

Cerebrovascular Events: Diagnostic Aspects

Echocardiography as a Tool in the Evaluation of Conditions with a High Likelihood of Cardiogenic Embolism

Itzhak Kronzon MD¹, Paul A. Tunick¹ MD and Leon H. Charney²

¹Department of Medicine and ²Division of Cardiology, New York University School of Medicine, New York, NY, USA

Key words: transthoracic echocardiography, transesophageal echocardiography, cardiogenic embolism, stroke, aortic atherosclerosis

IMAJ 2006;8:768–772

This review focuses on the utility of echocardiography in conditions with a high likelihood of cardiogenic (and “aortogenic”) embolism. Another review in this special issue of *IMAJ* deals with the echocardiographic evaluation and clinical implication of patent foramen ovale, which is clinically more relevant to the individual whose medical problems are the main theme of this special publication [1]. Because of space limitations this review cannot be comprehensive. The interested reader is referred to larger texts [2].

Stroke is the third leading cause of death in western countries (after cancer and heart disease). The human toll in disability in stroke patients is enormous. Most strokes are ischemic, which may be the result of major vessel atherosclerosis, small vessel occlusion (lacunar stroke), cardiogenic embolism, other defined etiologies, and cryptogenic (unexplained) stroke. It is estimated that 15–50% of all strokes are cardiogenic and 30–40% cryptogenic [3].

Since its earliest days echocardiography has been considered a promising tool in the evaluation of patients with cardiogenic embolism. Even single dimensional (M-Mode) technology was capable of detecting and diagnosing conditions known to be associated with central and peripheral embolization, such as mitral stenosis, left ventricular systolic dysfunction, left atrial enlargement and myxoma. The introduction of two-dimensional echocardiography further expanded the diagnostic capability and accuracy of this non-invasive technique in the evaluation of cardiogenic embolism. Wall motion abnormalities could be better defined, intracardiac normal and abnormal structures better assessed, and valvular abnormalities better visualized and quantitated.

Transthoracic echocardiography vs. transesophageal echocardiography

The quality of routine transthoracic echocardiography examination varies from patient to patient. It depends on body habitus,

the size of the intercostal spaces, the relation of the heart to the chest wall, and the presence of conditions such as emphysema (air in the lung does not allow sound penetration) and chest wall deformities. In many patients the image quality is suboptimal, and in a few, images are unobtainable. In addition, the ultrasound beam loses energy during its penetration, and therefore structures that are distant from the chest wall (and the transducer) are not well imaged. Lower transducer frequency improves the penetration but decreases the image resolution.

Cardiogenic and aortogenic embolism are the causes of 15–50% of all strokes

Therefore, deep (posterior) structures are not well imaged. Structures such as the posteriorly located left atrium, the interatrial septum, the mitral valve and the thoracic aorta – all potential sources of embolism – may be suboptimally demonstrated and the culprit lesion responsible for a stroke or peripheral embolization may be overlooked.

Transesophageal echocardiography was first introduced by Frazin et al. in 1976 [4]. With the transducer in the esophagus, many of the technical difficulties discussed in the previous paragraph are overcome. The close anatomic proximity between the esophagus and the posterior aspect of the heart requires a shorter distance of beam penetration and thus enables the use of higher frequency transducers. In addition, the heart is not masked by extracardiac structures, such as bones and lung tissue that may interfere with the penetration of the ultrasound beam. Finally, the thoracic aorta, which is not well seen on TTE, is very well demonstrated by TEE. TEE provides higher resolution images of the heart and the aorta. Therefore, TEE is considered superior to TTE in the evaluation of most conditions that lead to cardiogenic embolism. In our laboratory and in many echocardiography

TTE = transthoracic echocardiography

TEE = transesophageal echocardiography

laboratories worldwide, TEE is used primarily to determine the source of emboli.

Conditions with a high likelihood of embolization include intracardiac clots and masses, valvular vegetations and severe (complex) aortic plaque. Conditions with a lower likelihood of embolization include patent foramen ovale and atrial septal aneurysm. Most of these conditions are better visualized and diagnosed by TEE.

While TEE is usually safe, it is still semi-invasive. Complications are rare but include the dreaded esophageal perforation, which occurs in approximately 1:10,000 examinations [5]. Other reported complications include trauma to the oral cavity, the pharynx and the trachea. Potential complications associated with patient sedation mandate careful monitoring of vital signs and arterial oxygen saturation during and after the procedure.

Echocardiographic findings and stroke

Unless there are clinical findings suggesting conditions that explain the stroke (e.g., atrial fibrillation, mitral stenosis or endocarditis), TTE is usually negative. It has therefore been suggested that TTE need not be done in patients with cryptogenic stroke and negative clinical evaluation [6]. However, we, like many other echocardiographers, believe that the totally harmless TTE before TEE may occasionally provide information not seen on TEE, or it may clearly reach the diagnosis and eliminate the need for the more invasive (and costly) TEE.

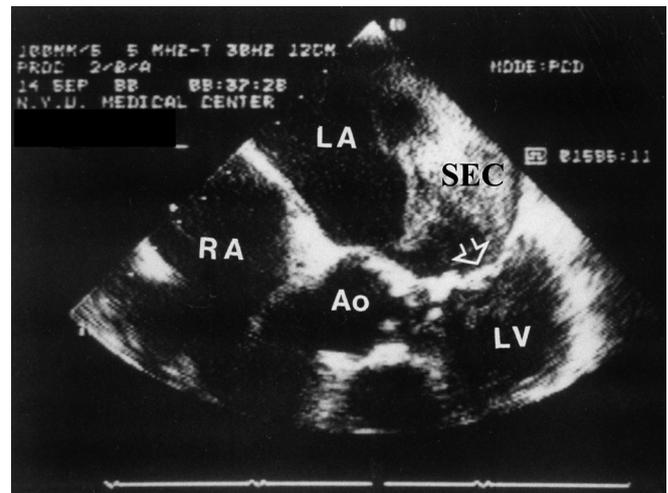


Figure 1. TEE frame from a patient with mitral stenosis. Note a dilated left atrium (LA), with spontaneous echo contrast (SEC). The mitral valve (arrow) is thickened. Ao = aorta, LV = left ventricle, RA = right atrium.

Left atrial size, best measured by echocardiography, has a major impact on prognosis. It was Dr. James Seward who recently phrased the analogy that the estimation of left atrial size in the cardiovascular patient has an impact similar to that of the estimation of hemoglobin A1C levels in the diabetic patient [7]. The normal LA volume index (corrected for body surface area) is < 33 ml/m.

Left atrial spontaneous echo contrast [Figure 1]

Spontaneous echo contrast, also known as “smoke” because of its slow swirling motion, is seen on echocardiography in cardiac chambers with stagnant blood flow. The exact mechanism that creates this echocardiographic finding is not fully understood. Theories include erythrocyte rouleaux formation and an expression of rheological phenomena associated with low flow. Left atrial SEC is frequently seen in patients with atrial fibrillation, but is also present in patients with normal sinus rhythm and one or more of the following: LA dilatation, left ventricular dysfunction (systolic and/or diastolic), mitral stenosis, and low cardiac output.

SEC is much better seen on TEE. In one study of patients with mitral stenosis, SEC was found on TEE in 61 of 120 patients (50%). In only one of those patients was the SEC detected by TTE. A history of embolization was present in 48% of all patients with SEC, and in only 7% of those without [8]. SEC is frequently more obvious in the LA appendage, a dead-end recess with stagnation and low blood flow velocity. Almost all patients with LA clots also have SEC. It is therefore felt that while SEC is not a clot, it is a precursor or harbinger of clot formation. We recommend that patients suspected of cardiogenic embolism and who have TEE evidence of SEC should be treated with anticoagulation regardless of their heart rhythm.

Transesophageal echocardiography is superior to transthoracic echocardiography in the evaluation of cardiogenic embolism

The clinical importance of left atrial dilatation

Left atrial dilatation is a very common finding. It can be associated with numerous cardiovascular conditions, including arterial hypertension, coronary artery disease, myocardial diseases and valvular heart disease. The presence of LA dilatation has a major impact on patient prognosis: it is a marker of the associated abnormality, but dilatation *per se* may start a vicious cycle and lead to increased atrial wall stress, decreased atrial contractility and further enlargement of the atrium. The blood in the dilated and poorly contracting atrium is stagnant, and the risk of clot formation increases. Atrial dilatation is frequently complicated by atrial fibrillation, this common arrhythmia being observed in 4% of individuals over 60 years old and in 15% of those over 75. Without effective atrial contraction, atrial fibrillation results in further increases in atrial size and leads to interatrial blood stagnation, clot formation, embolic stroke and peripheral embolization. In the absence of long-term anticoagulation therapy, one-third of all patients with atrial fibrillation will develop stroke.

LA = left atrial

SEC = spontaneous echo contrast



Figure 2. TEE frame showing left atrial appendage clot (arrow) in a patient with atrial fibrillation.

Left atrial clots [Figure 2]

Left atrial clots were found in 20% of patients who underwent surgery for mitral stenosis. The presence of LA clots was associated with a threefold increase in embolic events. Fifty percent of LA clots in patients with rheumatic valvular disease, and nearly 90% of LA clots in patients with non-valvular atrial fibrillation are limited to the LA appendage. TEE is superior to TTE in the evaluation of LA thrombi. TTE does not demonstrate the majority of LA appendage clots, since the appendage is frequently not well seen on TTE.

TEE, on the other hand, is a very reliable tool for evaluating LA clots. In a group of patients who underwent both TTE and TEE prior to cardiac surgery, TTE sensitivity for the presence of LA clots was 59% compared to 100% for TEE! [9]. Demonstration of an atrial clot mandates anticoagulation therapy (in the absence of contraindications).

TEE is also recommended to rule out left atrial thrombi before elective cardioversion of patients with atrial flutter or fibrillation, before LA ablation for the treatment of atrial fibrillation and before mitral balloon valvuloplasty. In these patients a clot in the left atrium may be dislodged and may embolize during such procedures. Therefore, if a clot is found, the procedure is usually postponed and anticoagulation therapy is given until the clot is dissolved or no longer present [10,11].

Paradoxical emboli may also occur if a thrombus reaches the left atrium via a patent foramen ovale. This is discussed elsewhere in this issue [1].

Left ventricular clots [Figure 3]

Clots are usually attached to the left ventricular endocardium in patients with LV wall motion abnormalities. The latter may be diffuse, as seen in dilated cardiomyopathy, or segmental, as in coronary artery disease and myocardial infarction. Clots are more common in the apex of the left ventricle. They occur more

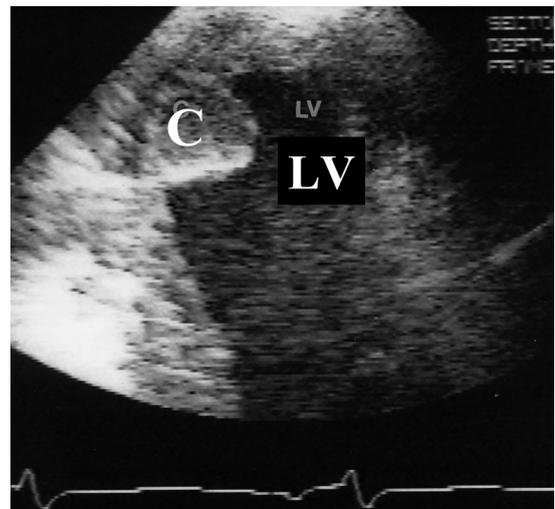


Figure 3. TTE, apical view, showing a patient with previous anteroseptal myocardial infarction. Note apical clot (C)

frequently in anteroseptal infarction than in inferior, posterior or lateral infarctions. It is estimated that up to 20% of LV clots will embolize and that one-third of those will produce stroke [12]. Since the cardiac apex is close to the chest wall (and is not in close proximity to the esophagus), LV apical clots are better visualized with TTE than with TEE. High frequency high resolution transducers may improve the image quality.

Occasionally, when image quality is suboptimal, transvenous echo contrast injection may provide better endocardial and clot delineation. Unlike agitated saline injection, which produces microcavitations that are trapped by the lung and therefore do not normally reach the left heart, these very small fluorocarbon 'microbubbles' travel through the lungs to reach and opacify the left heart chambers.

LV clots are rarely seen in the presence of normal wall motion. This may occur in patients with eosinophilic endomyocardial disorders (such as Loeffler's syndrome) and in patients with hypercoagulable states.

Left heart tumors [13] [Figure 4]

Primary tumors of the heart are rare. Benign primary cardiac tumors are more common than malignant ones. Since tumor fragments that protrude into the left heart chambers may embolize, stroke and other embolic events may be the first manifestations of such tumors. In addition, clots formed on the surface of intracardiac tumors may represent an additional embolic risk.

The most common primary myocardial tumor is a left atrial myxoma. Characteristically, it is attached by a stalk to the interatrial septum. The tumor may move into the mitral orifice during diastole, creating LV inflow obstruction with symptoms that may be similar to those of mitral stenosis. The tumor is usually diagnosed by TTE. TEE will better show the anatomic relations, the mode of attachment, and also small cysts within the tumor that are considered characteristic.

The second common left heart tumor is benign papillary fibroelastoma. This is usually smaller than a myxoma, may be

LV = left ventricular

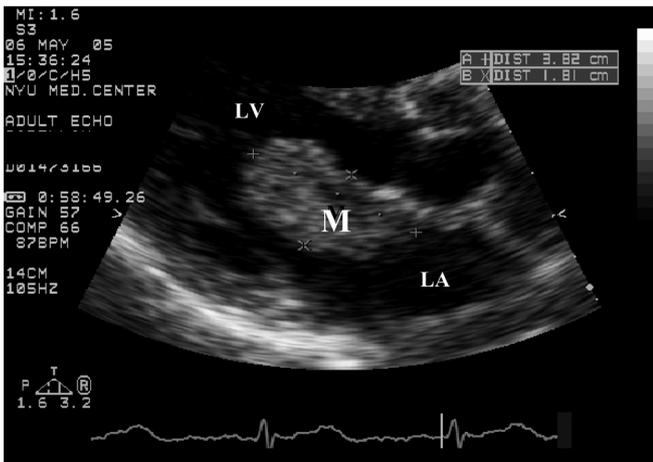


Figure 4. TTE, long axis view, diastolic frame showing a large left atrial myxoma (M) entering the mitral orifice

attached to the valves (aortic more than mitral) as well as to the cardiac walls, and may have characteristic small fingerlike mobile fronds seen best on TEE.

Valvular vegetations [Figure 5]

The diagnosis of endocarditis is frequently made clinically and then confirmed by blood cultures. The demonstration of valvular vegetations further establishes the diagnosis, stratifies embolic



Figure 5. TEE frame showing large, shaggy mitral valve vegetation (arrow) in a patient with bacterial endocarditis.

while TEE missed only 10% and 23% respectively [15]. In another study that compared TTE with TEE, TTE was only 55% sensitive for the detection of vegetations [16].

Because of its higher sensitivity and its ability to better define embolic risk and other complications of endocarditis (such as myocardial abscess or valvular destruction), TEE is recommended for all patients with suspected or diagnosed endocarditis

Aortic plaque [16,17] [Figure 6]

Imaging of the aorta is a vital part of the evaluation of the patient with embolic disease. Aortic atherosclerosis is an important and common source of embolic stroke and peripheral embolization. It should be considered a possible source of embolism even in the presence of other potential etiologies such as carotid stenosis or patent foramen ovale. The prevalence of severe aortic plaque in stroke patients is 14–21%, which is on the same order of magnitude as the two other important causes of embolic stroke – carotid artery disease (10–13%) and atrial fibrillation (18–30%).

The prevalence of aortic plaques increases from the ascending

Echocardiography can evaluate and diagnose many causes of embolic stroke, such as intracardiac shunts, blood clots and other masses, valvular vegetations, and aortic plaques

risk, dictates treatment modalities, and monitors the response to therapy. Valvular vegetations have been described as shaggy mobile masses that vary in size from a few millimeters to several centimeters. They are usually (but not always) associated with valvular pathology, regurgitation, stenosis or prosthetic valves.

Embolism may be an early manifestation of endocarditis. The risk of embolization is related to the vegetation site, size, mobility and age. Mitral vegetations have a higher embolic potential than aortic vegetations. Mitral valve vegetations of 1 cm or more have more than a 50% chance of producing a clinically significant embolic event [14]. Mobile vegetations have a higher embolic potential than do sessile ones, and fresh untreated vegetations are more risky than old treated lesions. (Echocardiographically, more acute vegetations are less dense than the myocardium, while older, fibrotic or even calcified vegetations are denser).

While many vegetations are visualized with TTE, TEE has higher sensitivity. In one study, where surgical or autopsy findings served as the gold standard, TTE missed 42% of all native valve vegetations and nearly 75% of all prosthetic valve vegetations,

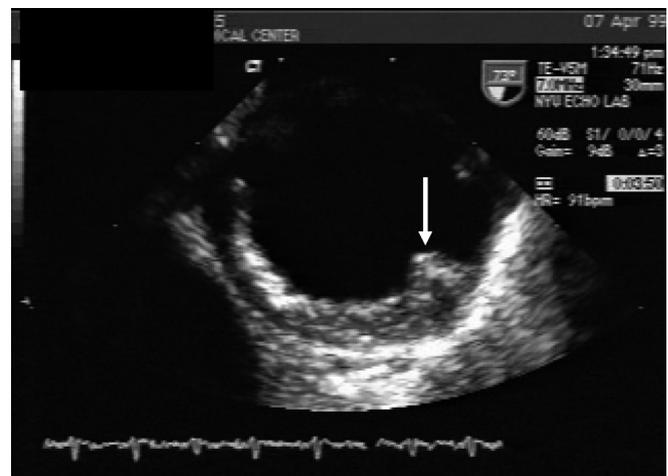


Figure 6. TEE frame, longitudinal view of the aortic arch. Note the large aortic plaque (arrow)

aorta distally. Complex plaques (defined as aortic plaque with a thickness of 4 mm or more and/or plaques with superimposed mobile thrombus) are associated with very high embolic risk. Almost one-third of all patients with complex plaques will have vascular events within one year. Twelve percent will suffer from stroke.

The mechanism for the majority of the events is embolic occlusion of medium- and large-size arteries by a blood clot that originates from the surface of an unstable plaque in the aorta. Plaques with a large high lipid core and thin cap are therefore more dangerous.

Patients with complex aortic plaque who undergo open heart surgery have a sixfold increased risk of embolic event or death. Direct plaque disruption and clot dislodgement during aortic cannulation and manipulation are the mechanism for this often devastating complication.

In most patients, TTE cannot show the details of the thoracic aorta beyond the aortic root. TEE is the echocardiographic technique of choice for the imaging of aortic plaque. It can evaluate plaque thickness and composition (lipid-laden plaques are less dense), visualize superimposed thrombi, and assess the risk of embolic events.

Patients with complex plaque who were treated with statins had significantly fewer embolic events [18]. It is therefore recommended that all patients with aortic plaques be treated with statins, regardless of their lipid levels. The role of anticoagulant versus antiplatelet agents in the treatment of these patients is less clear and warrants further study.

Occasionally, aortic imaging can disclose other conditions responsible for embolic or ischemic stroke. This includes aortic aneurysm, clots, tumors (rare) and dissection.

References

1. Kronzon I. Patent foramen ovale: echocardiographic evaluation and clinical implications. *IMAJ* 2006;8:793-7 (this issue).
2. Daniel WG, Kronzon I, Mugge A, eds. *Cardiogenic Embolism*. Philadelphia: Williams and Wilkins, 1996.
3. Foulkes MA, Wolf PA, Price TR, Mohr JP, Hier DB. The stroke data bank: design, methods and baseline characteristics. *Stroke* 1988;19:547-54.
4. Frazin L, Talano JV, Stephanides L, Loeb HS, Kopel L, Gunnar RM. Esophageal echocardiography. *Circulation* 1976;54:102-8.
5. Daniel WG, Erbel R, Kasper W, et al. Safety of TEE, a multicenter study of 10,419 examinations. *Circulation* 1991;83:817-21.

6. de Belder MA, Lovat LB, Tourikis, Leech G, Camm AJ. Limitations of TEE in patients with focal cerebral events. *Br Heart J* 1992;67:297-303.
7. Takemoto Y, Harnes ME, Seward JB, et al. Usefulness of left atrial volume in predicting first congestive heart failure. *Am J Cardiol* 2005;96:832-6.
8. Daniel WG, Nellesswen U, Schroder E, et al. Left atrial spontaneous echo contrast in mitral valve disease: an indicator for increased risk. *J Am Coll Cardiol* 1988;11:1204-11.
9. Aschenberg W, Schultze K, Kremer P, Schroeder E, Siglow V, Bleifeld W. Transesophageal two dimensional echocardiography for the detection of left atrial appendage thrombus. *J Am Coll Cardiol* 1986;7:163-6.
10. Kronzon I, Tunick PA, Glassman E, Slater J, Schwinger M, Freedberg RS. TEE to detect atrial clots in candidates for percutaneous mitral valvuloplasty. *J Am Coll Cardiol* 1990;16:1320-2.
11. Klein A, Grimm RA, Murray RD, et al. Use of TEE to guide cardioversion in patients with atrial fibrillation. *N Engl J Med* 2001;344:1411-20.
12. Visser CA, Kan G, Meltzer RS, Dunning AJ, Roelandt J. Embolic potential of left ventricular thrombus after myocardial infarction: a two dimensional echocardiographic study of 129 patients. *J Am Coll Cardiol* 1985;5:1276-80.
13. Friedberg RS. Cardiac and vascular tumors as a source of emboli. In: Daniel WG, Kronzon I, Mugge A, eds. *Cardiogenic Embolism*. Philadelphia: Williams and Wilkins, 1996:169-76.
14. Sanfilippo AJ, Picard MH, Newell JB, et al. Echocardiographic assessment of patients with infectious endocarditis: prediction of risk for complications. *J Am Coll Cardiol* 1991;18:1191-9.
15. Mugge A, Daniel WG, Frank G, Lichtlen PR. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by transthoracic and transesophageal echocardiography. *J Am Coll Cardiol* 1989;14:631-8.
16. Reynolds HR, Jagen MA, Tunick PA, Kronzon I. Sensitivity of transthoracic echocardiography vs. transesophageal echocardiography for the detection of native valve vegetations in the modern era. *J Am Soc Echocardiography* 2003;16:67-70.
17. Kronzon I, Tunick PA. Atheromatous disease of the thoracic aorta: pathologic and clinical implications. *Ann Intern Med* 1997;126:629-37.
18. Tunick PA, Kronzon I. Atheromas of the thoracic aorta: clinical and therapeutic update. *J Am Coll Cardiol* 2000;35:545-54.
19. Tunick PA, Nayar AC, Goodkin GM, et al. Effect of treatment on the incidence of stroke and other emboli in 519 patients with severe thoracic aortic plaque. *J Am Cardiol* 2002;15:1333-5.

Correspondence: Dr. I. Kronzon, 560 First Avenue, New York, NY 10016, USA.

Phone: (1-212) 263-5665

Fax: (1-212) 263-8461

email: itzhak.kronzon@med.nyu.edu