: Apical four-chamber view shows a large thrombus near the apex of LV lateral wall (white arrow). B: Two thrombi were also detected at LV apex (white arrow).

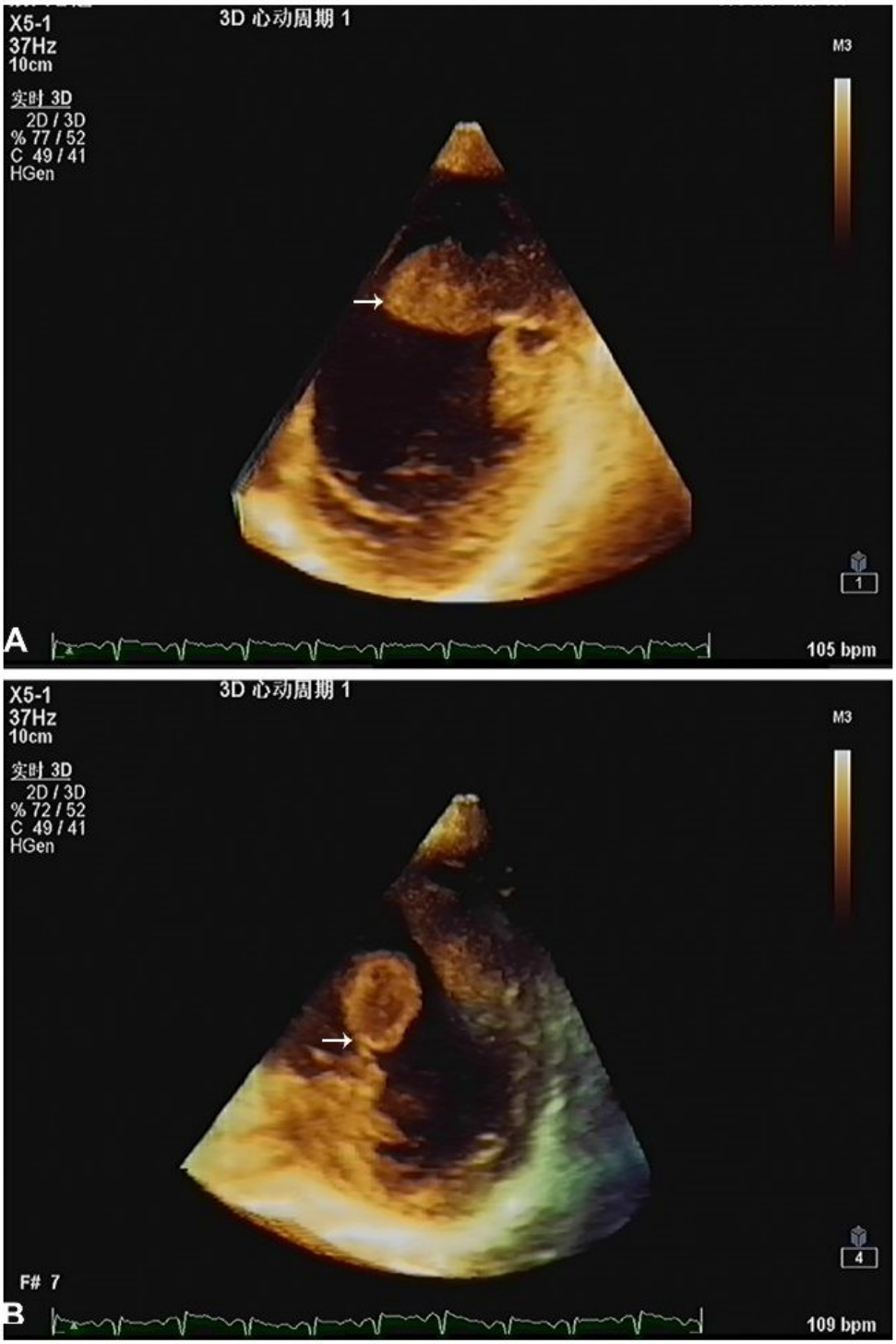


Figure 2

Still image derived from 3D echocardiography. A. Thrombus protrudes from LV lateral wall with a wide base (white arrow). B. Thrombus with short and thin stem (white arrow) protrudes from LV apex.

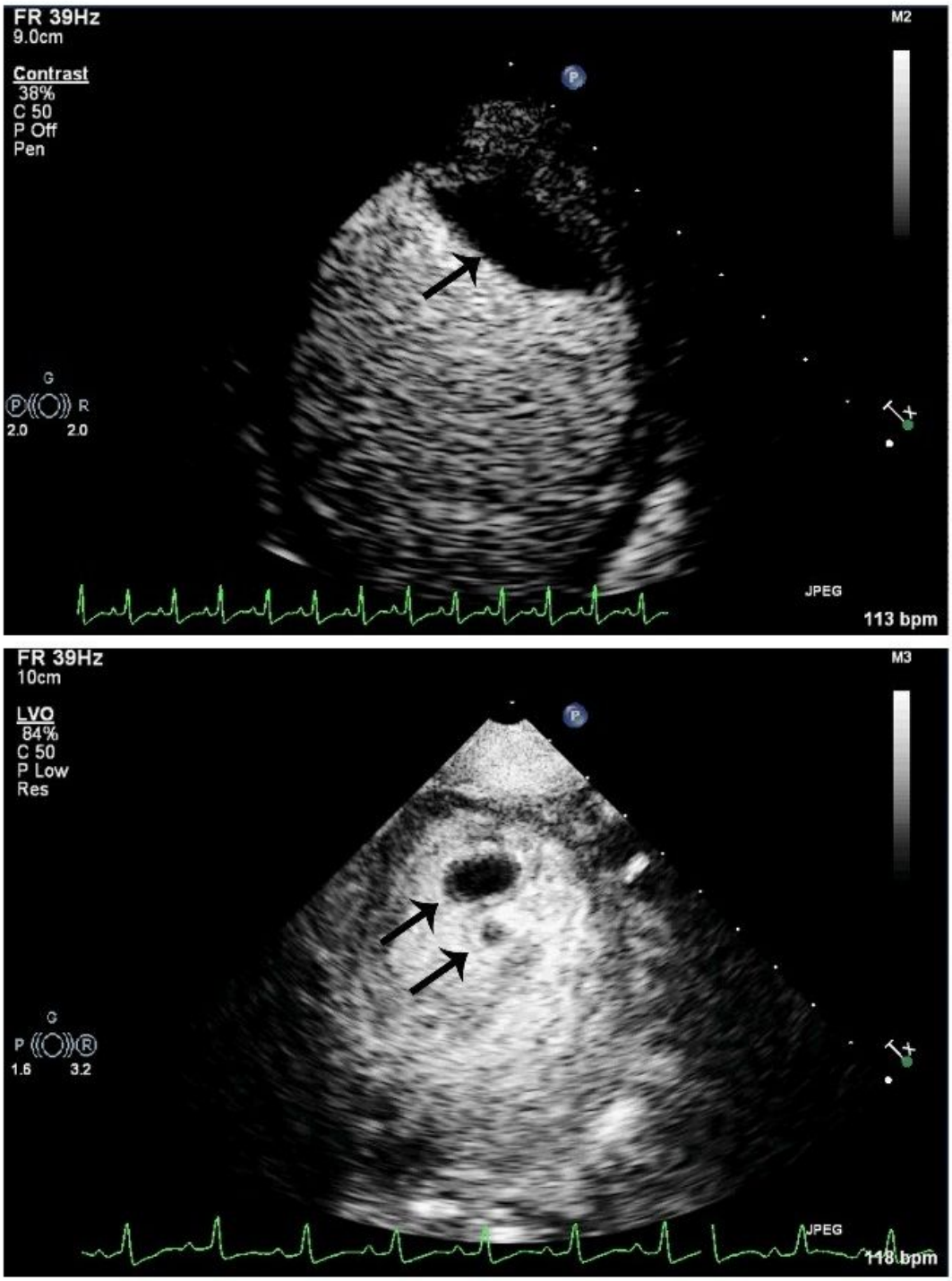


Figure 3

Contrast echocardiography thrombi imaging. A: Contrast agent entered at a part of the junction between thrombus base and LV wall. The inner portion of the thrombus had no contrast enhancement (black arrow). B. Contrast enhancement was detected in the peripheral part of the two thrombi in LV apex (black arrows), while most of the central region was not contrast-enhanced.

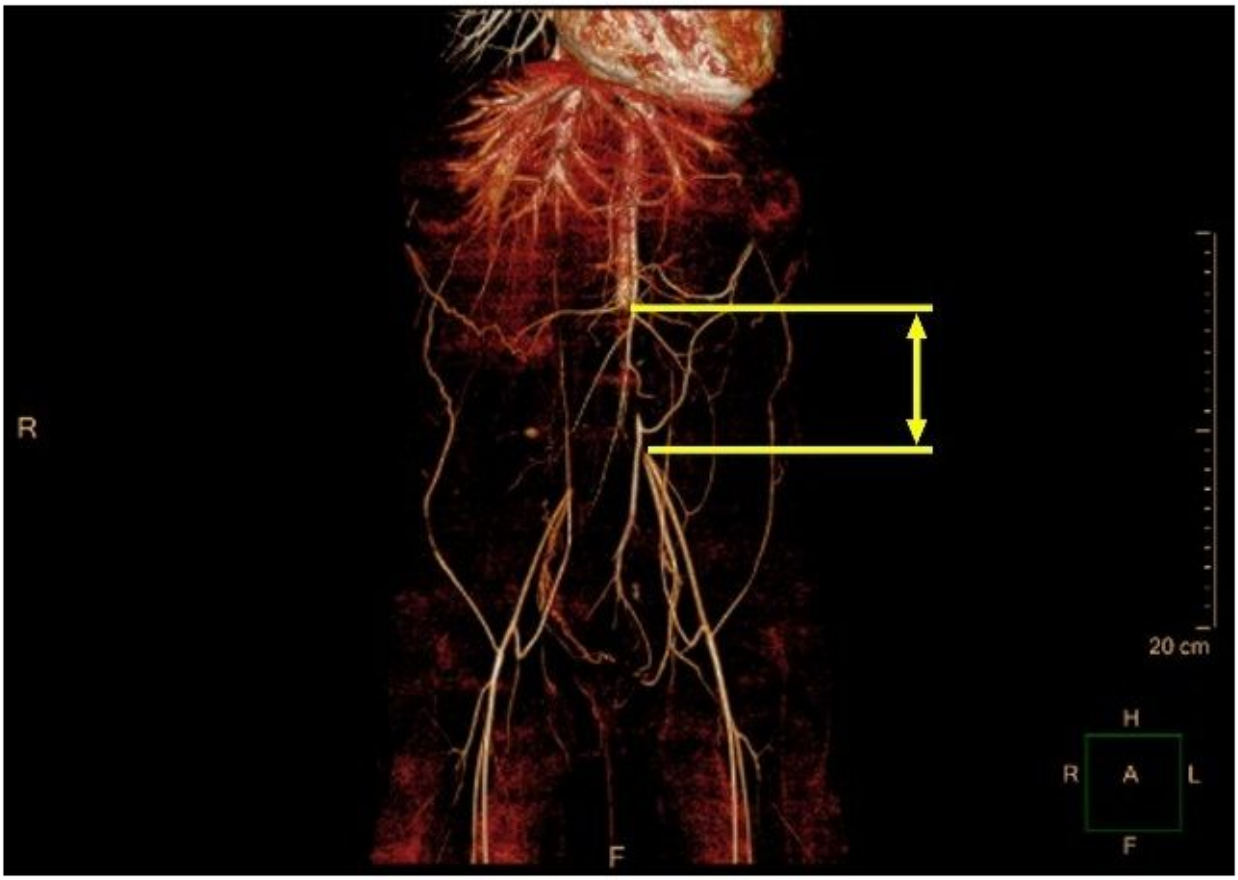


Figure 4

3D-CTA thromboembolism view. Thrombosis was detected between abdominal aorta and bilateral common iliac arteries (yellow lines indicate thrombus between abdominal aorta and left common iliac artery).