Cardiac CT and MRI for Assessment of Cardioembolic Stroke

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Cardioembolic stroke is generally severe with a high risk for both early and long-term recurrence, requiring early diagnosis. Cardiac CT and MRI are accurate noninvasive alternatives to echocardiography which can demonstrate the potential cardiac source of an embolism and exclude other potential sources. The major sources of cardioembolic stroke include atrial fibrillation, recent myocardial infarction, valvular heart disease, endocarditis, and atrial myxoma. Minor sources of cardioembolism are paradoxical embolism due to patent foramen ovale and atrial septal aneurysm, atrial or ventricular septal defects, calcific aortic stenosis, and mitral annular calcification. The appropriate clinical application of cardiac CT and MRI can allow an exact and timely diagnosis to be made in embolic stroke patients.

Key words Intracranial embolism · Stroke · EKG-triggered imaging techniques · Tomography, spiral computed · Magnetic resonance imaging.

INTRODUCTION

Cardioembolic stroke accounts for 14–30% of all ischemic strokes and is generally severe with a high risk of early and long-term recurrence, and high mortality [1]. Therefore, early diagnosis of cardioembolic stroke is critical so that anticoagulation therapy can be initiated for secondary prevention. Variable cardiac disorders have been proposed as potential sources of embolism. The major sources of cardioembolic stroke include atrial fibrillation, recent myocardial infarction, valvular heart disease, endocarditis, and atrial myxoma. Major sources carry a relatively high risk of initial and recurrent stroke and are convincingly linked to a cardioembolic mechanism [2]. Minor sources are paradoxical embolism due to patent foramen ovale (PFO) and atrial septal aneurysm (ASA), atrial or ventricular septal defects, calcific aortic stenosis, and mitral annular calcification (MAC) [2]. Minor sources are common in the general population, and these conditions have a low or uncertain associated risk of initial and recurrent stroke [2]. Imaging of potential sources allows the identification of the potential cardiac embolism

source and can exclude other potential sources of cerebral ischemia. Given the noninvasive nature and wide availability of transthoracic echocardiography (TTE), it is one of the initial cardiac imaging tools used for diagnosis of potential cardioembolic sources. Transesophageal echocardiography (TEE) provides more detail of the atria and aorta than TTE, although it is more invasive and requires more training to be performed adequately [3]. Cardiac CT or MRI can be accurate noninvasive alternatives to TEE or TTE in the following circumstances: 1) patients who cannot tolerate TEE, 2) questionable results from TTE for the detection of thrombus in the left ventricle, 3) inconclusive results of TEE, or 4) characterization of a cardiac mass detected on TTE or TTE (Table 1). The aim of this review is to present recent investigations on using cardiac CT or MRI in cardioembolic stroke cases.

ATRIAL FIBRILLATION

Atrial fibrillation is the most common cause of embolic sources, and about 60% of cardioembolic strokes are caused by left atrium (LA) and left atrial appendage (LAA) thrombi secondary to atrial fibrillation or flutter [4]. Atrial fibrillation causes strokes because of inadequate LA or LAA contraction

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Table 1. Comparison of cardiac CT, cardiac MRI, TTE, and TEE for the identification of the potential source of cardioembolic stroke

	Cardiac CT	Cardiac MRI	TTE	TEE
Atrial fibrillation	Requires administration of iodinated contrast and considerable use of ionizing radiation to obtain a delayed contrast-enhanced image for detection of thrombus in the left atrial appendage	Prolonged examination duration, dependence on breath holds, inability to be performed in patients with implanted cardiac devices	Widely available, loss of acoustic window in patients with obesity or limited inter-rib spaces	Requires the passage of a probe
Myocardial infarction	Simultaneous depiction of coronary artery disease and other potential anatomic structures of cardioembolic stroke including aorta	Differentiating thrombus and myocardium or tumor, prolonged examination duration, dependence on breath holds, inability to be performed in patients with implanted cardiac devices	Widely available	Requires the passage of a probe
Valvular heart disease	Lower temporal resolution than MRI or TTE or TEE	Lower temporal resolution than TTE or TEE	Easily maneuvered imaging plane in real-time to optimize visualization	Easily maneuvered imaging plane in real-time to optimize visualization
Endocarditis	Limited evaluation of small vegetation due to lower spatial resolution than TEE or TTE	Limited evaluation of small vegetation, lower spatial resolution than TEE or TTE	High temporal and spatial resolution demonstrating small vegetation	High temporal and spatial resolution demonstrating small vegetation
Atrial myxoma	Tissue characterization is inferior to MRI	Can distinguish the tumor from the myocardium, thrombus, and blood flow artifacts through the addition of contrast material	Inferior tissue characterization to MRI	Inferior tissue characterization to MRI
Foramen ovale and atrial septal aneurysm	Multiplanar reconstructed images along different planes	Lower spatial resolution than TEE or TTE	Real-time display of shunt flow with contrast echo such as agitated saline injection	Real-time display of shunt flow with contrast echo such as agitated saline injection
Calcific aortic stenosis or mitral annular calcification	Accurate detection of calcification		Limited visualization of the aorta	Limited visualization of the distal ascending aorta and proximal aortic arch

TTE: transthoracic echocardiography, TEE: transesophageal echocardiography

Fig. 1. A left atrial appendage thrombus in a 67-year-old woman. (A) A diffusion weighed brain MR image shows a small area of high signal intensity (arrow) in the right occipital lobe suggesting an acute cerebral infarction. (B) Cardiac CT shows a mural thrombus (arrows) in the left atrial appendage. (C) Cardiac CT also demonstrates aortic and mitral valvular thickening (arrows) suggesting rheumatic valvular disease.

Fig. 2. Circulatory stasis in the left atrial appendage in a 78-year-old man. (A) Cardiac CT shows a filling defect in the left atrial appendage (arrows). (B) Delayed image acquisition reveals contrast enhancement in the left atrial appendage, differentiating circulatory stasis from thrombi.

Fig. 3. A left atrial appendage thrombus in a 73-year-old man. (A) A diffusion weighed brain MR image shows small areas of high signal intensity (arrows) in the left occipital lobe suggesting an acute cerebral infarction. (B) Cardiac CT shows a filling defect (arrows) in the left atrial appendage. (C) Delayed image acquisition reveals a persistent nodular filling defect in the left atrial appendage (short arrows) suggesting a thrombus.

which leads to stasis that predisposes thrombus formation, and consequently an increased rate for cerebral embolization [2]. TEE is usually chosen for examination of LAA thrombi due to its high sensitivity and specificity for the detection of thrombi [5]. However, TEE is a semi-invasive test, and may not be adequate in various circumstances including multilobed appendages, large pectinate muscles, and dense spontaneous echo contrast, which can obscure a thrombus in the LAA [6].

With recent improvements in temporal and spatial resolution, cardiac CT has emerged as an acceptable alternative for evaluating an intracardiac thrombus, which is observed as a filling defect (Fig. 1) [7]. Delayed scanning has been reported to improve the specificity and positive predictive value of cardiac

CT for the detection of LAA thrombi (Figs. 2 and 3). In a recent meta-analysis, the sensitivity and specificity of cardiac CT was 0.957 (95% confidence interval: 0.928–0.977) and 0.917 (95% confidence interval: 0.905–0.927), respectively [8]. This study showed that diagnostic accuracy improved significantly with delayed imaging, ECG gating, and heart rate control with a sensitivity of 0.991 (95% confidence interval: 0.951–1.000) and specificity of 0.989 (95% confidence interval: 0.977–0.995). Dual-energy cardiac CT can also be used for differentiating LAA thrombi from circulatory stasis with high sensitivity [7]. Regarding delayed phase scanning, contrast enhancement of the first contrast materials in the LAA results in a different attenuation between a thrombus and circulatory stasis. A recent study

Fig. 4. A left ventricular thrombus in a 36-year-old man with a history of acute myocardial infarction two weeks prior. (A) A diffusion weighted brain MR image shows high signal intensity (arrow) in the right frontal lobe precentral gyrus suggesting acute cerebral infarction. (B) A two chamber view image of cardiac CT shows a nodular filling defect (arrows) in the left ventricular apex surrounded by contrast material. (C) Myocardial thinning and aneurysm (short arrows) in the left ventricle apex on the four chamber view image suggest a recent myocardial infarction. (D) Delayed image acquisition demonstrates a perfusion defect (short arrows) in the left ventricular apex and apical segment with non-enhancement of thrombus in the apex (arrow).

revealed that a cardiac CT measurement with a LAA/aorta Hounsfield units (HUs) ratio <0.245 in the arterial and venous phases can be a quantitative indicator for the presence of a thrombus [9], whereas another study concluded that additional calculation of the HU ratio did not improve the diagnostic performance of cardiac CT for detecting LAA thrombi [10]. Because a two-phase protocol increases patient radiation exposure, the supplementary role of CT can be most valuable in cases where performing TTE or TEE is hampered by limited experience or contraindication due to medical reasons [11]. Cardiac MRI can be proposed as an effective, safer, and comprehensive imaging modality comparable to TEE for the evaluation of LAA thrombi, although its slower image acquisition

and inability to be used in patients with implanted metallic devices interfere with the feasibility of cardiac MRI [12].

RECENT MYOCARDIAL INFARCTION

Approximately 1.0–2.5% of patients with acute myocardial infarction experience a stroke during the first 4 weeks after the infarction [13]. Factors that increase the risk of stroke are severe left ventricular (LV) dysfunction with low cardiac output and LV aneurysm or thrombus. The incidence of LV mural thrombus remains high (15–40%) after anterior infarction [14]. The incidence of early embolism is also high (up to 22%) in the presence of a mural thrombus that is mobile or protrudes into

Fig. 5. A left atrial thrombus in a 46-year-old woman with mitral stenosis. (A) Cardiac CT shows a thickened leaflet and diastolic bowing of the leaflets in a hockey-stick shape deformity (arrows). (B) A volume rendering reformatted image shows the mitral valvular area measurement (short arrows). (C) Cardiac CT demonstrates a diffuse mural thrombus in the left atrium (arrows) and (D) persistent nodular filling defect in the left atrial appendage (arrows) on the delayed image acquisition.

the ventricle [2]. Cardiac CT and MRI are both excellent tools to evaluate a LV thrombus. On cardiac CT, a thrombus is observed as a low-attenuation area surrounded by an infarcted myocardium (Fig. 4). In a study on 31 patients by Bittencourt et al. [15], CT attenuation within LV thrombi was significantly lower than myocardial attenuation, and a threshold of 65 HU yielded 94% sensitivity and 97% specificity to differentiate a thrombus from the myocardial wall. Contrast-enhanced cardiac MRI is not only an excellent technique to depict myocardial in-

farcion and scar tissue, but also a sensitive method for detecting a LV thrombus [16]. Delayed enhancement cardiac MRI using gadolinium contrast differentiates a thrombus from the surrounding myocardium as a thrombus is avascular and thus characterized by the absence of contrast uptake. Srithai et al. [17] reported that contrast-enhanced cardiac MRI, incorporating delayed enhancement cardiac MRI and cine-cardiac MRI (n=160), showed the highest sensitivity and specificity for thrombus detection (88% and 99%, respectively) compared to

Fig. 6. Infective endocarditis in a 41-year-old woman who underwent prosthetic mitral valve replacement. Cardiac CT shows a small low attenuating nodule attached to the prosthetic mitral valve suggesting vegetation (arrows). Cardiac surgeries revealed a pannus and abscess around the prosthetic mitral valve.

Fig. 7. Cardiac myxoma in a 60-year-old woman. (A and B) Cardiac CT shows about a 5 cm sized left atrial intraluminal protruding mass attached to the interatrial septum with multiple nodular calcifications (arrows). (C) Delayed image acquisition demonstrates diffuse enhancement in the mass (arrows). Cardiac MRI demonstrates high signal intensity in the mass (arrows) on both T1 (D) and T2 (E) weighed images and gadolinium enhancement (F).

TTE (23% and 96%, respectively) and TEE (40% and 96%, respectively). In a study by Weinsaft et al. [16], among 784 patients with systolic dysfunction, delayed enhancement cardiac MRI detected a thrombus in 55 patients (7.0%) and cine-cardiac MRI in 37 patients (4.7%), $p < 0.005$.

Rheumatic valvular heart disease and mechanical prosthetic valves are well-known risk factors for cardioembolic stroke [2]. The two most common valve abnormalities are mitral stenosis and calcific aortic stenosis. Systemic embolism occurs in 9–14% of patients with mitral stenosis and may be the initial presentation of mitral stenosis [18]. The risk of stroke in mitral stenosis is amplified in the presence of atrial fibrillation. Valvular atrial fibrillation is commonly accompanied by mitral stenosis, requiring anticoagulation treatment. Cardiac CT can demonstrate a thickened leaflet and diastolic bowing of the leaflets in a hockey-stick shape deformity as well as calcification in the mitral valve leaflet or commissure in patients with mitral stenosis (Fig. 5) [19]. Geometric measurement of the mitral orifice area on car-

diac CT is well correlated with TEE [20]. Cardiac CT demonstrates valvular vegetation as an oval or round filling defect on the mitral or aortic valve [21]. Because small vegetation can be disregarded as mere valvular thickening on cardiac CT, careful interpretation is needed to avoid false-negative results [11].

ENDOCARDITIS

Systemic embolization occurs in 22–50% of infective endocarditis cases [22]. Although TEE has great sensitivity in the detection of vegetations, cardiac CT can be used as an alternative tool for the assessment of endocarditis (Fig. 6) [23]. In a recent study by Feuchtner et al. [23], the diagnostic performance of cardiac CT for the detection of valvular abnormalities related to infective endocarditis was compared with TEE. Cardiac CT had a sensitivity of 97% (95% confidence interval: 82–100%) and specificity of 88% (95% confidence interval: 47–100%) on a per-patient basis. In their study, cardiac CT correctly identified 26

Fig. 8. An atrial septal defect in a 57-year-old woman. A reformatted image (A) and short-axis image (B) of cardiac CT show a 1.8 cm sized defect in the interatrial septum suggesting a secundum type atrial septal defect (arrows).

Fig. 9. A mitral annular calcification in an 83-year-old woman. Cardiac CT in the diastolic (A) and systolic phase (B) shows an extensively calcified mitral annulus (short arrows) with left atrial dilatation and severe aortic stenosis (arrows).

of 27 (96%) patients with valvular vegetations and 9 of 9 (100%) patients with abscesses/pseudoaneurysms compared to the intraoperative specimen. Regarding the lower temporal resolution of cardiac CT as compared to echocardiography, cardiac CT can be a complementary imaging modality by providing more accurate anatomic information regarding the perivalvular extent of abscesses/pseudoaneurysms than TEE [24] and allows concurrent imaging of coronary arteries prior to valve replacement surgery [25].

ATRIAL MYXOMA

Cardiac tumors such as myxomas and papillary fibroelastomas are associated with a high frequency of embolic events. Myxomas occur in the LA in 75% of cases, often originating from the fossa ovalis area of the interatrial septum [26]. Myxomas tend to embolize to the systemic circulation in 30 to 40% of cases, and to the cerebral circulation in over 50% of cases. Embolization may be caused by tumor fragmentation, or be secondary to superimposed thrombus formation. Although TEE is the mainstay for the clinical diagnosis of cardiac mass, cardiac MRI is the reference imaging technique for further differentiation and characterization of cardiac tumors. In addition to cine imaging and steady-state free precession, black blood imaging, fat-suppressed sequences, perfusion, and late gadolinium enhancement are used as MR protocols [4]. Cardiac CT is also an excellent method for assessment of a mass due to its higher spatial resolution and its ability to evaluate calcification, fat, thrombi, and fibrous material (Fig. 7). In some cases, an atrial thrombus may have pedunculation and can be misdiagnosed as a myxoma, which can lead to an unnecessary surgical resection [27]. According to a cardiac CT study by Scheffel et al. [28], myxomas are significantly larger than thrombi, most often originate from the fossa ovalis, and are predominantly polypoid, with a minority having a villous shape [26], whereas thrombi are smaller than myxomas and most often originate from the appendage. It is reported that villous-shaped myxomas and mobile polypoid thrombi are highly associated with embolic strokes [29]. Regarding differentiating between benign and malignant intracardiac masses, cardiac MRI is excellent due to its multiplanar capabilities and soft tissue characterization. For example, lipomatous hypertrophy of the interatrial septum, which is a common benign variant mimicking mass, can be correctly identified using cardiac MRI [30].

PARADOXICAL EMBOLI

PFO is present in a third of stroke patients, and is found in up to 40% of patients with ischemic stroke younger than 55 years of age [31]. The association between PFO and cryptogenic

strokes has been well established [32]. It is frequently considered as a possible cardioembolic source since it allows for potential paradoxical embolism, a systemic arterial embolus from a venous source [3]. PFO and atrial septal defect (ASD) can be differentiated based on the direction of the contrast jet from the left to right atrium and the appearance of the atrial septum on cardiac CT [33]. A contrast jet flowing toward the inferior vena cava with the channel-like appearance of atrial septum can confirm a PFO. On the other hand, a contrast jet flowing perpendicular to the atrial septum with the appearance of a membrane with a hole is an ASD (Fig. 8). An ASA can cause a stroke by paradoxical embolism of a thrombus originating in the aneurysm or by inducing supraventricular arrhythmia. ASA is defined as the presence of interatrial septal bulging with an excursion of >1.0 cm with >1.5 cm of base span [21]. Paradoxical embolism, supraventricular arrhythmia, and thrombus from a coexistent ASA are possible mechanisms of stroke in PFO. Patients with PFO and ASAs had an increased risk ratio (4.2) for recurrent stroke [34].

CALCIFIC AORTIC STENOSIS AND MITRAL VALVE CALCIFICATION

Aortic stenosis is a rare cause of stroke which is usually calcific. Large emboli in patients with calcific aortic stenosis have been associated with cardiac catheterization and balloon valvuloplasty [35]. Regarding cardiac CT imaging in aortic stenosis, the measurement value for the aortic valve area is larger than the echocardiographic result [36] and valvular calcification adversely affects the accuracy of aortic valve area measurement [37]. MAC is also a possible source of cerebral embolism with a 2.1 increase in the relative risk of stroke, and a fivefold increase in the risk of stroke in the presence of atrial fibrillation [1]. MAC is chronic degeneration of the mitral valve fibrous ring. In patients with suspected embolic stroke of uncertain etiology, dense MAC is an important marker for aortic atherosclerosis associated with a high risk of embolism [38]. On cardiac CT, MAC can be defined as calcification located at the junction between the LA and LV (Fig. 9). When liquefaction necrosis develops in the calcification, it can look like the left atrial mass in the posterior mitral annulus on TTE, mimicking a left atrial fibroma [39]. With the use of cardiac CT or MRI, MAC can be accurately diagnosed by revealing areas of calcifications in the mass along with their exact locations [40].

CONCLUSION

Cardioembolic stroke can arise from various cardiac disorders. Appropriate clinical application of cardiac CT or MRI can be useful to quickly identify or exclude the cardiac source and

make an exact diagnosis in patients with embolic stroke.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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