

The Indian Academy of Echocardiography Practice Guideline for the Performance of Transesophageal Echocardiographic Evaluation of a Patient with Cerebrovascular Stroke

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Abstract

Ischemic stroke remains a major cause of morbidity and mortality. Cardiac sources of embolism account for almost up to 40% of all the ischemic strokes. Accordingly, echocardiography is an important investigation in the evaluation of clinically suspected cardioembolic stroke or cryptogenic stroke. Both transthoracic echocardiography and transesophageal echocardiography (TEE) are complementary to each other for this purpose. However, because of its superior resolution and the ability to image structures that are the most likely sources of cardioembolism (e.g., left atrial appendage), TEE is the preferred imaging modality in the cardiac evaluation of stroke. This document describes the systematic TEE evaluation of the patients referred with a clinical diagnosis of either cryptogenic stroke or cardioembolic stroke.

Keywords: Atrial septal aneurysm, cardiac tumor, infective endocarditis, intracardiac thrombus, Lambl's excrescences, left atrial appendage, paradoxical embolism, patent foramen ovale, RoPE score, spontaneous echo contrast, Valsalva maneuver

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INTRODUCTION

Cardiac source of embolism accounts for 15%–40% of all strokes.^[1] Undetermined (cryptogenic) causes are responsible for 25%–40% of ischemic strokes.^[2] In a significant proportion of the cryptogenic stroke population, a cardiac source is implicated or discovered. Echocardiography is an important investigation in the evaluation of clinically suspected cardioembolic stroke or cryptogenic stroke. Both transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are complementary to each other, and most neurologists frequently prefer both in the evaluation of majority of the patients with stroke.

SCOPE OF THE DOCUMENT

This document describes the systematic TEE evaluation of patients referred with a clinical diagnosis of either cryptogenic stroke or cardioembolic stroke. A primary physician or a neurologist routinely refers such patients for cardiac evaluation after neuroradiological imaging of the cerebrovascular system. Electrocardiogram (ECG) and TTE remain the initial modalities in the cardiac evaluation of stroke. By the time TEE is contemplated, the results of blood investigations, neurovascular imaging, ECG, and TTE are usually already available and are helpful in guiding TEE examination. This document discusses TEE imaging of common cardiovascular pathologies, which form definite or potential sources of cerebral embolism.

APPROACH TO A PATIENT WITH STROKE REFERRED FOR TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Cerebrovascular stroke is classified clinically as follows:^[3]

1. Cardioembolic stroke
2. Cryptogenic stroke (typically defined as an ischemic stroke in a patient with age 35–55 years, no hypertension, no atrial fibrillation [AF], no valvular heart disease, no intracardiac or intracerebral mass, no hypercoagulability syndrome, etc.)
3. Cerebral small vessel disease (lacunar infarcts)
4. Atherothrombosis of major vessels
5. Space-occupying lesions (tumor, hemorrhage) or neurodegenerative.

A cardiologist performing the TEE should systemically and concisely review the pertinent data from the clinical history, investigations, and imaging before undertaking the procedure. Table 1 provides a checklist for the workup of a patient with suspected cardioembolic stroke.

History should document the presence or absence of atherosclerotic cardiovascular disease (ASCVD) risk factors, viz., hypertension, diabetes mellitus, smoking, and dyslipidemia; any cardiac illness such as previous myocardial infarction, AF, congestive heart failure, and valvular heart disease; and any other relevant findings such as history of prolonged fever. In addition, any history of deep vein thrombosis, collagen vascular disease, or thrombophilia syndromes is also important as it may suggest paradoxical embolism. Further, certain features in clinical presentation may itself suggest an embolic stroke. A cardioembolic stroke often presents with a dense sensory-motor deficit which is maximum at onset and may be recurrent. Clinical cardiac examination may indicate the presence of valvular or congenital heart disease. The neuroradiological imaging in cardioembolic stroke may show infarcts involving predominantly the superficial gray matter involving single or multiple cerebral artery territories which are morphologically distinct from white matter lacunar infarcts.

Causes of cardioembolic stroke

A cardiac source of embolism may arise from a variety of structural or functional pathologies which can either be “definite, evidence based, and associated with high risk of recurrence” or be “potential, hypothetical, and with low risk of recurrence.” The embolic material may be thrombotic, infective, tumor fragment, calcium chunks, atheroembolic, fat, or air. A comprehensive list of common cardiac sources of embolism classified according to various cardiac segments, nature of embolic material, and risk of recurrence is presented in Table 2.

INDICATIONS FOR TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Transthoracic versus transesophageal echocardiography

TTE is the first-line imaging technique in the cardiac evaluation of a stroke patient. It provides a lot of useful information, and in many cases, it can itself lead to the underlying diagnosis. Left ventricular (LV) apical pathology is best seen with TTE coupled with LV opacification with intravenous (IV) contrast. Further, even in the noncardioembolic stroke patients, pathological changes in the heart due to associated systemic hypertension, diabetes, coronary atherosclerotic heart disease, etc., can be diagnosed by TTE, which are useful for the management of these patients. Findings of an obvious pathology (e.g., LV apical clot) may obviate the need for TEE. If TTE is negative and inconclusive or further evaluation of

Table 1: Clinical approach to cardioembolic stroke

Evaluation modality	Salient information
History	Atherosclerotic cardiovascular disease risk factors: age, smoking, hypertension, diabetes, dyslipidemia Fever, hypercoagulability syndrome Any history suggestive of deep vein thrombosis, collagen vascular disease, etc., In women, history of repeated abortions
Clinical examination	Valvular or congenital heart disease
Ambulatory blood pressure monitoring	Labile hypertension
Electrocardiogram, extended Holter monitoring, implantable loop recorder	Rhythm for atrial fibrillation, flutter
Hematological investigations	Complete blood count, lipid profile, fasting blood glucose, glycosylated hemoglobin, thrombophilia profile, D-dimer, anti-nuclear antibody, double-stranded deoxyribonucleic acid, and other collagen vascular disease profile
Neuroradiological imaging	Carotid ultrasound and color Doppler Computed tomography of brain and computed tomographic angiography of neck vessels Magnetic resonance imaging of brain and magnetic resonance angiography of neck vessels Transcranial Doppler
Transthoracic echocardiography	Left ventricular systolic function/regional wall motion abnormalities Valvular disease Any intracardiac thrombus/mass

pathology (e.g., infective endocarditis [IE] or intracardiac mass) is needed, one should proceed with TEE.

Among the indications for TEE, cardiac source of embolism forms about 30% of the cases in which TEE is performed. TEE provides high-quality images of the interatrial septum (IAS), patent foramen ovale (PFO), left atrium (LA) left atrial appendage (LAA), and arch of the aorta, not achievable by TTE. Compared to TTE, TEE is superior for the identification of cardiac sources of emboli.^[4] In stroke patients with no history of cardiac disease, TEE more frequently identifies a cardiac source of embolism than TTE.^[5] TEE findings also significantly influence the therapeutic decision regarding anticoagulation in stroke.^[6]

Indications for transesophageal echocardiography

TEE is indicated in the following conditions:

1. Patients aged <45 years without known cardiovascular disease, for detecting PFO/atrial septal aneurysm (ASA)
2. Patients with high probability of cardioembolic stroke with negative TTE
3. Patients with AF and stroke (though many would prefer to straightaway proceed with anticoagulation without performing TEE)
4. Patients with mechanical prosthetic heart valve and stroke
5. Patients with high ASCVD risk where aortic atheroembolism is likely.

Following TEE findings are considered as high-risk cardiac sources of embolism:

1. Aortic thrombi or plaques ≥ 4 mm in size
2. Thrombi in LA cavity/LAA
3. Spontaneous echo contrast (SEC)
4. LAA flow velocity <30 cm/s on pulsed-wave Doppler.

And these are the potential sources of embolism on TEE:

1. PFO
2. ASA
3. Aortic plaques <4 mm
4. Lambl's excrescences.

SYSTEMATIC SEGMENTAL APPROACH FOR TRANSESOPHAGEAL ECHOCARDIOGRAPHY EVALUATION IN STROKE

This guideline document proposes a protocol for systematic scanning sequence for various cardiac segments. The word "segment" used in this document does not mean embryological derivative but means a "structure or chamber" with "potential and frequent" source of cardioembolism requiring focused and thorough imaging.

The sequence of imaging is arranged with the following principles:

1. To increase the diagnostic yield in a time-efficient manner, with least discomfort to the patient
2. Less manipulation of TEE probe by sequential selection of windows
3. To focus on one segment at a time to avoid missing inconspicuous pathologies
4. To visualize more frequent sources first and less frequent sources later
5. Valsalva maneuver (VM), requiring patient's effort, to be performed as the penultimate step
6. High esophageal arch imaging causing patient discomfort and associated with the likelihood of termination of the test is positioned in the last.

Table 2: Causes of cardioembolic stroke

Cardiac segment	Structure	Cardiovascular disease/condition	Thrombotic	Nonthrombotic	Risk of recurrence
Left atrium	Left atrial appendage	Atrial fibrillation/flutter Mitral stenosis	+	-	High
	Left atrial cavity	Atrial fibrillation/flutter Mitral stenosis Congestive heart failure Spontaneous echo contrast in the absence of atrial fibrillation or mitral stenosis	+	-	High
Valves and annuli	Mitral valve	Infective endocarditis	+	-	High
		Nonbacterial thrombotic endocarditis in systemic lupus erythematosus, antiphospholipid antibody syndrome, malignancies, sepsis	+	-	High
		Papillary fibroelastoma	-	+	High
		Calcific degeneration, caseoma of annulus	-	+	Low
	Aortic valve, aortic root, ascending aorta	Infective endocarditis	+	-	High
		Nonbacterial thrombotic endocarditis	+	-	High
		Papillary fibroelastoma	-	+	High
		Lambl's excrescences	-	+	Low
		Degenerative calcification and atherosclerotic plaques	+/-	+	Low
Prosthetic valves or devices	Mitral or aortic position or right atrial/right ventricular cavity	Infective endocarditis	+	-	High
		Suboptimal anticoagulation	+	-	High
		Fibrin strands	+	-	Low
Left ventricle	Left ventricular wall	True or pseudo aneurysm, left ventricular noncompaction	+	-	High
	Left ventricular cavity	Acute myocardial infarction, regional wall motion or global left ventricular systolic dysfunction	+	-	High
Interatrial septum	Patent foramen ovale±atrial septal aneurysm with right-to-left shunt on Valsalva maneuver, atrial septal defect	Paradoxical venous thromboembolism, fat/air embolism, paradoxical embolism of right atrial tumor or tricuspid valve vegetation	+	-	Low
	Interatrial septal pouch	Local stasis	+	-	Low
	Myxoma	Primary cardiac tumor	+/-	+/-	High
Arch of aorta, Descending thoracic aorta	Atherosclerotic plaques	Mobile atherothrombi	+	-	High
	>4 mm protruding	Atheroemboli from ulcerated plaques	-	+	High

Based on the most common etiologies of stroke [Table 2], the cardiac segments which deserve focused TEE imaging to rule out or rule in a cardiac source of embolism are as follows [Figure 1]:

1. LAA
2. LA cavity
3. Mitral valve and annulus
4. Aortic valve, annulus, ascending aorta
5. Prosthetic valve(s)
6. LV cavity and apex
7. IAS
8. Right atrium (RA)/right ventricle/tricuspid valve/pacemaker leads
9. Descending thoracic aorta and arch of aorta.
2. Careful setting of probe frequency, focus position, and gain
3. A thorough multiplanar electronic sweep of imaging plane from 0° to 120° at gradual 5°–10° increment
4. For every imaging plane (at approximately 0°, 30°, 60°, 90°, and 120°), a gentle “right–left or clockwise–counterclockwise turn” and gentle “inward–outward push–pull” of TEE probe
5. Special maneuvers for IAS (VM with agitated saline-bubble contrast) and for the arch of the aorta
6. Color flow mapping (CFM) and pulsed-wave Doppler/continuous-wave Doppler interrogation at appropriate locations.

Sequence of segmental imaging

A comprehensive TEE imaging of each cardiac segment should include the following:

1. Positioning of the segment at the center of the imaging sector

Proper precautions should be observed during TEE examination of this special group of patients with recent stroke. Enquire about swallowing difficulties and dentures and then administer

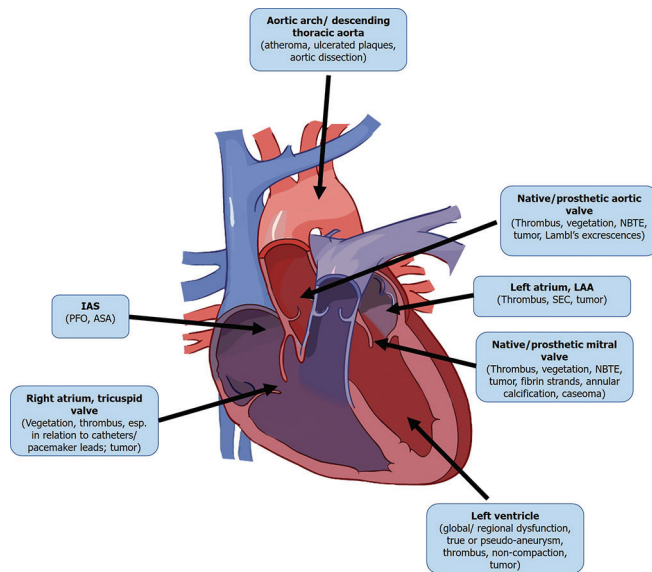


Figure 1: Cardiac structures of interest during transesophageal echocardiography in a patient with suspected cardioembolic stroke. ASD: Atrial septal defect, IAS: Inter atrial septum, NBTE: Non bacterial thrombotic endocarditis, PFO: Patent foramen ovale

pharyngeal local anesthetic spray. In a hospitalized patient with a Ryle's (nasogastric or orogastric feeding) tube *in situ*, it may be prudent to perform stomach aspiration and removal of the tube as it may interfere with imaging. In mechanically ventilated patients, it is helpful to top up the sedation by IV bolus of fentanyl and midazolam, give short-acting muscle relaxant, deflate the endotracheal tube cuff, and use a laryngoscope to gently introduce the TEE probe under vision.

Following is a suggested sequence of imaging that should be followed to obtain the maximum diagnostic yield [Figure 2]:

1. Introduce the TEE probe to the mid-esophageal (ME) position obtaining the 5-chamber view. Turn the probe leftward to identify and focus LAA. Scan the LAA by 0°–120° forward and 120°–0° reverse sweep
2. Return to 0° and slightly advance the probe to ME 4-chamber view. Focus on mitral valve leaflets, annulus, and LA cavity and scan from 0° to 120° in a forward sweep. Turn on/off CFM. In native mitral valve disease, use CFM to evaluate regurgitant orifice, vena contracta, and mechanism of mitral regurgitation. In a prosthetic mitral valve, the CFM should encompass both valvular and paravalvular regions during 0°–120° electronic sweep of the imaging plane
3. At 120°, in the ME view, slightly withdraw the TEE probe to focus on the aortic valve, annulus, and aortic root. Scan the aortic valve by 120°–0° reverse sweep. While at 120° and 0° imaging planes, withdraw the probe slightly to scan the ascending aorta in long-axis (120°) and short-axis (0°) views, respectively, up to the level of posterior crossing of the right pulmonary artery. In native aortic valve disease, use CFM to evaluate regurgitant orifice, vena contracta, and mechanism of aortic regurgitation. In a prosthetic aortic valve, the CFM should encompass both valvular and paravalvular regions during 120°–0° electronic sweep

of the imaging plane

4. Return to the ME 4-chamber view (0°) and focus on the LV cavity. Scan the LV cavity by a 0°–120° forward and 120°–0° reverse sweep, with careful visualization of submitral apparatus, LV regional wall motion abnormality, and intracardiac mass, if any. Visualization of the LV apex on TEE can be optimized by reducing the probe frequency, shifting the focus position to the apex, and ensuring the apical myocardium appears as thin as possible to avoid foreshortening. However, LV apical clot and aneurysm are better visualized by TTE
5. At 0° ME 4-chamber view, turn the TEE probe toward the right to focus on the IAS. Scan the IAS thoroughly with 0°–120° forward sweep and 120°–60° reverse sweep. CFM should be performed to visualize the PFO channel, if present, between the overlapping segments of septum primum and septum secundum in the region of fossa ovalis. Any drop out in the IAS should be evaluated with CFM to confirm the presence of a true atrial septal defect. The sinus venosus region should be evaluated carefully at 0° and 90°–110° imaging planes
6. At 30°–90° ME view, while focusing on the fossa ovalis region, agitated saline-bubble-contrast study should be performed. The saline bubble study may first be performed without VM, and if this shows definite right-to-left shunt, no further injections are required. However, often the study needs to be combined with VM as described below [Videos 1 and 2]
7. From the vantage point of rightward turned TEE probe, at 0° ME 4-chamber imaging plane, the focused view of RA, tricuspid valve, and right ventricle is obtained. Scan the right heart structures with 0°–60° forward and 60°–0° reverse sweep
8. At 0° ME 4-chamber view, turn the TEE probe toward extreme left until the descending thoracic aorta is visualized in its short axis. Then, gradually, withdraw the probe millimeter by millimeter to obtain multiple cross-sectional views of the descending thoracic aorta. After reaching the upper thoracic portion of the descending aorta, sweep the imaging plane to 90° to visualize the descending thoracic aorta in its long axis. From this vantage point, turn the TEE probe clockwise (which will turn the imaging plane medially and to the right), very gradually, millimeter by millimeter, to obtain multiple cross-sectional views of the arch of aorta. The origins of the left subclavian, left common carotid, and right brachiocephalic arteries can be visualized by this maneuver.

The above maneuvers are described for a two-dimensional TEE probe. When a three-dimensional TEE probe is available, biplane imaging can be utilized to enhance visualization of the cardiac structures from different planes simultaneously.

Performance of agitated saline-bubble-contrast echocardiography

The following sections describe the steps involved in the performance of agitated saline-contrast TEE for the detection

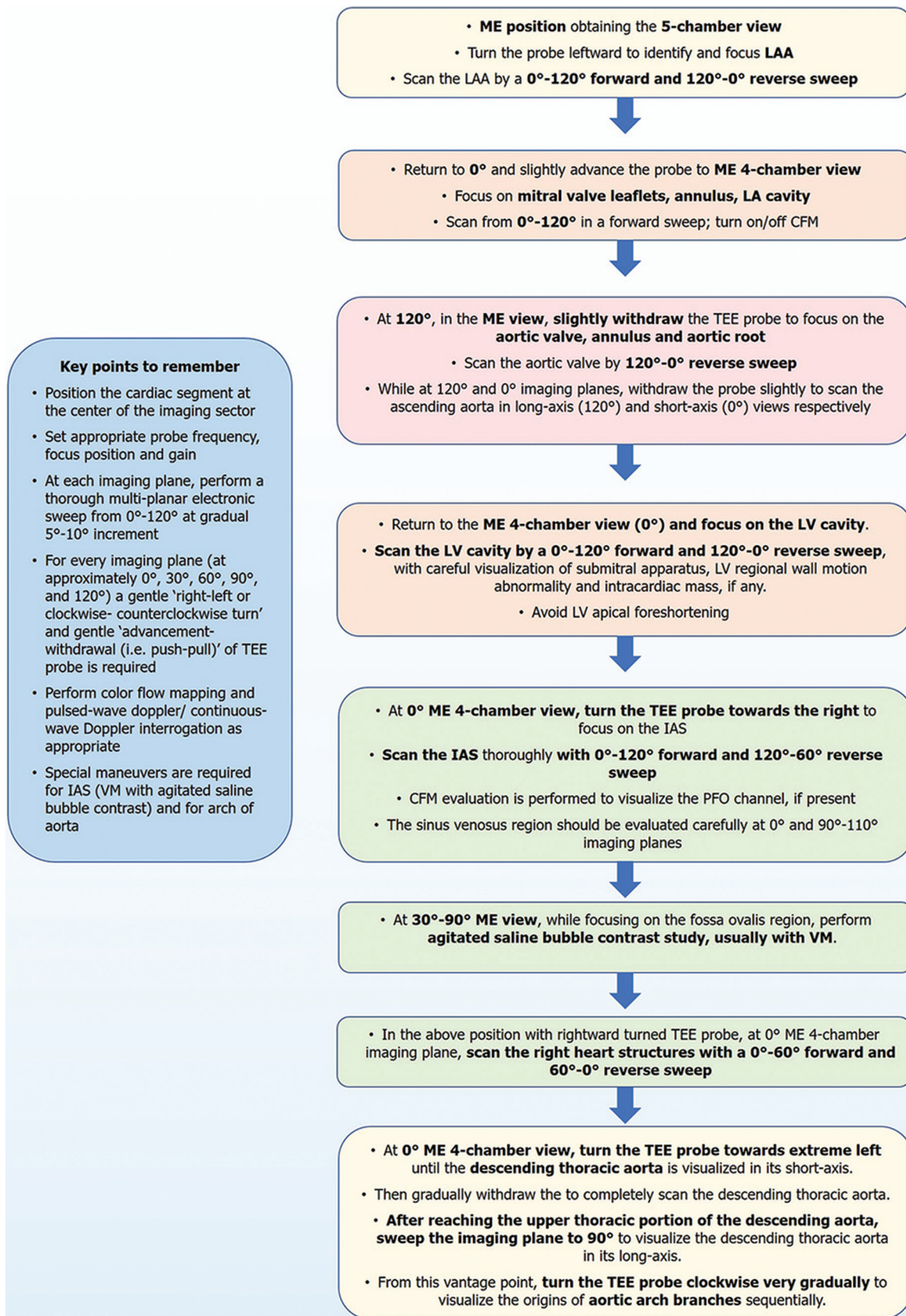


Figure 2: Suggested sequence of imaging for transesophageal echocardiography in a patient with suspected cardioembolic stroke
CFM- color flow mapping; IAS- interatrial septum; LA- left atrial; LAA- left atrial appendage; LV- left ventricular; ME- mid-esophageal; PFO- patent foramen ovale; TEE- transesophageal echocardiography; VM- valsalva maneuver

of intermittent right-to-left shunting through a PFO.^[7]

1. Explain the entire procedure to the patient before introducing the TEE probe. Teach and practice the performance of VM with the patient. The VM involves forced expiration against a closed glottis, and the strain should be maintained for at least 10 s. At the start of VM, the lab assistant can firmly put his or her palm against the patient's abdomen and ask the patient to forcefully push the hand by distending the abdominal wall with a sustained effort. The patient's strain effort can be adequately judged by this method. The patient should be instructed to maintain the strain till he/she is asked to cease the effort after which he/she can exhale out and immediately take a deep breath
2. In the patients on a mechanical ventilator, ventilation can be briefly paused at end expiration with simultaneous sustained firm pressure by palm on the patient's abdomen
3. Insert an 18–20-gauge IV cannula in the left antecubital vein. Connect a bivalve and two 10 ml syringes, one syringe containing 8 ml of normal saline and 0.5 ml of air. Withdraw 1 ml of patient's blood in the same syringe. After closing the bivalve toward the cannula, vigorously agitate the contents between the two syringes to make a fine frothy contrast. The contrast should be injected from the vertically oriented syringe so that the macrobubbles are allowed to float upward (away from the cannula) when the contrast is idle, preventing macro-air-embolism. Alternately, agitated gelatin-based plasma expander (3.5%) with a small amount of air (5%–10% mixture) can also be used
4. Introduce the TEE probe and position it at ME level. Rotate the multiplane angle to 30°–90° to visualize the fossa ovalis region and bring the area of fossa ovalis to the center of the image. If the TEE equipment has three-dimensional imaging capability, then X-plane imaging proves very helpful. Keeping one imaging plane at 30°–60° and the other at 90°–110° allows much better visualization of PFO, and the contrast bubbles entering from superior vena cava into the RA can also be visualized. Check the movement of imaging plane with the first VM without injecting the contrast
5. Ask the patient to start the VM. After 3–4 s from the start of the sustained effort, ask the nursing staff to inject 5–8 ml of agitated saline-bubble contrast while taking care to avoid injecting the macrobubbles floating on the top. This should be quickly followed by a 5–10 ml of saline flush. The patient should continue to perform VM with a sustained effort for 8–10 s without break
6. With the sustained strain of VM, there is a reversal of LA–RA pressure gradient and the septum primum starts bulging toward LA. At that moment, the injected contrast bolus should reach and completely opacify the RA. Immediately, ask the patient to release VM and take a deep breath. The septum primum further bulges to LA with opening of PFO and a puff of contrast can be seen entering into the LA cavity across the PFO channel [Figure 3 and Videos 1, 2]. It is very essential to ensure that the fossa ovalis territory of RA is fully opacified by the contrast before

release of VM. The noncontrast inferior vena cava blood preferentially flows toward the fossa ovalis diluting or clearing the contrast and is a major cause of false-negative studies for right-to-left shunt, despite the septal shift

7. Alternately, 10-ml contrast bolus can be injected into a foot vein, followed by a 5–10 ml of saline flush. In case of femoral injections, contrast preferentially flows from inferior vena cava toward the PFO
8. For complete evaluation of PFO, total four arm injections, with two during VM, one during cough, and one during 10° head-up bed tilt combined with VM, are recommended
9. After VM sustained effort, in healthy individuals, faint, thin, and smoke-like echoes are seen entering LA through the pulmonary veins on high gain setting. These are thought to be due to roulette formation of red blood cells during temporary stasis in the LA
10. Pulmonary arteriovenous malformation (PAVM): The agitated saline contrast will reach the LA in 3–5 beats after RA opacification. To avoid missing PAVM in the presence of PFO in conditions such as chronic liver disease or hereditary hemorrhagic telangiectasia, administer additional contrast injections and examine each pulmonary vein carefully
11. Injection into a vein in the left antecubital fossa is essential to avoid missing persistent aberrant left superior vena cava draining into the LA or unroofed coronary sinus.

TRANSESOPHAGEAL ECHOCARDIOGRAPHY EVALUATION OF INDIVIDUAL PATHOLOGIES

Infective endocarditis

Sensitivity and specificity of transthoracic and transesophageal echocardiography

TEE has consistently shown higher diagnostic yield for IE [Figures 4, 5 and Videos 3, 4] than TTE in various studies. Vegetations < 2–3 mm in size are missed by TTE due to limited

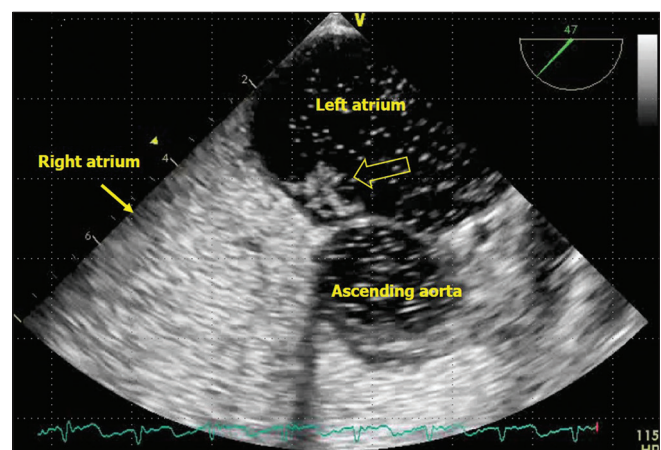


Figure 3: Agitated-saline-contrast transesophageal echocardiography with Valsalva maneuver for detection of right-to-left shunt across a patent foramen ovale. A large bolus of contrast bubbles (open arrow) is seen traversing from right atrium to the left atrium

spatial resolution. For the diagnosis of IE, TTE and TEE have diagnostic sensitivity of 63% and 94%, specificity of 98% and 100%, positive predictive value of 92% and 95%, and negative predictive value of 91% and 100%, respectively.^[8,9] In the presence of prosthetic mitral and aortic valves,^[9-11] the sensitivity of TTE is further reduced to approximately 20%–40%, while sensitivity of TEE remains at approximately 80%–90%.

TEE is superior to TTE in diagnosing complications of IE. For diagnosis of paravalvular abscess [Figure 6 and Videos 5a, b], the sensitivity and specificity of TTE are 28% and 98%, respectively, and that of TEE are 87% and 95%, respectively.^[12] For diagnosis of native leaflet perforation, the sensitivity and specificity of TTE are 45% and 98%, respectively, and that of for TEE are 95% and 98%, respectively.^[13]

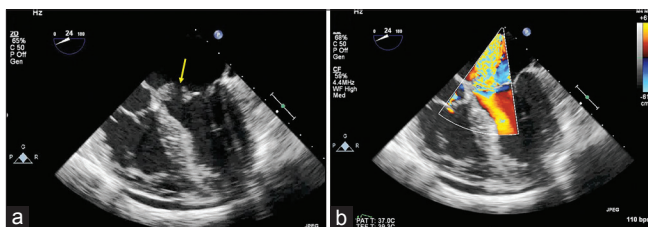


Figure 4: Infective endocarditis involving native mitral valve. (a) There is thickening of anterior mitral leaflet with central perforation (arrow) suggestive of a leaflet abscess; (b) large jet of mitral regurgitation through the leaflet perforation

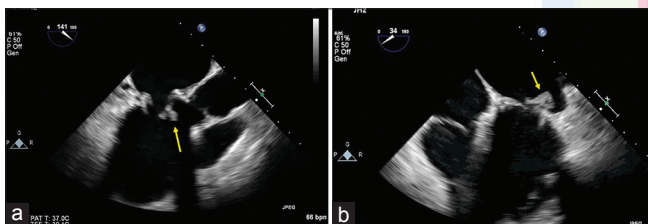


Figure 5: Infective endocarditis involving a bioprosthetic mitral valve. The vegetation (arrow) is attached to one of the valve leaflets and is moving with it. (a) Valve in open position; (b) valve in closed position

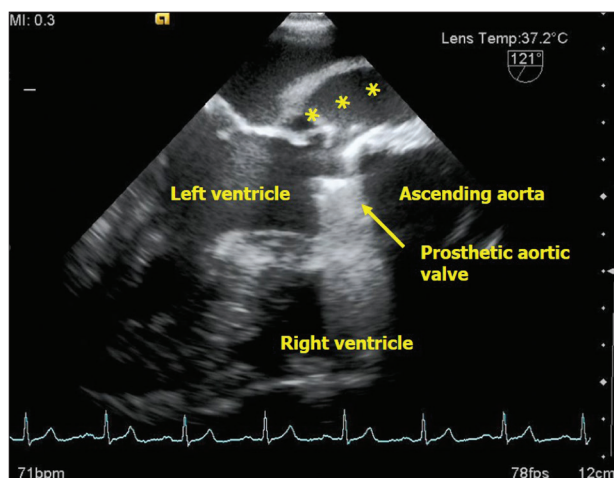


Figure 6: A large para-aortic abscess (asterisks) in a patient with prosthetic aortic valve infective endocarditis

Determinants of embolism in infective endocarditis

Approximately 20%–30% of patients with IE have clinical signs and symptoms of cerebral embolization. However, more than 30%–50% of patients with IE show silent cerebral embolism on neuroradiological imaging.^[14] Vegetation length >10 mm and excessive mobility are independent predictors of embolic events.^[15,16] The incidence of embolism is 60% in patients with vegetation length >10 mm, 62% in patients with highly mobile vegetations, and 83% in patients with both highly mobile and large vegetations (>15 mm).

Nonbacterial thrombotic endocarditis

In systemic diseases such as primary antiphospholipid syndrome, systemic lupus erythematosus (SLE, lupus anticoagulant and/or immunoglobulin G anti-cardiolipin antibodies), sepsis, burns, or disseminated malignancy, circulating inflammatory cytokines cause focal endothelial injury on the valve leaflets. Sterile, noninfective, fragile thrombi develop on the valve leaflets (usually mitral valve) at the site of endothelial injury [Figure 7 and Video 6]. The nonbacterial thrombotic endocarditis (NBTE) vegetations are more fragile than IE vegetations and have high potential for embolization. This may lead to infarcts in various organs, including the brain, kidney, and spleen. The incidence of embolic events is reported to be very high, ranging from 14.1% to 90.9% (average 42%), with cerebral circulation being the most common site for embolism.^[17]

In the autopsy studies, neoplasms are the most frequently encountered underlying disease,^[18] whereas surgical series have shown that NBTE is more frequent in patients with connective tissue and autoimmune diseases.^[19] The prevalence of NBTE is as high as 32% in patients with primary antiphospholipid syndrome.^[20] The patients with SLE and antiphospholipid antibodies have 3-fold higher risk for developing NBTE, compared with those without antiphospholipid antibodies.^[21] Cardioembolism from NBTE plays a crucial role in the neuropsychiatric manifestations of SLE.

Lambl's excrescences

TEE may show filamentous echo densities on native aortic and mitral leaflets and on prosthetic valves, especially in elderly patients [Figure 8 and Video 7]. These filamentous structures may represent fibrin strands on degenerated valve tissue. The prevalence of strands is five times higher among patients with an embolic event, compared to patients without any embolic event.^[22] Among patients with strands, more than one-third of the patients develop embolic events. Higher prevalence of Lambl's excrescences has been described in patients with ischemic stroke with no other detectable source of embolism.

Prosthetic valves

The annualized risk of thrombosis is estimated to be 1%–2% for mechanical prosthetic valves and 0.5%–1% for bioprosthetic valves^[23] [Figures 9–11 and Videos 8, 9, 10a, b]. Despite optimal anticoagulation, thrombosis is more common at tricuspid and mitral positions than at the aortic position. IV thrombolysis is an established therapeutic strategy in the presence of prosthetic valve

thrombosis. Independent predictors of risk of stroke or embolic event, related to thrombolysis, include thrombus size (measured as thrombus area by planimetry) on TEE and a history of stroke.^[24]

Besides valve thrombosis, any other structural abnormality of the prosthetic valves such as IE and structural degeneration of the bioprosthetic valves may also result in an embolic stroke. When IE is suspected, the entire circumference of the sewing ring and paravalvular area should be carefully inspected using multiplanar (0°–180°) TEE and CFM.

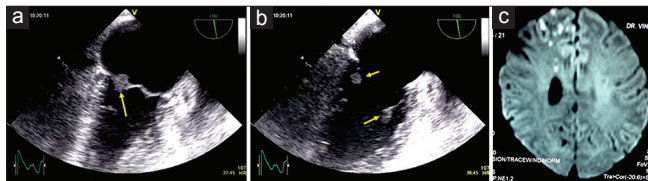


Figure 7: Nonbacterial thrombotic endocarditis involving mitral valve leaflets (a and b) in a patient with systemic lupus erythematosus. (c) Multiple cerebral infarcts in the same patient

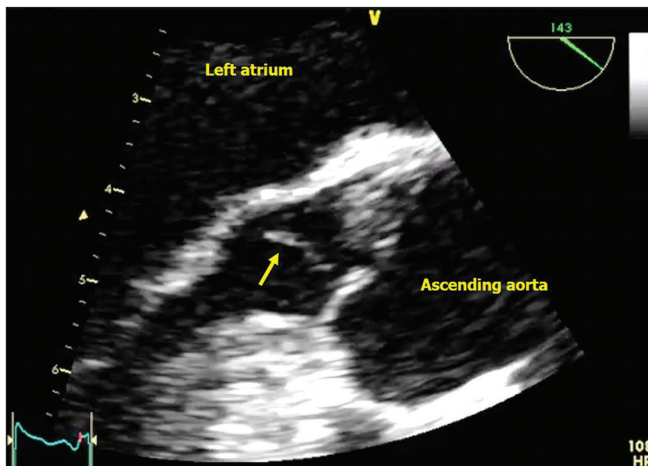


Figure 8: A thin, filamentous, oscillating structure suggestive of Lambert's excrescence is seen attached to one of the aortic valve leaflets

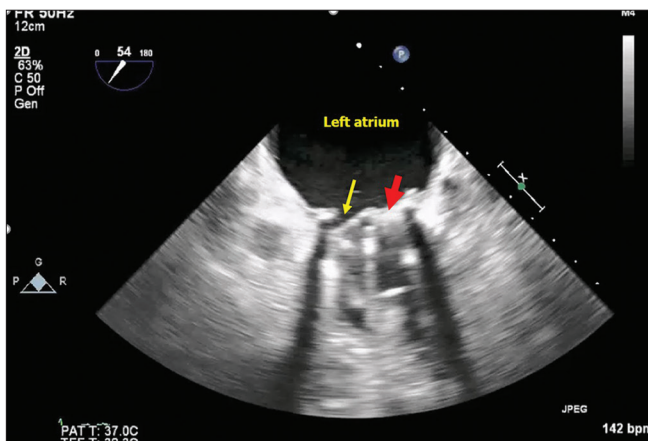


Figure 9: Bileaflet prosthetic valve at mitral position with valve thrombosis. One leaflet is completely stuck (red arrow) because of echogenic material deposited on it, which is likely to be thrombus. The other leaflet also opens only partially (yellow arrow)

Mitral annular calcification

Mitral annular calcification (MAC) is a common echocardiographic finding in elderly individuals and may sometimes be the cause of embolic stroke [Figure 12 and Video 11]. MAC is defined as mild if it involves less than one-third of the mitral annulus and severe if it involves more than two-thirds of the annulus. The postulated mechanisms of stroke due to MAC are as follows:^[25]

1. IE of MAC lesion
2. MAC being a marker of atherosclerotic vascular disease
3. Ulcerated MAC may develop overlying thrombus
4. Calcific mobile components of MAC can embolize
5. MAC may be associated with degenerative mitral stenosis, leading to LA dilation and AF.

Sometimes, caseous degeneration occurs within the calcified mitral annulus. This is known as caseoma [Figure 13 and Videos 12a, b]. Posterior mitral annulus is the most common site for caseoma formation. Contents of caseoma may sometimes leak into the LA, LV cavity, resulting in embolic events.

Valvular calcification

Apart from MAC, calcification involving any other part of the aortic or mitral valvular structure (leaflets, subvalvular apparatus, etc.) may also rarely cause embolic stroke.

Cardiac tumors

Myxoma

Myxomas most commonly arise from fossa ovalis region of the IAS with protrusion into the LA [Figure 14 and Video 13] or RA cavity and rarely from the LAA, valves, or ventricles. The embolization of tumor material itself or of overlying thrombi causes embolic events.

Papillary fibroelastomas

The size of papillary fibroelastomas varies from 2 to 70 mm, with a mean of 9 mm. More than 80% of the papillary fibroelastomas are located on the left-sided heart valves (aortic 36%, mitral 29%, tricuspid 11%, and pulmonic 7%)^[26,27] [Figure 15 and Video 14]. The remaining papillary fibroelastomas are located throughout the atria and ventricles. Multiple tumors are present in 9% of patients. The tumor material of papillary fibroelastomas can cause embolism and recurrent strokes.

Left atrial and left atrial appendage thrombus

The LAA is known to have different morphologies termed as cactus, chicken wing, windsock, and cauliflower appearances. The chicken-wing LAA morphology may be less likely to have thromboembolic events.^[23] The pathophysiological conditions which cause LA dilatation, atrial systolic-diastolic dysfunction, and blood stasis lead to the formation of SEC and thrombi within the LA and/or LAA [Figures 16, 17 and Videos 15-17]. TEE shows 100% sensitivity, 99% specificity, 86% positive predictive value, and 100% negative predictive value for detecting thrombi of sizes ranging from 3 to 80 mm.^[28] In comparison, the sensitivity of TTE is only 39%–65% for

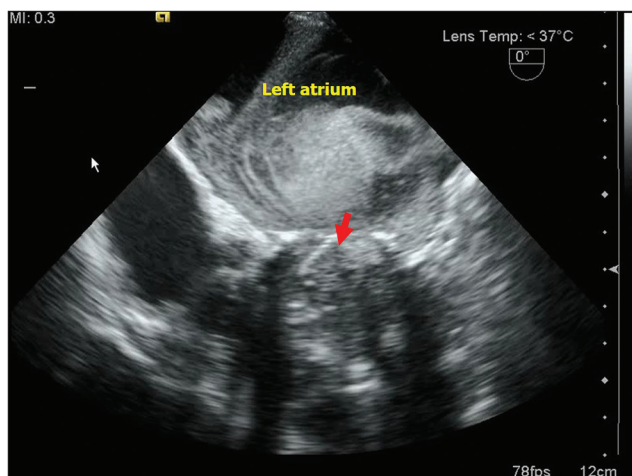


Figure 10: Another example of thrombosed bileaflet mitral prosthetic valve (arrow). There is extensive thrombosis around the valve leaflets with only one leaflet opening slightly. The left atrium is full of dense spontaneous echo contrast and evolving thrombus

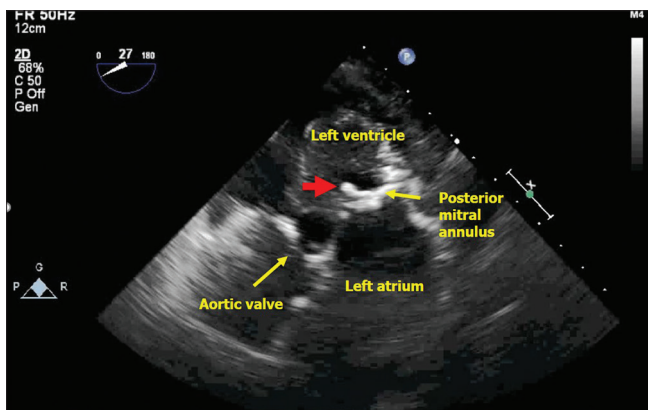


Figure 12: Deep transgastric view showing posterior mitral annular calcification with a mobile, echo-dense, oscillating structure (red arrow) seen attached to the calcified annulus. The patient had presented with stroke

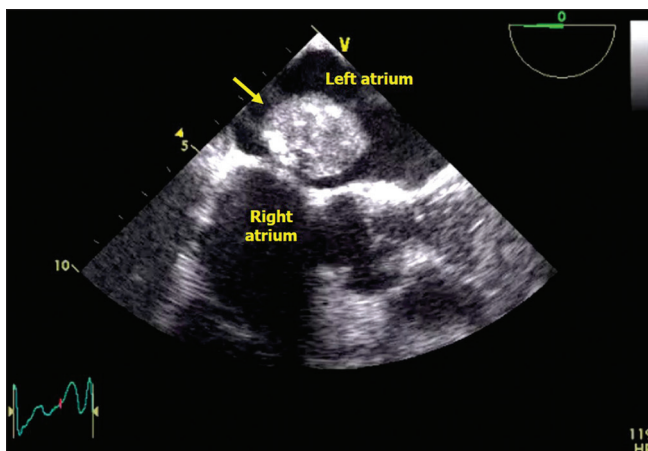


Figure 14: A large left atrial myxoma (arrow) attached to the left atrial side of the interatrial septum

LA/LAA thrombi because of poor visualization of LAA on TTE.

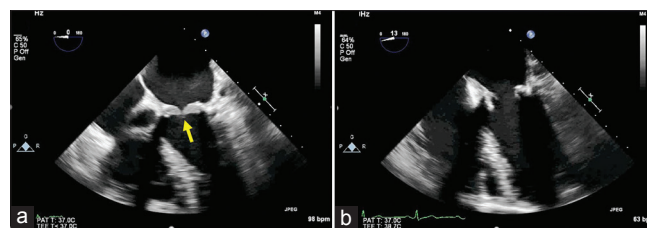


Figure 11: Thrombosis of a bioprosthetic mitral valve. (a) The mitral leaflets are markedly thickened with markedly reduced valve opening (arrow); (b) After adequate anticoagulation, the leaflet thickness has reduced significantly, and the leaflets are opening well now

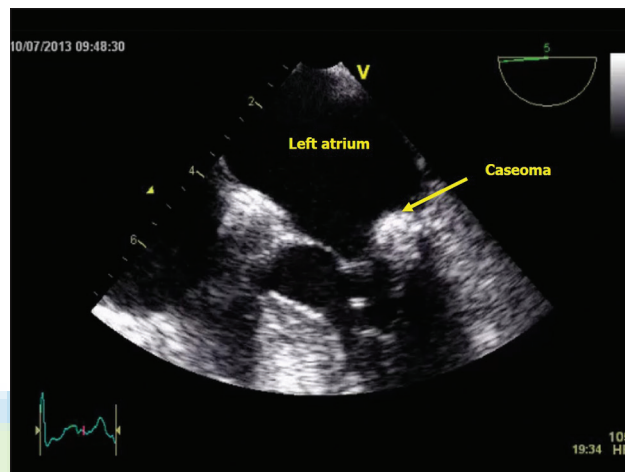


Figure 13: Caseoma (arrow) of the posterior mitral annulus. This entity represents chronic caseous degeneration within the calcified mitral annulus

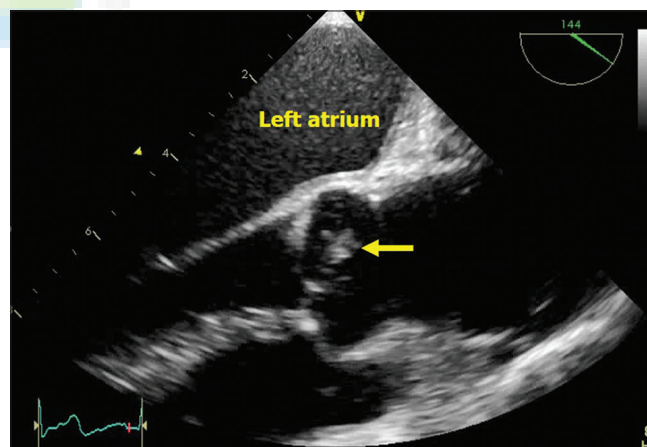


Figure 15: A small papillary fibroelastoma (arrow) on the aortic valve. The tumor has characteristic frond-like appearance

The incidence of LA thrombi on TEE is obviously much higher in patients with AF compared with patients in sinus rhythm. The LAA thrombi are known to cause thromboembolism even in patients in sinus rhythm, and this may occur even in an otherwise normal heart or when there is severe mitral stenosis or severe LV cardiomyopathy with LA chamber dilatation. The incidence of LA/LAA thrombus formation is higher in persistent (>7 days duration) or long-standing (>12 months)

AF compared to paroxysmal AF.^[29] However, in patients with a recent cardioembolic event, the frequency of LAA thrombus does not differ between those with paroxysmal AF and those with persistent, long-standing, or permanent AF.^[29] Patients with LAA thrombi in sinus rhythm and those with LAA thrombi in AF show similar degree of LA dilatation and LV dysfunction, increased LAA area, decreased peak emptying velocity of LAA, or presence of LA SEC.^[30]

LA systolic stunning occurs after cardioversion from AF to sinus rhythm, leading to continued stasis and risk of embolism. The LAA “stunning” is seen on TEE as an increase in the intensity of SEC and a decrease in LAA Doppler flow velocities immediately after direct current cardioversion.^[31] TEE-guided cardioversion for AF has similar low risk of embolism as the conventional method of precardioversion 3-week

anticoagulation and has significantly lower incidence of bleeding than the conventional method.^[32]

In the Stroke Prevention in AF III (SPAF-III) trial,^[33] the risk factors for embolism in nonvalvular AF as identified by TEE were presence of LAA thrombus, LAA peak flow velocity <27 cm/s, and presence of aortic plaque. In patients with LA thrombus detected on TEE, the stroke or embolic event rate is 10.4%/year and cardiovascular mortality rate is 15.8%/year.^[34] The strongest predictors of thromboembolism are thrombus size >1.5 cm, history of thromboembolism, and mobility of thrombus, irrespective of gender, age, warfarin therapy, AF, and location (cavity vs. appendage) of thrombus.

Left atrial spontaneous echo contrast

The blood stasis produced by mitral stenosis, AF, or severe LA dilatation leads to erythrocyte aggregation in low shear rate conditions, which is seen as SEC on echo [Figure 16 and Videos 15-17]. LA SEC is a common finding in 19% of patients undergoing TEE for various reasons. However, 95% of the patients with SEC have AF or mitral stenosis. SEC is also an independent predictor of LA thrombus formation or cardioembolism.^[35]

In the SPAF-III trial, SEC was detected in 20% of the patients.^[36] The rate of stroke in patients with SEC was 18.2%/year with combination therapy (2.9 times the rate in patients without SEC) and 4.5%/year with adjusted-dose warfarin. LAA thrombus was detected in 10% of patients and was associated with dense SEC. LAA thrombus was seen more frequently after 2 weeks of combination therapy (15%) than after 2 weeks of adjusted-dose warfarin (4%). The presence of persistent LAA thrombus tripled the overall rate of stroke.

Left ventricular thrombus

In acute myocardial infarction, an LV thrombus often develops over an akinetic wall segment, which has sustained subendocardial injury, in the milieu of a hypercoagulable state and blood stasis due to low cardiac output. These predominantly red thrombi can occur as early as 24 hour after an acute myocardial infarction. However, the majority (90%) of LV thrombi are detected within 14 days of myocardial infarction.^[23] The risk factors for developing LV thrombi are large infarct size, anterior wall myocardial infarction, LV apical wall akinesia, and LV aneurysm.^[37] LV apical thrombi may also be seen in LV endomyocardial fibrosis, LV noncompaction cardiomyopathy, and LV apical outpouching in the presence of LV mid-cavity obstructive hypertrophic cardiomyopathy.

TTE is superior to TEE in diagnosing LV apical clot. TTE has sensitivity of 95% and specificity of 85%–90% for detecting LV thrombi.^[38] Poor transthoracic echo window, near-field apical clutter, and LV apical trabeculations or false tendon may reduce the diagnostic accuracy of TTE. The use of IV echocardiographic contrast agents for LV opacification significantly improves the accuracy of diagnosis by “ruling in” or “ruling out” LV apical thrombus [Figure 18 and Video 18] and has direct impact on clinical decisions and outcomes.^[39,40]

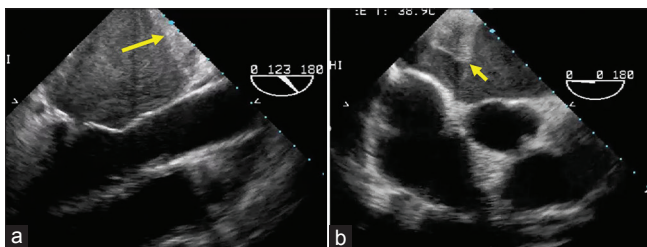


Figure 16: Two examples of spontaneous echo contrast with clot (arrows in image a & b) in the left atrium. Both the patients had mitral stenosis

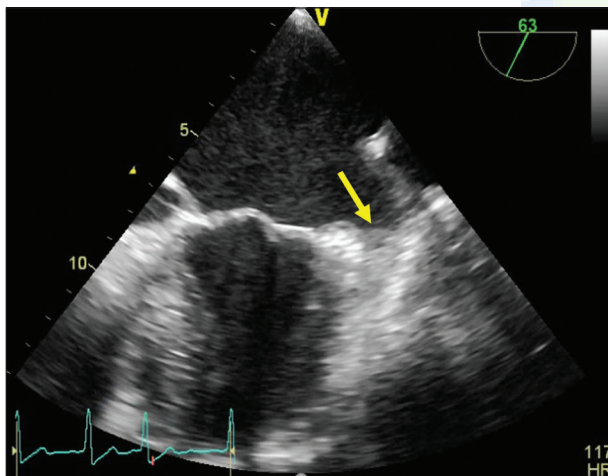


Figure 17: Thrombus in the left atrial appendage along with spontaneous echo contrast in the left atrium

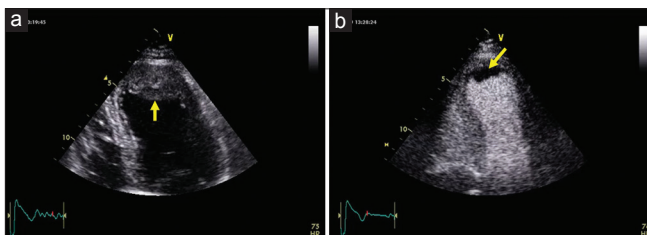


Figure 18: Apical four-chamber view during transthoracic echocardiography demonstrating a left ventricular apical clot. (a) Without contrast; (b) with contrast

LV thrombi which are mobile and/or protruding into the LV cavity have a higher incidence of embolization.

Patent foramen ovale, atrial septal aneurysm, and pulmonary arteriovenous fistula

PFO [Figure 19 and Video 19] or ASA [Figures 20, 21 and Videos 20, 21] are often implicated in the pathogenesis of paradoxical embolic events in cryptogenic stroke [Box 1]. However, identification of PFO and/or ASA in a patient with an ischemic stroke does not always prove a causal relationship in every patient. In the presence of abnormalities of the IAS, two pathophysiologic mechanisms are suggested for embolic events: [41] first, right-to-left shunting with Valsalva across the PFO; and second, blood stasis and thrombus formation in the ASA/atrial septal pouch [Figures 21, 22 and Videos 21, 22]. A large Eustachian valve [Figure 20 and Video 20] or a Chiari network directs inferior vena cava blood toward the PFO aiding in the paradoxical embolism. Trapped thrombi in the PFO, while traversing from RA to LA, have been shown in many case reports.[42] Thrombi from lower extremity or pelvic veins, tricuspid valve vegetations, right-sided papillary fibroelastoma or other cardiac tumor, air emboli, fat emboli, and clots or vegetations on pacemaker or defibrillator leads may lead to paradoxical embolism to the left circulation via PFO.

A PFO is defined on agitated-saline contrast as follows:[7]

- A PFO is defined as at least three bubbles reaching the LA within three beats from opacification of RA and/or the PFO channel (overlap of septum primum and secundum) is visualized as the site of contrast passage
- A large PFO is defined as >20 bubbles passing from RA to LA after a single injection. The investigators of the Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current

Standard of Care Treatment (RESPECT) trial^[43] used a semi-quantitative system for grading PFO shunt as Grade I (mild, 1–9 bubbles), Grade II (moderate, 10–20 bubbles), and Grade III (large, >20 bubbles).

For any PFO identified during TEE, the following parameters should be reported which can help in device selection for PFO closure:[44]

- Amount of right-to-left shunt (small, medium, or large)
- The length of tunnel-like overlap between septum primum and septum secundum (absent to large length of overlap)
- The maximum width of the PFO channel during the cardiac cycle
- Diameter of the fossa ovalis (measured on three-dimensional TEE)
- Presence of and diameter of ASA and its mobility
- Thickness of the septum secundum.

Ischemic strokes in younger patients that are large, radiologically prominent, superficially located in the cerebral cortex, or without prior radiological lacunar infarcts are more likely to be PFO associated. Ischemic strokes in older patients, which are clinically unobvious, radiologically smaller, lacunar, detected in deep white matter and those accompanied by chronic infarcts, are likely to be related to atherosclerotic vascular disease.[45] In the setting of cryptogenic stroke and incidental PFO, the risk of stroke recurrence is lower if there is a higher likelihood of PFO being responsible for the first stroke.

The presence of PFO, ASA, or both (PFO + ASA) has been shown to be significantly associated with an ischemic stroke in patients aged <55 years.[46] However, the association of these atrial septal abnormalities with ischemic stroke is less certain in those aged ≥55 years. The following characteristics of PFO

Box 1: The role and relevance of patent foramen ovale and atrial septal aneurysm in stroke

- A PFO is defined as at least three bubbles reaching the left atrium within three beats from opacification of right atrium and/or the PFO channel (overlap of septum primum and secundum) is visualized as the site of contrast passage
- An atrial septal aneurysm is defined as septal excursion of >10 mm, with a base diameter of >15 mm or a sum of total excursion into left or right atrium >14 mm
- PFO and atrial septal aneurysm frequently coexist, and both have been shown to have significant association with cardioembolic stroke in case-control studies. However, identification of PFO and/or atrial septal aneurysm in a patient with an ischemic stroke does not always prove a causal relationship
- PFO and/or atrial septal aneurysm are implicated in the pathogenesis of paradoxical embolic events in cryptogenic stroke, either because of intermittent right-to-left shunting across the PFO or due to blood stasis and thrombus formation in the atrial septal aneurysm/atrial septal pouch
- Transesophageal echocardiography with agitated-saline-contrast injection with VM has the highest diagnostic accuracy for diagnosing PFO
- RoPE score has been proposed for estimating contribution of PFO -attributable fraction for index stroke as well as stroke/transient ischemic attack recurrence rates. Maximum score is 10. A higher score is associated with greater likelihood of PFO being responsible for the stroke
- Regarding transcatheter device closure of PFO, the earlier trials (2012-2013), viz., CLOSURE I, PC Trial and the RESPECT-early outcome, did not show benefit of PFO device closure in reducing recurrent ischemic strokes. However, the recent, late-breaking trials (2017), viz., RESPECT-late outcome, Gore REDUCE and CLOSE, have shown statistically significant reduction in recurrent ischemic strokes, likely due to longer follow-up, reduced device complications, and strict entry criteria of moderate-to-large right-to-left PFO shunts and/or atrial septal aneurysm

CLOSE: Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence, CLOSURE I: Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a Patent Foramen Ovale trial, Gore REDUCE: GORE HELEX™ Septal Occluder and Antiplatelet Medical Management for Reduction of Recurrent Stroke or Imaging-Confirmed TIA in Patients with Patent Foramen Ovale, PC trial: the Clinical Trial Comparing Percutaneous Closure of Patent Foramen Ovale Using the Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism, PFO: Patent foramen ovale, RESPECT- Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment, RoPE: Recurrence of paradoxical embolism, VM: Valsalva maneuver

were proposed to be related to an increased risk of recurrent stroke- larger PFO size, large right-to-left shunt, spontaneous right-to-left shunt, greater PFO flap mobility, prominent Eustachian valve, presence of Chiari network, and ASA.^[47,48]

There are discrepant findings in the literature regarding the association of PFO and its characteristics with ischemic stroke. While the case-control studies have reported a positive association, the population-based cohort studies have only revealed an uncertain association.^[49] The PFO-attributable fraction of stroke in different age groups differs significantly, and it may explain the discrepant findings of the case-control and population-based cohort studies.

A point score system^[50] (Recurrence of Paradoxical Embolism or RoPE score) has been proposed for estimating contribution of PFO-attributable fraction for index stroke as well as stroke/transient ischemic attack recurrence rates. The clinical variables and the score assigned are shown in Table 3. Total score is calculated as sum of the individual points with maximum score being

10 (patients aged <30 years with no hypertension, no diabetes, no history of stroke or transient ischemic attack, nonsmoker, and cortical infarct) and the minimum score being 0 (patient aged ≥ 70 years with hypertension, diabetes, prior stroke, current smoker, and no cortical infarct). The RoPE score stratum-specific prevalence of PFO, PFO-attributable fraction estimate for index stroke, and the risk of recurrence of stroke are shown in Table 4.^[50] A patient with RoPE score 9–10 (younger age, presence of a cortical stroke on neuroimaging, and absence of risk factors) has PFO prevalence of 73%, PFO-attributable fraction estimate for the index stroke of 88%, and estimated stroke/transient ischemic attack 2-year recurrence rates of approximately 2%.

An ASA is defined as septal excursion of >10 mm, with a base diameter of >15 mm or a sum of total excursion into LA or RA >14 mm [Figure 20 and Video 20]. ASA is frequently associated with PFO. Approximately 56%–84% of the patients with ischemic stroke and an ASA also have an interatrial shunt via a PFO.^[51,52] Conversely, PFOs are

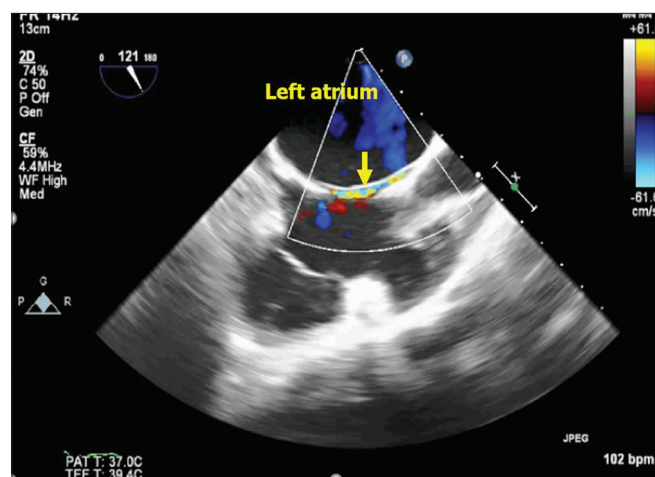


Figure 19: Color flow imaging showing left-to-right shunting across a patent foramen ovale. As demonstrated in Video 2, the shunt direction reverses intermittently on performing Valsalva maneuver

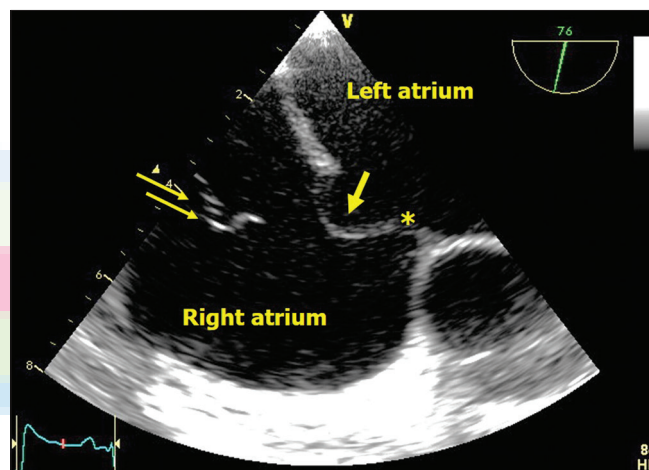


Figure 20: Interatrial septal aneurysm (single arrow) with a patent foramen ovale (asterisk). The patient also had a large, redundant Eustachian valve (double arrows)

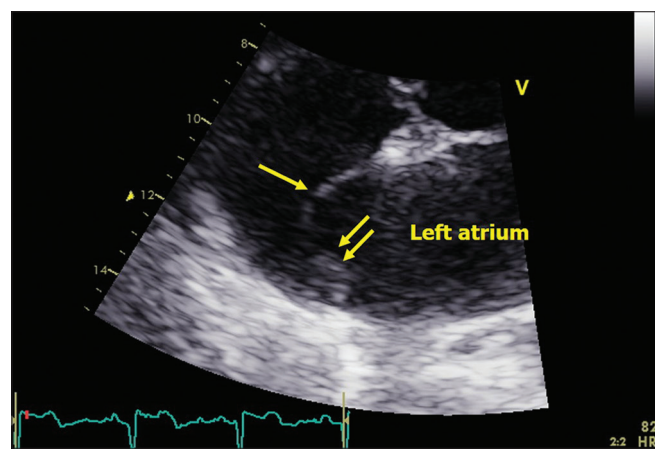


Figure 21: Transthoracic echocardiography showing short-axis view at atrial level. The interatrial septum is aneurysmal (single arrow) with a thrombus attached to it (double arrows)

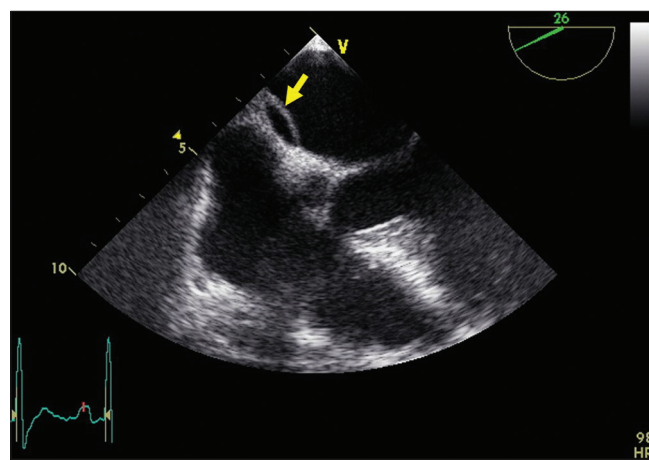


Figure 22: Interatrial septal pouch (arrow) due to incomplete fusion of septum primum and septum secundum. This may sometimes be the site for thrombus formation and subsequent embolic events

also approximately 4–5 times more frequent in patients with ASAs compared to those with nonaneurysmal IAS.^[51] ASAs are three times more common in stroke patients with normal carotids compared to normal population.^[52] In patients with ASA and stroke aged <45 years, TEE may not detect another source of embolism other than PFO in a vast majority of the cases. In patients with ASA without PFO, it is hypothesized that fibrin-platelet particles adhere to the LA side of the aneurysm and the oscillations of the aneurysmal flap result in embolization. Sometimes, even thrombi may form in relation to the ASA [Figure 21 and Video 21].

TTE with CFM has low sensitivity for the detection of a PFO compared with TTE with agitated-saline contrast. The latter has 99% sensitivity and 85% specificity for diagnosing PFO with shunt and has good agreement with TEE.^[53] However, nearly half of the patients with positive contrast study require VM to detect the right-to-left shunting. False-positive contrast TTE studies occur due to transpulmonary shunting (PAVM) and the false-negative results occur due to suboptimal RA opacification. Transcranial Doppler ultrasound with IV agitated-saline contrast detects air bubbles in the cerebral circulation and is

a sensitive method for detecting the presence of right-to-left shunt. However, unlike echocardiography, transcranial Doppler cannot differentiate between intracardiac (i.e., PFO) and extracardiac (i.e., PAVM) sources of shunting.

The hypothesis of paradoxical embolism across PFO as a cause of cryptogenic stroke led to the concept of transcatheter device closure of PFO to abolish recurrence of ischemic strokes. Till date, five randomized trials^[43,54-58] have compared the efficacy of transcatheter device closure against oral antithrombotic therapy in patients with cryptogenic stroke and TEE-defined PFO. The earlier trials (2012–2013), viz., the Evaluation of the STARFlex Septal Closure System in Patients with a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism through a PFO (CLOSURE I) trial,^[54] the Clinical Trial Comparing Percutaneous Closure of PFO Using the Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism (PC Trial),^[55] and the RESPECT-early outcome,^[43] did not show benefit of PFO device closure in reducing recurrent ischemic strokes. However, the recent, late-breaking trials (2017), viz., RESPECT-late outcome,^[56] the GORE HELEX™ Septal Occluder and Antiplatelet Medical Management for Reduction of Recurrent Stroke or Imaging-Confirmed TIA in patients with PFO (Gore REDUCE),^[57] and the PFO Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence (CLOSE),^[58] showed statistically significant reduction in recurrent ischemic strokes, likely due to longer follow-up, reduced device complications, and strict entry criteria of moderate-to-large right-to-left PFO shunts and/or ASA.

While considering PFO device closure in a patient with cryptogenic stroke, the following lessons learned from these trials^[43,54-58] should be taken into consideration:

1. The patients should have truly cryptogenic stroke and be thoroughly evaluated to rule out non-PFO-related causes
2. The patient should have high RoPE score which implies younger age, absence of atherosclerotic risk factors, and nonlacunar infarcts
3. The TEE should show large right-to-left shunt across PFO at rest or on Valsalva or the presence of true ASA with PFO
4. The antiplatelet therapy should be continued after PFO device closure to reduce non-PFO-related strokes
5. There is no conclusive evidence of superiority of device closure with antiplatelet therapy over oral anticoagulants alone (either direct oral anticoagulants or international normalized ratio-guided Vitamin K antagonists)
6. The PFO-attributable strokes have low recurrence rate. Hence, the benefits of PFO closure are accrued over longer period of time
7. The choice of the closure device (except STAR Flex) does not matter, but higher rate of effective closure of the shunt is the principal factor
8. There are small but definite device and procedure-related complications. These can be minimized by performing the procedure only at the centers of excellence.

Table 3: Recurrence of Paradoxical Embolism (RoPE) score

Variables	Score
No history of hypertension	1 (0 if hypertensive)
No history of diabetes	1 (0 if diabetic)
No history of stroke or transient ischemic attack	1 (0 if history present)
Nonsmoker	1 (0 if smoker)
Cortical infarct on imaging	1 (0 if no cortical infarct)
Age years	
18-29	5
30-39	4
40-49	3
50-59	2
60-69	1
≥70	0

Table 4: RoPE score and prevalence of PFO, attributable fraction estimate, and risk of recurrence of stroke

RoPE score	Prevalence of PFO (%), (95% CI)	PFO-attributable fraction (%), (95% CI)	Estimated two-year stroke/transient ischemic attack recurrence rate (%), (95% CI)
0-3	23 (19-26)	0 (0-4)	20 (12-28)
4	35 (31-39)	38 (25-48)	12 (6-18)
5	34 (30-38)	34 (21-45)	7 (3-11)
6	47 (42-51)	62 (54-68)	8 (4-12)
7	54 (49-59)	72 (66-76)	6 (2-10)
8	67 (62-73)	84 (79-87)	6 (2-10)
9-10	73 (66-79)	88 (83-91)	2 (0-4)

CI: Confidence interval, PFO: Patent foramen ovale, RoPE: Recurrence of paradoxical embolism

Arch atheroma Thromboembolism

TEE imaging of the arch of the aorta or descending thoracic aorta many times reveals mobile structures attached to the aortic walls. These mobile structures are usually thrombi superimposed on underlying ulcerated plaques [Figure 23 and Videos 23 and 24]. Thromboemboli from these plaques are generally large and occlude single, medium-sized cerebral arteries in the index stroke or transient ischemic attack.^[59]

Atheroembolism

Atherosclerosis of aorta can also lead to formation of cholesterol crystal emboli or micro-atheroemboli resulting in multiple small arteries occlusion causing tissue or organ damage (e.g., “blue toe” syndrome, retinal ischemia, renal failure, livedo reticularis, and intestinal infarction).^[23]

The risk factors for embolization are as follows:

1. Plaque thickness >4 mm
2. Plaque ulceration
3. Mobility of a component of the plaque
4. Overlying thrombus
5. Plaque location.

Approximately one-fourth of the patients with cerebrovascular strokes show ulcerated aortic plaques on autopsy. The ulcerated aortic plaques are seen in more than half of the patients with no known cause of cerebral infarction.^[60] The presence of ulcerated plaques in the aortic arch has no association with the presence of extracranial internal carotid artery stenosis, suggesting that arch atheroma and carotid stenosis are independent risk factors for stroke.

Approximately one-third of the patients with protruding atheroma detected on TEE and no other source of emboli develops vascular events on follow-up over 2 years which amounts to nearly 5-fold higher incidence than normal population.^[61] Protruding atheroma is the strongest independent predictor of stroke events [Video 25]. Ischemic strokes are 9-fold more common among patients with >4 mm thick plaques. In a French study,^[62] 331 patients >60 years of age, consecutively admitted for brain infarction, were divided into three groups according to the size of arch atheroma on TEE (>4 mm, 1–3.9 mm, and <1 mm). The incidence of recurrent brain infarction in the three groups over 4 years

of follow-up was 11.9, 3.5, and 2.8 per 100 person-years, respectively. The overall incidence of vascular events (brain infarction, myocardial infarction, peripheral embolism, and death from vascular causes) over 4 years was 26.0, 9.1, and 5.9 per 100 person-years, respectively.

The arch atheromas also have independent and additional contribution to stroke in the population of nonvalvular AF. In the SPAF-III trial,^[36] 134 (35%) of the 382 patients with AF had complex aortic plaque (>4 mm in thickness or mobile) on TEE. Patients with complex aortic plaque had a 4-fold increased rate of stroke compared with plaque-free patients. Adjusted-dose warfarin decreased risk by 75%. In patients with AF, dense SEC and complex aortic plaque were independent predictors of thromboembolism.

Complex atherosclerotic plaques are more prevalent in the mid or distal aortic arch or descending aorta and are relatively less prevalent in the ascending aorta. The presence of protruding atheroma in the arch causes more strokes than the atheroma in descending thoracic aorta. The incidence of stroke is nearly 7-fold higher in patients with plaques > 4 mm in the aortic arch compared to the plaques in the descending aorta.^[63]

The perioperative stroke incidence during cardiopulmonary bypass surgery is 12% (i.e., six-time higher) when aortic arch atheromas are detected on TEE.^[64] In the presence of arch atheroma, procedures such as diagnostic catheterization, percutaneous coronary intervention, intra-aortic balloon pump insertion, cross-clamping, and performance of the proximal anastomosis during cardiac surgery are associated with an increased risk of stroke. In such patients, an embolic event occurs in nearly one-fifth of the patients after femoral catheterization and in one-half of the patients after intra-aortic balloon pump insertion.^[65]

DISCLAIMER

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Conflicts of interest

There are no conflicts of interest.

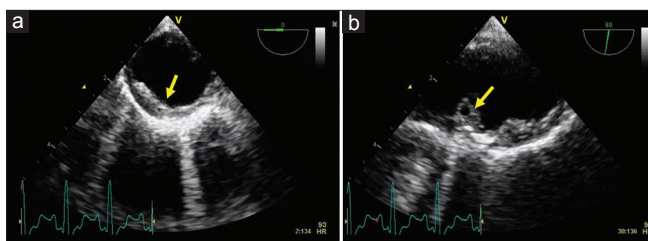


Figure 23: A short-axis view of the aortic arch showing (a) atheroma; (b) large, protruding atheroma in the aortic arch with mobile components (arrow)

Video legends

Video 1: Performance of agitated saline contrast transesophageal echocardiography with Valsalva maneuver for detection of right-to-left shunt across a patent foramen ovale. The saline contrast bubbles appear in the left atrium within three cardiac cycles of their appearance in the right atrium. The interatrial septum is highly mobile and the shunting increases intermittently as the septum bulges towards the left atrium.

Video 2: Another example of agitated saline contrast echocardiography with Valsalva maneuver for detection of right-to-left shunt across a patent foramen ovale. There is visible passage of saline bubbles across the patent foramen ovale, which increases as the interatrial septum bulges towards the left atrium.

Video 3: Infective endocarditis involving both the native aortic valve and the bioprosthetic mitral valve.

Video 4: Large vegetation attached to one of the leaflets of the bioprosthetic mitral valve.

Video 5: A patient with bileaflet prosthetic aortic valve with infective endocarditis. There is a large paraaortic abscess in the region of aortomitral curtain (a); the abscess cavity is communicating with the left ventricle, which can be easily appreciated on color flow imaging (b).

Video 6: An example of non-bacterial thrombotic endocarditis in a patient with systemic lupus erythematosus with antiphospholipid antibody syndrome. A sessile mass can be seen attached to the atrial surface of the anterior mitral leaflet.

Video 7: Lambl's excrescences, which are thin, filamentous, oscillating structures attached to the aortic valve leaflets.

Video 8: Bileaflet prosthetic valve at mitral position with valve thrombosis. One leaflet is completely stuck because of echogenic material deposited on it, which is likely to be thrombus.

Video 9: Another example of thrombosed bileaflet mitral prosthetic valve. There is extensive thrombosis around the valve leaflets with only one leaflet opening slightly. The left atrium is full of dense spontaneous echo contrast and evolving thrombus.

Video 10: Thrombosis of a bioprosthetic mitral valve. (A) The mitral leaflets are markedly thickened with markedly reduced valve opening; (B) After adequate anticoagulation, the leaflet thickness has reduced significantly and the leaflets are opening well now.

Video 11: Deep transgastric view showing posterior mitral annular calcification with a mobile, echo-dense, oscillating structure seen attached to the calcified annulus. The patient had presented with stroke.

Video 12: A and B- Two examples of caseoma of the posterior mitral annulus. This entity represents chronic caseous degeneration within the calcified mitral annulus.

Video 13: A large left atrial myxoma attached to the left atrial side of the interatrial septum.

Video 14: A small papillary fibroelastoma on the aortic valve. The tumor has characteristic frond-like appearance with multiple oscillating structures on its surface.

Video 15: Spontaneous echo contrast with a clot in the left atrium in a patient with mitral stenosis.

Video 16: Another example of spontaneous echo contrast with left atrial clot. The clot in this example is much larger and is pyramidal in shape.

Video 17: Thrombus in the left atrial appendage along with spontaneous echo contrast in the left atrium in a patient with mitral stenosis.

Video 18: Transthoracic echocardiography with contrast demonstrating a left ventricular apical clot.

Video 19: The same patient as in Video 2. Left-to-right shunting across the patent foramen ovale is seen on color flow imaging. As demonstrated in Video 2, the shunt direction reverses intermittently on performing Valsalva maneuver.

Video 20: Aneurysmal interatrial septum with patent foramen ovale with large, redundant eustachian valve.

Video 21: Transthoracic echocardiography showing short-axis view at atrial level. The interatrial septum is aneurysmal with a mobile thrombus attached to it

Video 22: Interatrial septal pouch due to incomplete fusion of septum primum and septum secundum. This may sometimes be the site for thrombus formation and subsequent embolic events.

Video 23: Short-axis view of the aortic arch showing an atheroma.

Video 24: An aortic arch atheroma with superimposed mobile clot.

Video 25: A large, protruding atheroma in the aortic arch.

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