Evaluation of Patients with Suspected Cardiac Sources of Emboli

39

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Abstract

The presentation of a patient with an acute arterial embolic event is not only dramatic for the acuity and severity of symptoms; it is also the harbinger of potentially life-threatening disease. Recognition of the many clinical manifestations that can result as emboli travel through the arterial system is the first step in the evaluation for cardiac sources of emboli. While nearly every organ in the body is a potential embolic target, the incidence of clinically apparent embolic events is approximately three times higher in the cerebral circulation than the peripheral circulation. The most common source of cardiac emboli is a left atrial thrombus due to atrial fibrillation, whereas the second most common source is a left ventricular thrombus following an acute myocardial infarction. Other etiologies include endocarditis, cardiac tumors, and aortic atherosclerosis. While a transthoracic echocardiogram (TTE) is the initial imaging test for most patients, transesophageal echocardiography (TTE) has been shown to be superior to TTE at detecting cardiac sources of emboli and is also more cost effective. Once a cardiac source of emboli is identified, management depends on the underlying etiology and patient comorbidities.

Keywords

Emboli • Thrombus • Stroke

Introduction

The presentation of a patient with an acute arterial embolic event is not only dramatic for the acuity and severity of symptoms; it is also the harbinger of potentially life-threatening disease. Because of the cardiovascular nature of the embolic syndromes, cardiologists are frequently the primary consultants for affected patients. Therefore, recognizing the many clinical manifestations that can result as emboli travel through the arterial system is the first step in the evaluation for cardiac sources of emboli. While nearly every organ in the body is a potential embolic target, the incidence of clinically apparent embolic events is approximately three times higher in the cerebral circulation than the peripheral circulation [1, 2]. This may be due to the fact that most cerebral arteries are functional end arteries, whereas the peripheral circulation tends to have a rich anastomotic blood supply that can stave off clinically significant ischemia while the thrombus resolves. Other potential end organs of arterial emboli include the spleen, kidney, gut, eye, and, although commonly overlooked, the heart itself. Finally, diseases of the right heart can result in pulmonary emboli. The most common source of cardiac emboli is a left atrial thrombus due to atrial fibrillation (AF) [3], whereas the second most common source is a left ventricular (LV) thrombus following an acute myocardial infarction (MI) [1].

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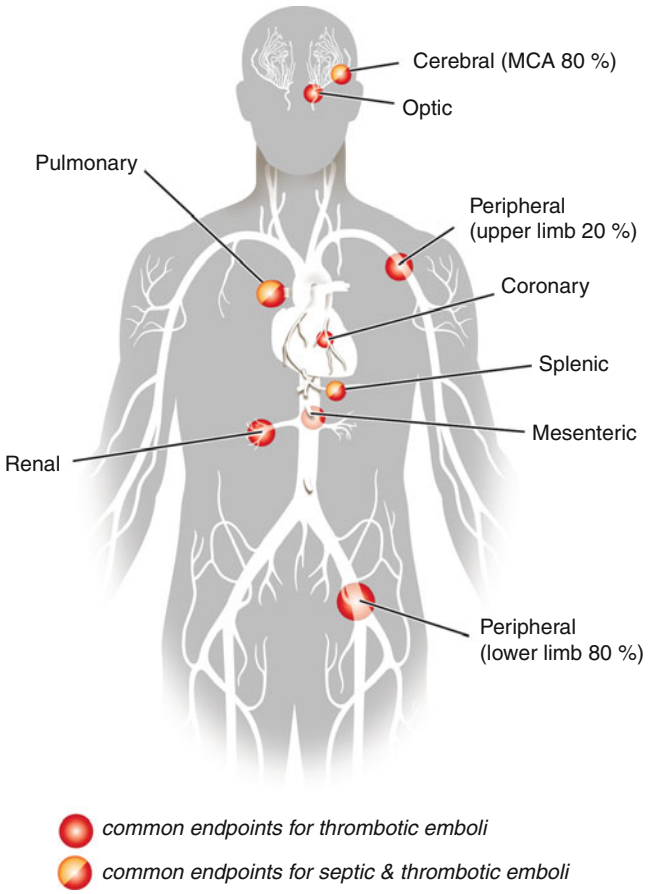

Fig. 39.1 Common destinations for cardiac emboli

Other etiologies include endocarditis, cardiac tumors, and aortic atherosclerosis.

The cornerstone of the evaluation for cardiac sources of emboli is the echocardiogram. While a transthoracic echocardiogram (TTE) is the initial imaging test for most patients, transesophageal echocardiography (TEE) has been shown to be superior to TTE when evaluating for cardiac sources of emboli [4, 5] and is also more cost effective [6]. As a result, the evaluation for cardiac sources of emboli is the most common indication for using TEE [5]. Once a cardiac source of emboli is identified, management depends on the underlying etiology and patient comorbidities.

Clinical Syndromes of Cardiac Emboli (Fig. 39.1)

Cerebral Vascular Accidents (CVA)

Embolisms of cardiac origin account for approximately 15–20 % of all ischemic strokes [7]. The overwhelming majority (80 %) of cardiogenic emboli lodge in the middle cerebral artery and its branches, while 10 % lodge in the posterior cerebral circulation and the remaining 10 % in the vertebral arteries. It is very rare for cardiac emboli to reach the anterior cerebral artery [8]. If the embolic thrombus is lysed quickly, only a transient ischemic attack (TIA) will occur. TIAs are defined as symptoms of stroke that last less than 24 h; however, most last less than 1 h. Patients with a history of TIA are at a very high risk for subsequent stroke, with an incidence of approximately 17 % by 90 days if untreated [9]. Immediate work-up and treatment of the underlying cause of embolism are imperative when TIA is suspected as the risk of subsequent stroke is highest in the days and weeks immediately after the TIA [10].

Peripheral Arterial Embolization

Cardiac emboli are by far the most common cause of peripheral artery embolization, with ischemic heart disease and AF accounting for approximately 80 % of cases. The lower extremities are involved in approximately 80 % of cases and the upper extremities in only 20 % [11]. As opposed to chronic limb ischemia in which collateral vessels develop over time to compensate for decreased antegrade flow, peripheral artery embolization results in an acute reduction of blood flow to the affected limb and is a medical emergency. Acute limb ischemia is a clinical diagnosis; symptoms include the 6 "Ps": pain, pulselessness, pallor, poikilothermia, paresthesias, and paralysis. Pain is generally the earliest and the most dominant symptom [12].

Renal Emboli

The incidence of renal emboli in the general population is quite rare. In a study involving nearly 30,000 patients with AF followed for 13 years, the incidence of renal thromboemboli was only 2 % [3]. Symptoms of renal infarction are vague and overlap with more common conditions making the diagnosis difficult. Patients generally have abdominal or flank pain, nausea, and vomiting and may report hematuria. Laboratory findings can be helpful in raising suspicion for the diagnosis. Patients tend to have an elevated white blood cell count (WBC), elevated creatinine concentration, and markedly elevated serum lactate dehydrogenase (LDH). Finally, an elevation of urinary LDH is very suggestive of intrarenal pathology as LDH is generally too large to be filtered and its excretion is generally only increased in renal infarction and renal transplant rejection [13].

Splenic Emboli

Both splenic infarction and abscess should prompt evaluation for cardiac sources of emboli. Abscesses can present with persistent fever despite antibiotic therapy, left upper

quadrant (LUQ) pain, and, sometimes, a left-sided plural effusion [14]. Splenic infarct presents similarly with LUQ pain, fever, LUQ tenderness, nausea and vomiting, elevated WBC count, and elevated LDH. The clinical presentation of splenic infarcts can be atypical, but the most consistent findings are LUQ pain and elevated LDH [15].

Optic Emboli

Central retinal artery occlusion is a relatively rare event, with an incidence of approximately 1.9 per 100,000 [16]. While the most common cause of retinal artery occlusion is carotid artery disease, cardiogenic sources may account for as many as 42 % of cases [17]. A cardiogenic source is more likely in younger patients and in patients with a history of cardiac disease such as AF or rheumatic heart disease [18]. Retinal artery emboli present clinically as acute onset, unilateral, painless, loss of vision. It is considered a form of stroke (if transient it is called amaurosis fugax) and should compel the clinician to investigate the source of the emboli to prevent other vascular events.

Mesenteric Emboli

Emboli to the mesenteric vasculature most commonly lodge in the superior mesenteric artery (SMA) because of its large caliber and the narrow angle of its departure from the aorta. Emboli to the SMA account for 5 % of peripheral emboli and approximately 50 % of cases of acute mesenteric ischemia [19]. Classic symptoms of mesenteric ischemia include nausea, vomiting, diarrhea, and acute periumbilical pain that appears "out of proportion" to the physical findings where tenderness is not prominent. The patient appears acutely ill and at least 50 % test positive for fecal occult blood with 15 % presenting with melena or hematochezia [20]. Acute mesenteric ischemia can be a catastrophic event, with mortality rates exceeding 60 % [21]. As such, when suspicion is high, physicians should have a low threshold for a definitive, invasive evaluation with angiography.

Pulmonary Emboli (PE)

While dislodged deep vein thrombi (DVT) are, by far, the most common cause of PE, cardiac sources of PE include right ventricular (RV) thrombi secondary to blood stasis, indwelling cardiac catheters, or pacemaker/defibrillator leads and right-sided endocarditis. In patients with right-sided endocarditis, which accounts for 5–10 % of cases of endocarditis [22], septic PE are common and can result in multiple pulmonary abscesses. The most common symptom in such patients is fever. Other symptoms include dyspnea, pleuritic chest pain, cough, and hemoptysis [23]. Hypoxia and paradoxical emboli are also possible when right atrial pressures increase sufficiently to cause right-to-left shunting [24] in patients with an atrial septal defect or a patent foramen ovale.

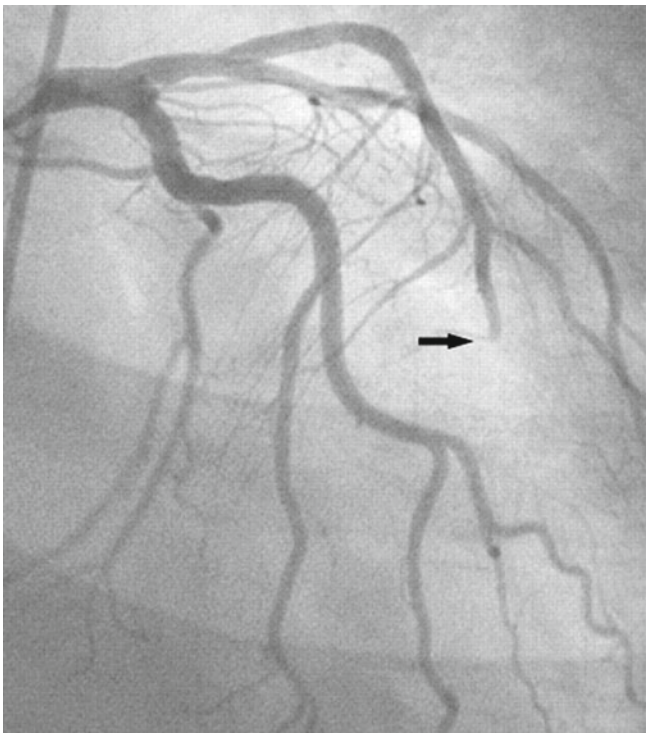

Fig. 39.2 Coronary angiogram showing normal coronary arteries with abrupt occlusion, as indicated by the *arrow*, (cut-off sign) of the distal left anterior descending coronary artery consistent with embolus (Reprinted with Permission Adachi and Kobayashi [88])

Coronary Emboli

Approximately 4–7 % of patients with acute MI are found to have otherwise normal coronaries [25]. In such cases, emboli to the coronary arteries are an important consideration, especially in patients with underlying conditions that predispose to embolization such as AF. Coronary emboli are usually located in the left anterior descending (LAD) artery at the level of the distal epicardial and intramural branches (Fig. 39.2). This observation may be due to the aortic valve morphology which results in preferential blood flow into the left main coronary [26].

Etiology (Fig. 39.3)

There are three types of masses that can embolize from the heart: thrombotic, infectious, and neoplastic.

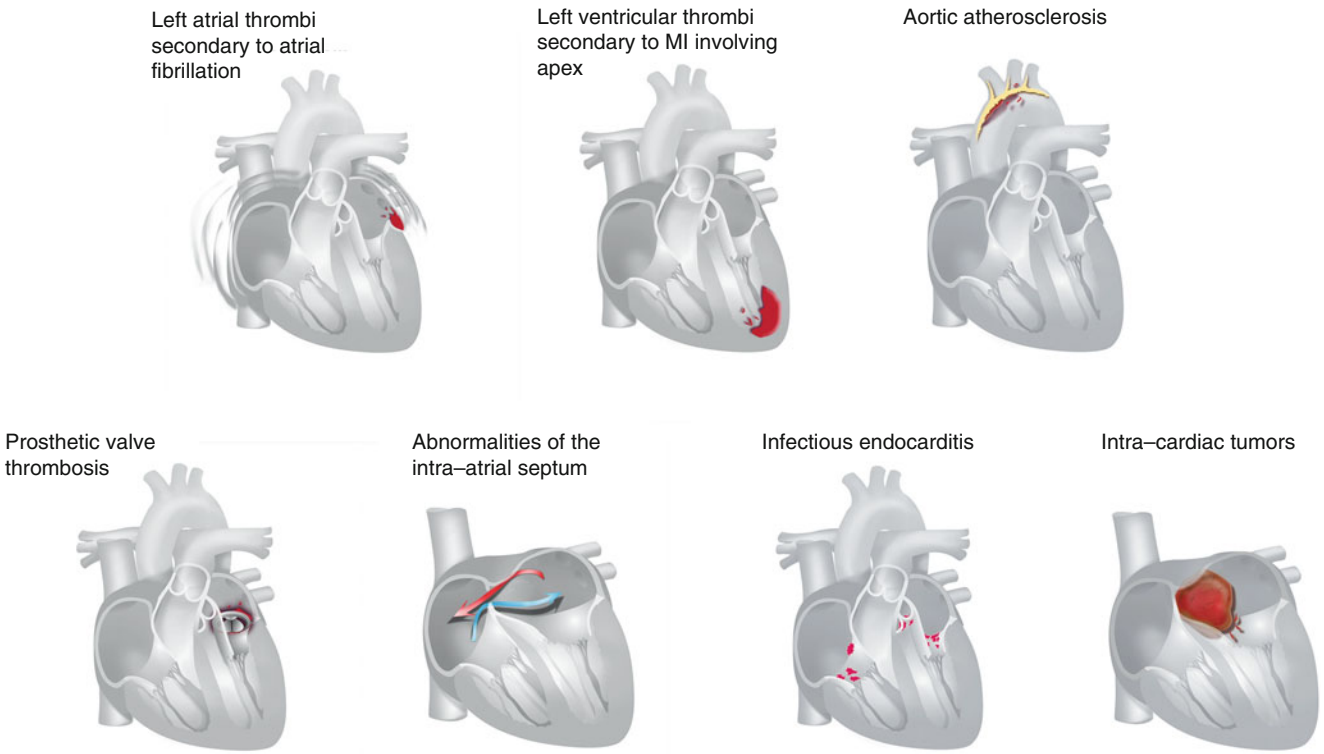

Fig. 39.3 Possible etiologies of cardiac emboli

Left Atrial (LA) Thrombi

A thrombus in the LA (Fig. 39.4) is the most common source of cardiogenic emboli. Most thrombi form in the LA appendage [27] secondary to blood stasis. Atrial fibrillation, rheumatic mitral stenosis, and LA enlargement are all conditions that predispose to stasis and subsequent thrombus formation. In the developed world, where rheumatic disease is less common, AF is the most common cause of LA thrombus formation [1, 3]. The association is so strong that in patients in sinus rhythm presenting with embolic strokes or TIA, only 1 % have LA thrombosis demonstrable by TEE as opposed to 14 % of those in AF [28]. Patients with dilated cardiomyopathy experience systemic emboli at a rate of approximately 4 % per year and more commonly are found to have thrombus in the LA rather than the LV suggesting that dilated cardiomyopathy is another important cause of LA thrombosis [29]. Mitral regurgitation does not appear to be associated with LA thrombus, possibly because the regurgitant flow prevents the stasis of blood in the LA [30].

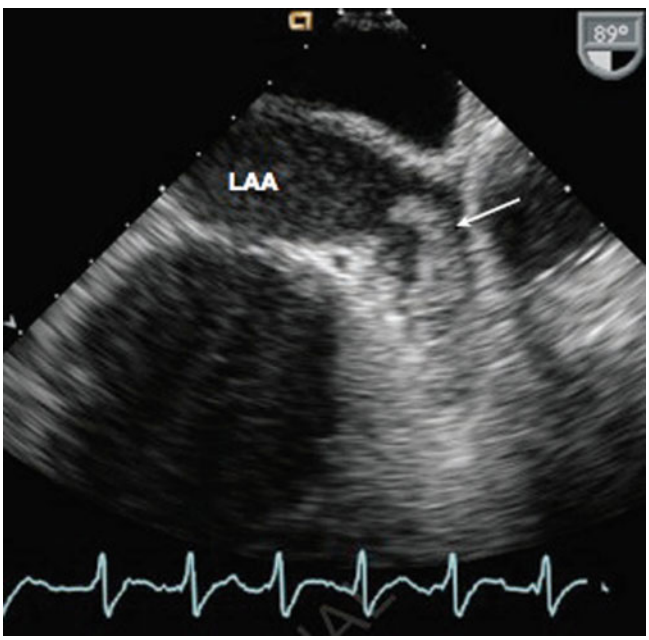

Fig. 39.4 Transesophageal echocardiogram showing left atrial thrombus (*arrow*) in the atrial appendage. This thrombus was visualized in two orthogonal views, using zoom mode and a high-frequency (7 MHz) transducer (Reprinted with Permission Otto [30])

Left Ventricular Thrombi

As in the case of LA thrombosis, LV thrombi also form under conditions of stasis. Ventricular aneurysms, diffuse ventricular hypokinesis (e.g., dilated cardiomyopathy), or segmental wall motion abnormalities (e.g., post-MI) are the main causes of stasis in the LV. In the absence of an aneurysm or severe global or regional LV dysfunction, LV thrombi are unlikely to occur. Conversely, LV thrombi are most likely to

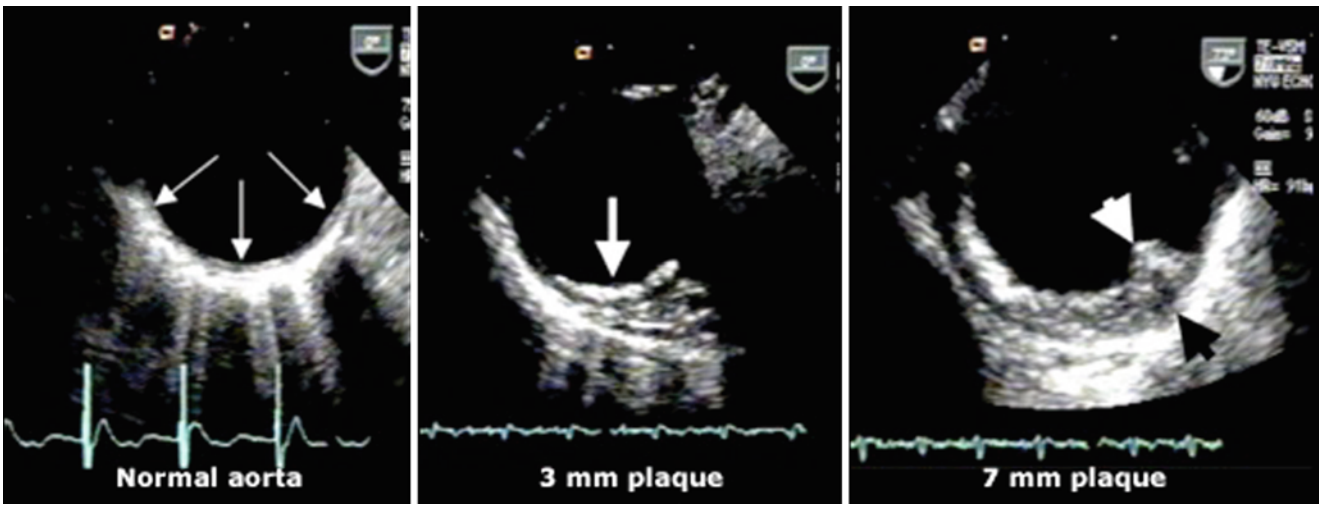

Fig. 39.5 Transesophageal echocardiograms of the thoracic aorta: *Left*: normal; *middle*: moderate (3 mm) plaque; and *right*: severe (7 mm) plaque (Reprinted with Permission Tunick [89])

occur in patients with large anterior wall infarction with apical wall motion abnormalities. LV thrombosis occurs in up to 46 % of these patients, while patients without apical involvement are at low risk for thrombosis. Thrombi tend to form between one and 11 days following an MI [31].

Aortic Atherosclerosis

Embolism related to aortic atherosclerosis can be secondary to either thromboembolism or atheroembolism (cholesterol embolism). Thromboembolism occurs when an aortic atherosclerotic plaque ruptures and the thrombus that forms at the site of rupture embolizes. These tend to be single large emboli with resulting clinical syndromes similar to those associated with cardiac emboli as noted above (TIA, stroke, limb ischemia, etc.). Atheroembolism, however, tends to result in multiple small artery occlusions leading to very variable clinical presentations. Vague symptoms such as fever, headache, and weight loss may be present, while more dramatic clinical presentations include "blue toe" syndrome, livedo reticularis, renal failure, and retinal ischemia [32]. Risk factors for embolization include characteristics of the plaque as observed on TEE (Fig. 39.5) and instrumentation during cardiac catheterization or surgery. Ulcerated, protruding, mobile plaques and plaques with thickness >4 mm are at the highest risk of embolism [33, 34].

Prosthetic Valve Thrombosis

The rates of prosthetic valve thrombosis range between 0.1 and 5.7 % per patient year depending on the valve characteristics [35]. Patients with bioprosthetic valves and those with mechanical valves with consistent therapeutic anticoagulation are at the lowest risk while patients with mechanical valves and inadequate anticoagulation and valves in the mitral position are at the highest risk. The risk of embolization in patients with mechanical valves is approximately 4 % per year without anticoagulation, 2 % per year on antiplatelet therapy, and 1 % per year on warfarin. Other risk factors for embolization such as AF and depressed LV function contribute to increased risks of embolization in patients who have undergone valve replacement [35]. However, it should be noted that the most common presenting symptom of prosthetic valve thrombosis is not an embolic event but rather congestive heart failure [36] due to an acute obstruction or restriction of valve opening.

Abnormalities of the Atrial Septum

Right-to-left shunting, which can occur in patients with a patent foramen ovale (PFO) or atrial septal defect (ASD), may lead to paradoxical emboli in which thrombi formed in the venous system cross the atrial defect to embolize systemically. A prerequisite for such an event is higher pressures in the right heart chambers than left. While several pathological conditions can increase right-sided pressures such as Eisenmenger syndrome or pulmonary hypertension from a variety of causes, right heart pressures can increase transiently under physiologic conditions, allowing the passage of paradoxical emboli from the venous to systemic circulations in otherwise normal patients. First, during the normal cardiac cycle, right atrial pressures transiently exceed left atrial during early systole. Second, under conditions where patients perform the Valsalva maneuver, there are two opportunities for right-to-left shunting. First, during straining, increased intrathoracic pressures disproportionately increase right heart pressure, and during release, the influx of venous blood again increases right-sided pressure above left-sided pressure

[37]. As such, patients who present with a history of straining immediately preceding an ischemic event should draw the clinician's attention to the possibility of paradoxical emboli.

It is estimated that approximately 25 % of the population has PFOs, and several studies have found an association between cryptogenic strokes (strokes with no clearly identifiable cause) and an increased prevalence of PFOs [38, 39]. Furthermore, patients with larger PFOs, patients in hypercoagulable states, patients with right-to-left shunting found on TEE, and patients with concurrent atrial septal aneurysms appear to have higher risks of embolism [40, 41]. However, population-based studies have not shown PFOs alone to be associated with statistically significant increases in the risk of stroke [42, 43]. This suggests that the role of PFO in cryptogenic strokes is likely only part of a multifactorial cascade that predisposes patients to paradoxical emboli.

Right Ventricular Thrombi

RV thrombi are quite rare but native RV thrombi can be seen in cases of severe RV dilatation or dysfunction and on indwelling catheters [30]. Another rare finding may be a floating RV thrombus. These likely represent thrombi in transit from the venous circulation and are associated with a high mortality. While native RV thrombi can be treated with anticoagulation, floating RV thrombi are an emergency and require emergent surgery or thrombolytic therapy [44].

Septic Emboli

Infectious intracardiac vegetations most commonly result from infective endocarditis (IE) on native valves. The infection likely begins with minor trauma secondary to the force of the valves opening and closing—which is supported by the relative frequency of the valves involved: mitral > aortic > tricuspid > pulmonic [45]—combined with transient bacteremia.

Although the brain and spleen are the most common sites of left-sided septic emboli, nearly any organ can be affected including the spinal cord, the paraspinal space, and the arteries themselves via the vasa vasorum which can lead to mycotic aneurysms [22]. Systemic embolization with subsequent abscess formation is a common cause of prolonged fever despite adequate antibiotic therapy. Right-sided IE commonly leads to septic pulmonary emboli with subsequent respiratory symptoms as noted above.

Nonbacterial Thrombotic Endocarditis (NBTE)

This entity, also known as marantic, Libman-Sacks, or verrucous endocarditis, refers to a large spectrum of valvular lesions that are usually associated with advanced malignancy [46] and autoimmune conditions such as systemic lupus erythematosus. While rare, these vegetations have the potential for embolization.

Table 39.1 Sensitivity and specificity of TTE and TEE in the evaluation of LA and LV thrombus formation

Test	Sensitivity (%)	Specificity (%)
LA thrombus		
TEE	99	100
TTE	53–63	95–99
CMR	100	94
LV thrombus		
TEE	40 ± 14	96 ± 3.6
TTE	92–95	86–88
CMR	88–93	85–99

Adapted from Otto [30]
TTE transthoracic echocardiogram, *TEE* transesophageal echocardiogram, *CMR* cardiac magnetic resonance imaging, *LA* left atrium, *LV* left ventricle

Intracardiac Tumors

Primary cardiac tumors are very rare, with an incidence of only 0.06 % [47]. Only two types are associated with embolization: myxomas and papillary fibroelastomas. Myxomas are the most common type of cardiac tumor. They are benign tumors; most are located in the left atrium as a pedunculated growth off the atrial septum. The morphology of the tumor dictates the likelihood of embolization. Friable or villous myxomas, which account for 35 % of all myxomas, are more likely to embolize [48].

Papillary fibroelastomas are the second most common type of primary cardiac tumors. These are pedunculated tumors most commonly located on left-sided cardiac valves but can also be found on the endocardium itself. Again, it is a benign tumor that has the potential to cause serious morbidity and mortality from emboli. Tumor mobility is independently associated with increased risks of embolization [49]. The embolized material in myxomas or papillary fibroelastomas can be either pieces of the tumor itself or thrombi which form on the tumor and subsequently dislodge.

Evaluation

Echocardiography is the imaging modality of choice when evaluating for cardiac sources of emboli. As noted above, TEE has been found to be superior to TTE in the evaluation of the most common causes of cardiac emboli [4, 5] and has been shown to be more cost effective [6]. However, the superiority of TEE depends on the source of the emboli (Table 39.1). A TEE is performed by passing a modified gastroscope with an ultrasound transducer at its tip down the esophagus. The esophagus travels immediately posterior to the aortic arch and left atrium with minimal intervening

tissue between the transducer and the heart, as opposed to TTE which has retrosternal airspace intervening. This close proximity allows for the use of high-frequency transducers which increase the spatial resolution of the resulting image. Therefore, TEE provides for improved detection of LA thrombi and tumors, PFOs, ASDs, valvular vegetations, atheromatous plaques within the aorta, and spontaneous left atrial echo contrast, which is a marker of blood stasis. On the other hand, TEE provides poor visualization of the LV apex, and as a result, when evaluating for LV thrombi (e.g., post-MI), TTE is still the imaging modality of choice.

It should be noted that TEE is an invasive procedure and therefore involves more risks than TTE. Minor complications occur in approximately 1/500 patients and include minor oropharyngeal trauma, transient bronchospasm, transient hypoxia (more likely in obese patients), nonsustained ventricular/atrial arrhythmias, and vomiting. More severe complications are rare but include esophageal perforation, gastrointestinal bleeding, pharyngeal hematoma, and methemoglobinemia [4, 50, 51]. Methemoglobinemia is a complication of the topical anesthetic benzocaine used for posterior pharyngeal anesthesia and is very rare, occurring in approximately 0.07 % of patients [52]. Endocarditis secondary to transient bacteremia during TEE is also rare; antibiotic prophylaxis is not recommended except in patients who are immunosuppressed and have prosthetic valves, cyanotic congenital heart disease, or a previous history of endocarditis [53].

As noted above, masses found in the heart may be of thrombotic, infectious, or neoplastic origin. However, since not all echo-dense objects found on echocardiogram are necessarily pathologic, one must be able to identify artifacts and normal variants to avoid misdiagnosis. Artifacts on echocardiogram in general lack clearly demarcated borders, do not have appropriate movement throughout the cardiac cycle, do not have clearly visualized attachment to the endocardial surface and cannot be seen in multiple views and different depths [54]. Also, normal anatomy may be misdiagnosed as intracardiac masses. These include normal trabeculae, aberrant chordae tendineae, the moderator band (especially in cases of right ventricular hypertrophy), or papillary muscles [30].

In situations in which TEE is inconclusive or cannot be performed, a cardiac magnetic resonance imaging (CMR) is a second-line option for the evaluation of cardiac sources of emboli. Studies have shown that for the detection of LV thrombi in post-MI patients, CMR has superior specificity with similar sensitivity [55] when compared to TTE, and is comparable to TEE for the evaluation of LA thrombi [56] (Table 39.1).

Left Atrial Imaging

TTE has two major limitations when evaluating the LA: first, in both the parasternal and apical views, the LA is in the far field limiting the resolution of the image [30]; second, most atrial thrombi originate in the left atrial appendage [27], and TTE has poor visualization of the atrial appendage limiting its sensitivity for the diagnosis of LA thrombi [57].

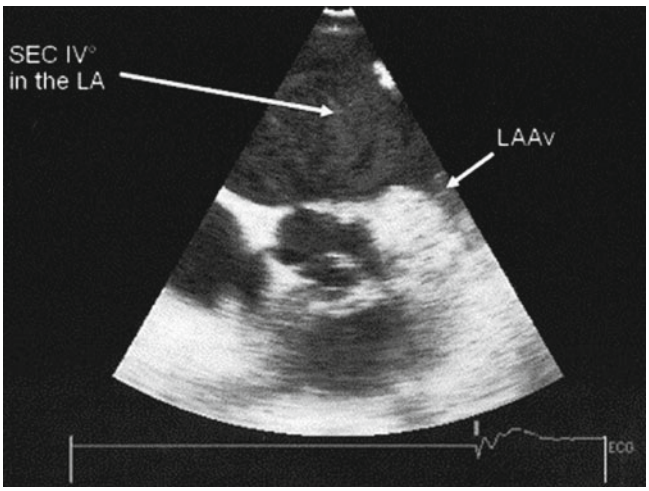

Fig. 39.6 Transesophageal echocardiography with dense spontaneous echo contrast (*SEC*). *LA* left atrium, *LAAv* left atrial appendage peak emptying velocity (Reprinted with Permission Bernhardt et al. [59])

As noted above, blood stasis is the major underlying cause of LA thrombosis, and it can be visualized on TEE with Doppler imaging or via the observation of spontaneous echo contrast (SEC) in the LA. On Doppler, flow velocity during LA contraction is normally above 0.4 m/s. Velocities lower than 0.4 m/s are associated with higher rates of thrombus formation [1].

SEC is best seen at high-frequency settings of TEE with low gain to be better able to distinguish SEC from noise artifact [1]. The echo density seen in SEC appears as white swirls (Fig. 39.6) and is thought to be the result of transient erythrocyte aggregation produced by interactions between erythrocytes and plasma proteins in low shear rate conditions [1, 58]. This hypothesis is supported by the finding that SEC is independently associated with hematocrit and fibrinogen levels in addition to stasis [58], suggesting that SEC also indicates a relatively hypercoagulable state. This finding helps to explain why SEC is so strongly associated with thrombus formation even when patients are on oral anticoagulation [59] and is an independent risk factor for thromboembolic events [60].

Imaging of the Atrial Septum

TEE also provides high-quality images of the atrial septum. TEE with bubble contrast, at rest, and with cough or Valsalva is the preferred method of evaluating right-to-left shunt (PFO or ASD) [5, 61] (Fig. 39.7). However, more recent studies have found TTE with Doppler and contrast to have similar sensitivity and specificity for the detection of PFO as TEE and can be used as an alternative approach [62, 63].

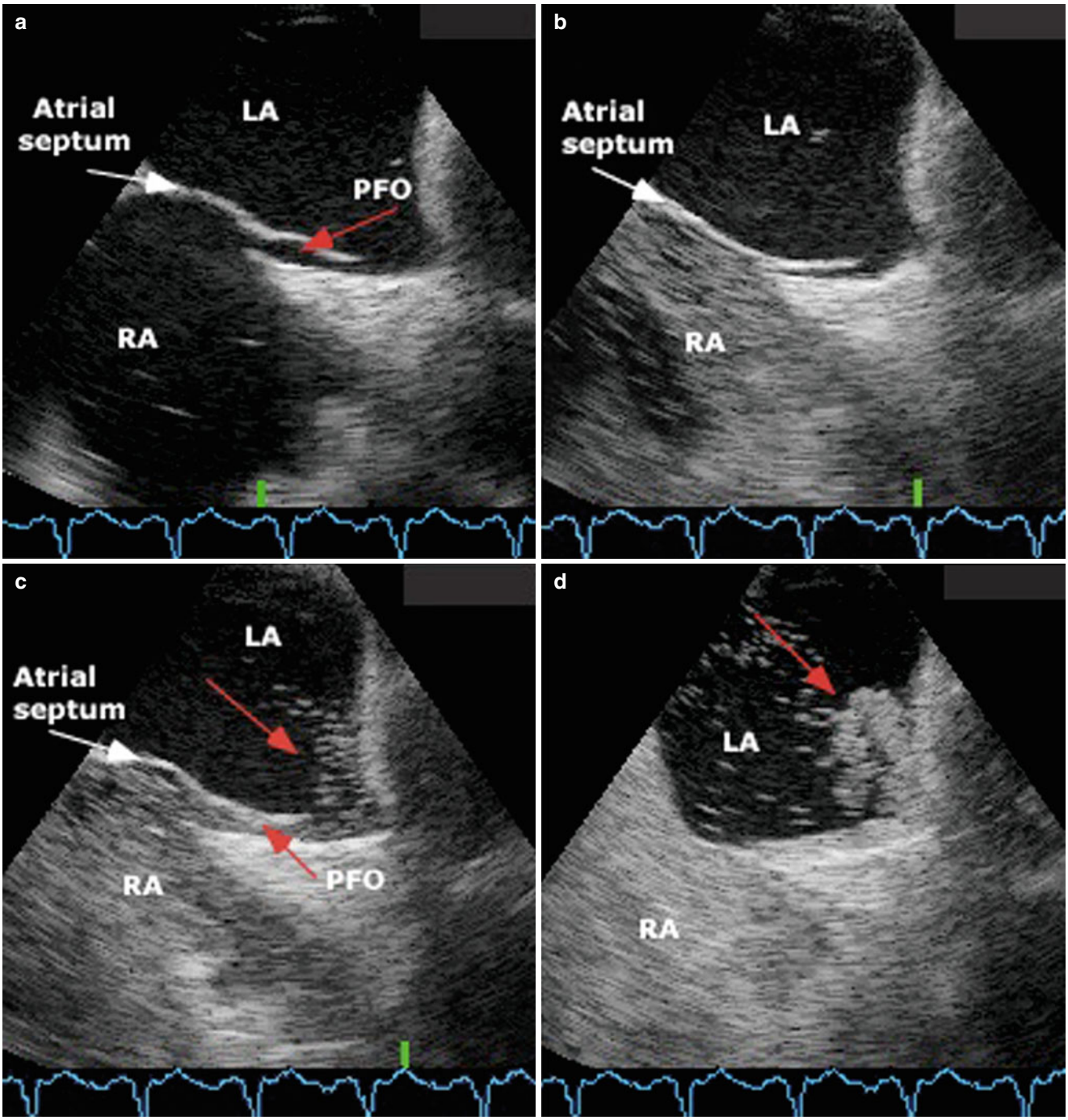

Fig. 39.7 Transesophageal echocardiography with contrast of a patent foramen ovale. The sequence of images shows the right and left atria during diastole (panel **a**); a flap of the atrial septum is seen covering the foramen ovale. There is opacification of the right atrium immediately after injection of agitated saline (panel **b**). Panel **c** shows the contrast passing through the right atrium (*RA*) to the left atrium (*LA*) through a patent foramen ovale (*PFO*) (*red arrow*). Panel **d** shows a large amount of contrast within the LA (*red arrow*) (Reproduced with Permission UpToDate, Waltham, MA 2012. Copyright © 2012 UpToDate, Inc.)

Valve Imaging

TEE has been found to be vastly superior to TTE in the evaluation of possible vegetations on native and prosthetic valves. Echocardiography, however, cannot distinguish between septic vegetations and NBTE [64].

Thoracic Aortic Imaging

TEE is the imaging modality of choice to evaluate the thoracic aorta for the potential source of embolism. TEE not only has been found to be highly sensitive and specific for detecting aortic atherosclerosis but is also able to define the

morphologic characteristics of the plaque such as ulcerations, mobility, and thickness [65] which are predictors of the risk for embolization.

Left Ventricular Imaging

Given the high prevalence of LV thrombi after MIs that involve the apex, TTE should be preformed routinely on these patients to identify those at highest risk of embolization. Two characteristics have been found to be associated with greater risks for embolization: thrombus mobility and thrombus protrusion [66]. As noted above, LV imaging is best accomplished by TTE. However, the sensitivity of TTE may be decreased due to poor image quality in patients who are obese or have severe chronic pulmonary disease. Prominent LV trabeculae or papillary muscles can also cause suboptimal imaging. In such instances, intravenous contrast can be used to improve the sensitivity and specificity of the study [67]. It should be noted, however, that even in conditions in which a thrombus is not visualized, TTE can guide treatment by indicating patients at high risk of developing LV thrombi such as those with LV ejection fraction less than 40 %, apical wall motion abnormality, or aneurysm.

Management

Anticoagulation

The prevention or treatment of thromboembolism is accomplished through anticoagulation (vitamin K antagonists (VKA), direct thrombin inhibitors, and factor Xa inhibitors) or antiplatelet therapy. Anticoagulation is not benign and must be weighed against the risk of bleeding. Therefore, whether the practitioner chooses anticoagulation as opposed to antiplatelet therapy or a combined approach is dependent on the underlying etiology and the patient's risk factors for thrombus formation (Table 39.2):

Atrial Fibrillation

Being the most common cause of thromboembolism, AF has been extensively studied. Both acute and chronic AF have significant risk of thrombus formation [69], and thus, treatment is indicated in paroxysmal and persistent AF. The most popular and best-studied risk stratification calculator is the $CHADS_2$ score [70]. Its simplicity makes it quickly and easily applicable in the clinical setting. The score is calculated as follows: 1 point for congestive heart failure, 1 point for **h**ypertension, 1 point for **a**ge >75 years, 1 point for **d**iabetes, and 2 points for **s**troke or TIA; the sum of points is the total $CHADS_2$ score. As noted in Table 39.2, a $CHADS_2$ score of 0 can be managed with antiplatelet therapy or without any antithrombotic therapy; a score of 1 can be managed with aspirin or with VKA; a score of 2 or greater should be managed with VKA With a goal INR of 2–3. To help further stratify patients with a score of 0 or 1, the $CHADS_2$-VASc score was devised. Unlike the $CHADS_2$ score, it takes into account age 65–74, female sex, and vascular disease. If patients have any of these

Table 39.2 Recommendations for use of chronic antithrombotic therapy for various cardiac conditions

Disease comorbidities	Recommendation
Nonvalvular atrial fibrillation	
$CHADS_2$ score 0	Aspirin or no antithrombotic
$CHADS_2$ score 1	Aspirin or VKA
$CHADS_2$ score >1	VKA
Rheumatic mitral valve disease	
With atrial fibrillation, previous embolization, or atrial appendage thrombus or left atrial diameter >55 mm	VKA
Embolization or appendage clot despite INR 2–3	VKA plus aspirin
Aortic arch mobile atheroma	
Otherwise cryptogenic stroke or TIA	Aspirin or VKA
Patent foramen ovale	
Otherwise cryptogenic ischemic stroke or TIA	Aspirin
Indication for VKA (deep venous thrombosis or hypercoagulable state)	VKA
Mechanical heart value	
Aortic position, bileaflet, or Medtronic Hall tilting disk with normal left atrial size and sinus rhythm	VKA (INR 2.5, range 2–3)
Mitral position tilting disk or bileaflet valve	VKA (INR 3.0, range 2.5–3.50)
Mitral or aortic position, antero-apical myocardial infarct, or left atrial enlargement	VKA (INR 3.0, range 2.5–3.5)
Mitral or aortic position, with atrial fibrillation, or hypercoagulable state, or low ejection fraction, or atherosclerotic vascular disease	Aspirin plus VKA (INR 3.0, range 2.5–3.5)
Systemic embolization despite target INR	Add aspirin and/or increase INR: prior target was 2.5 increase to 3.0, range 2.5–3.5; prior target was 3.0 increase to 3.5, range 3–4
Bioprosthetic valve	
No other indication for VKA therapy	Aspirin
Infective endocarditis	Avoid antithrombotic agents
Nonbacterial thrombotic endocarditis	
With systemic embolization	Full dose unfractionated heparin or subcutaneous LMWH

Adapted from Smith et al. [68]
Dose of aspirin is 50–325 mg/day; target INR for VKA is 2.5 unless otherwise specified
INR international normalized ratio, *LMWH* low-molecular-weight heparin, *TIA* transient ischemic attack, *VKA* vitamin K antagonist

additional risk factors with a $CHADS_2$ score of 0, it is reasonable to maintain them on aspirin therapy while those with a score of 1 should be managed with VKA [71]. Finally, several recent trials [72, 73] have demonstrated that direct thrombin and Xa inhibitors are equally effective at preventing thromboembolism as VKA with similar bleeding risks. In all patients, when considering therapeutic options, the risk of stroke prevention must be balanced against the risk of bleeding.

Mechanical Valves

As noted above, mechanical valves are associated with a significant risk of thrombosis, and that risk is increased with mechanical valves in the mitral position and other comorbid conditions such as AF or low ejection fraction. These patients require lifelong anticoagulation and possibly antiplatelet therapy with INR goal depending on comorbid conditions (see Table 39.2). Of note, unlike patients with AF, the use of direct thrombin inhibitors and factor Xa inhibitors has not approved for use in patients with mechanical valves, and therefore, these drugs should not be used in patients with mechanical mitral valves.

Left Ventricular Thrombi

As noted above, as many as 46 % of patients with an anterior MI involving the LV apex eventually develop LV thrombi. In the absence of anticoagulation, approximately 10 % will have clinically evident CVAs [74]. Several studies [75–77] have shown that heparin followed by warfarin therapy in patients with LV thrombi decreases the incidence of CVA to 1–3 %. While the optimal duration of treatment has not been investigated, several studies have shown a reduced risk of embolization after 3 months [78]; thus, anticoagulation is recommended for at least 3 months. According to the 2012 American College of Chest Physicians guidelines on Antithrombotic Therapy and Prevention of Thrombosis, patients at high risk for thrombus formation and embolization should begin anticoagulation with VKA and aspirin early and continue for 3 months. After that point, VKA can be discontinued but aspirin should be continued. Patients considered high risk include those with documented LV thrombus on TTE, those with an LVEF less than 40 %, and those with an antero-apical wall motion abnormality or aneurysm [79].

Aortic Atherosclerosis

All patients with established atherosclerotic disease should be treated for secondary prevention of cardiovascular disease. This includes aspirin, statins, controlling hypertension, smoking cessation, and lifestyle modifications [80]. However, the use of anticoagulation has not been firmly established; the 2008 American College of Chest Physician guidelines on valvular and structural heart disease give a weak recommendation (grade 2C) for VKA therapy in patients with ischemic stroke associated with mobile aortic arch thrombi [81].

Cardiac Tumors

Surgical excision is the treatment of choice in the case of cardiac tumors. Cardiac myxomas are generally removed under cardiopulmonary bypass. In familial cases, myxomas have a high rate of recurrence (up to 22 %), but in sporadic cases the procedure is generally curative with a recurrence rate of only 1–2 % [82].

PFO/ASD Treatment

In patients who present with cryptogenic strokes or TIA and a PFO, two treatment options are available: antithrombotic therapy or percutaneous closure. In the PICSS (PFO in Cryptogenic Stroke Study) trial, there were no significant differences in the 2-year event rates among those treated with VKA as opposed to aspirin [83]. Given the risks of bleeding involved with anticoagulation, The 2012 American College of Chest Physicians guidelines recommend antiplatelet (aspirin and/or clopidogrel) therapy in these patients [84].

Whether percutaneous closure of a PFO is superior to medical therapy at preventing recurrent stroke is a topic of much debate. Recently the 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 found no benefit of percutaneous PFO closure over medical therapy (warfarin, aspirin, or both) [85]. However, there has been much controversy over the validity of the results [86], and thus, no clear recommendations can be made at this point. However, given that the results of this randomized trial showed no benefit of closure, patients should be treated medically or recommended to participate in ongoing PFO closure trials that are attempting to address some of the limitations of CLOSURE I. Percutaneous closure can be considered in patients who have events on antithrombotic therapy. On the other hand, in ASD, where left-to-right shunting may result in right heart failure, percutaneous or surgical closure is recommended for all adults who have right ventricular enlargement or other signs of overload regardless of symptoms of embolization [87].

Key Points

- The 3 types of masses that can embolize from the heart are thrombotic, infectious, and neoplastic.
- A left atrial thrombus is the most common source of cardiogenic emboli.

- The incidence of clinically apparent embolic events is approximately three times higher in the cerebral circulation as opposed to the peripheral circulation.
- Embolisms of cardiac origin account for approximately 15–20 % of all ischemic strokes.
- Cardiac emboli are the most common cause of peripheral artery embolization, with ischemic heart disease and AF accounting for approximately 80 % of cases.
- The symptoms of acute limb ischemia include the 6 "Ps": pain, pulselessness, pallor, poikilothermia, paresthesias, and paralysis.
- Other potential end organs of arterial emboli include the spleen, kidney, gut, eye, and, although commonly overlooked, the heart itself.
- Stasis of blood is the main risk factor for thrombosis; this commonly occurs in the LA secondary to AF and in the LV secondary to apical wall motion abnormalities post-MI.
- When evaluating cardiac sources of emboli, TTE is the test of choice to visualize the LV while TEE is the test of choice to visualize the LA, aortic arch and cardiac valves.
- Treatment of patients with cardiogenic emboli depends on the source and composition of the embolus and the bleeding risks of the individual patient.

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