

Assessment of Ischemic Stroke or Transient Ischemic Attack of Undetermined Cause Using Cardiac Magnetic Resonance Imaging

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Abstract:

Background: Cardiac magnetic resonance imaging (CMR) has emerged as a crucial tool for evaluating cardiac sources of emboli, particularly in patients with ischemic stroke of undetermined origin. Accurate identification of potential cardiac embolic sources can significantly impact treatment strategies and improve patient outcomes. **Methods:** This study aimed to assess the efficacy of CMR in detecting cardiac sources of emboli in patients with ischemic stroke or transient ischemic attack (TIA) of unknown etiology. A total of 100 patients who met the inclusion criteria underwent CMR, focusing on identifying abnormalities such as left atrial enlargement, left atrial appendage thrombus, diastolic dysfunction, and other relevant cardiac anomalies. Data was analyzed to determine the prevalence and clinical significance of these findings. **Results:** CMR identified cardiac abnormalities in 24% of patients. Specifically, 4% had left atrial appendage thrombus, and 8% exhibited patent foramen ovale. Additionally, 12% had left ventricular thrombi or tumors. These abnormalities were significantly associated with an increased risk of recurrent embolic events, with a 50% higher likelihood of subsequent stroke or TIA. **Conclusion:** CMR proves to be an effective modality in identifying potential cardiac sources of emboli in patients with ischemic stroke or TIA of undetermined cause. Its ability to detect subtle cardiac abnormalities can guide targeted interventions and improve overall management strategies for these patients.

Keywords: Ischemic Stroke; Transient Ischemic Attack; cardiac MRI; CT Brain.

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Introduction

After an ischemic stroke or transient ischemic attack (TIA), generally there is a diagnostic workup in search of the cause of the event, as this information may guide treatment that aims at reducing the risk of recurrent ischemic events ⁽¹⁾.

In 20-25% of patients, ischemic stroke may be attributed to cardiac embolism. Cardiac embolism may not result only from atrial fibrillation but from a variety of structural abnormalities and conditions of the heart or the ascending aorta. major cardio embolic sources are conditions that are considered presumable causes of an ischemic stroke and require a change of therapy, whereas for minor cardio embolic sources the causal relationship is uncertain and in most cases no change of therapy is required ⁽²⁾.

Despite a routine in-hospital work-up that generally consists of imaging of the brain and carotid arteries, laboratory testing, electrocardiogram (ECG) and at least 24 h of cardiac rhythm monitoring, the underlying cause remains unknown in about 25% of patients ⁽³⁾.

In these patients the event is referred to as cryptogenic stroke or "ischemic stroke of undetermined cause "the term "embolic stroke of undetermined source ", which has been proposed as a more clearly defined concept, is confined to patients with an imaging –proven, non-lacunar cerebral infarction in the absence of more than or equal to 50% ipsilateral extra – or intracranial arterial stenosis, and in the absence of a major cardio embolic source or other specific cause of stroke ⁽²⁾.

After negative routine work –up, most guidelines advice cardiac imaging but it is much less defined how to examine the heart and what exactly to look for detecting a treatable, major cardio embolic source is of paramount importance, yet insights into the relation between cardiac conditions and ischemic stroke have shifted over the past years. several cardio embolic sources, such as aortic atheroma or dilated cardiomyopathy, are considered

to have therapeutic implications in this context ⁽⁴⁾.

Cardiac thrombus provides a substrate for embolic events and an indication for anticoagulant therapy. cardiac magnetic resonance (CMR) imaging enables thrombus to be detected based on intrinsic tissue characteristics related to avascular tissue composition. Delayed enhancement CMR tissue characterization has been well validated for thrombus assessment using references of both pathology and clinical thromboembolic outcomes. Comparative studies have demonstrated CMR to yield improved thrombus detection compared to echocardiography, which typically detects thrombus based on anatomic appearance. Experimental studies have demonstrated the feasibility of targeted CMR contrast agents for assessing thrombus composition and chronicity. This review examines established and emerging ⁽⁵⁾.

The purpose of this study was to assess cardio-embolic sources of acute ischemic stroke or transient ischemic attack of unknown cause by cardiac MRI (magnetic resonance imaging).

Aim of the Work

This study aimed to assess cardio-embolic sources of acute ischemic stroke or transient ischemic attack of unknown cause by cardiac MRI (magnetic resonance imaging).

Patients and methods

This prospective non-randomized observational study included 100 patients exposed to acute ischemic stroke or transient ischemic attack selected from Cardiology & Neurology Departments, in Benha University and Electricity Hospital in Cairo, during the period from 1st October 2023 to 30th March 2024.

An approval from the Research Ethics Committee of Benha faculty of medicine and Electricity hospital was obtained. An informed written consent from all participants before participation was obtained; it included data about the aim of

the work, study design, site, time, subject and methods, confidentiality.

Inclusion criteria were patients less than 30 y and more than 60 y, CT brain or MRI brain evidence of acute ischemic stroke or clinical criteria of TIA, neurological deficit, sinus rhythm, vitally stable, normal carotid duplex.

Exclusion criteria were AF or atrial flutter (excluded by ECG), carotid significant plaques more than 50% (excluded by cardiac duplex), coma or shock (excluded by proper examination and vital signs acquisition), echocardiographic findings of thrombus or vegetation (excluded by echo examination), old CVS (excluded by CT or MRI brain), intracerebral hemorrhage or cerebrovascular abnormalities (excluded by CT or MRI brain), recent fibrinolytic therapy, extreme body weight, obesity beyond the limits of scanner table capacity, claustrophobia or anxiety, allergy to gadolinium contrast, severe renal impairment, metallic implants, significant calcification of cardiac valves or mitral annulus, and patient refusal..

All studied cases were subjected to the following: Demographic data and history taking, including [age and sex and history of comorbid conditions]. Full Clinical Examination (Cardiological and Neurological), Laboratory Tests, Electrocardiogram (ECG) , CT or MRI Brain , Cardiac Magnetic Resonance Imaging (CMR), Carotid Duplex Ultrasonography , transthoracic Echocardiography (Echo) & CT Chest .

Electrocardiogram (ECG): Performed to exclude atrial fibrillation (AF) and other arrhythmias. It included heart rate, rhythm, P-wave morphology, PR interval, QRS complex, and QT interval.

CT Brain or MRI Brain: Conducted to confirm the presence of an acute ischemic stroke or transient ischemic attack. Assessment of the extent and location of the infarction, any signs of hemorrhage, and evaluation of brain structures.

Cardiac Magnetic Resonance Imaging (CMR): CMR was conducted by machine Model name: Magnetom Aera1.5T, Serial number: 142377 for evaluation of the following: Thrombus Detection: Specific sequences like LGE were utilized to identify thrombi based on their avascular nature. Structural and Functional Assessment: Cardiac volumes, function, and potential structural abnormalities (such as dilatation of the chambers or abnormal motion) were meticulously analyzed.

Carotid Duplex Ultrasonography: Used to exclude significant carotid plaques. It included intima-media thickness, the presence of atherosclerotic plaques, degree of stenosis, and blood flow velocity in the carotid arteries.

Echocardiography (Echo): Transthoracic echocardiography (TTE) was performed to evaluate cardiac structure and function. It included left ventricular ejection fraction (LVEF), presence of wall motion abnormalities, chamber sizes, valvular function, and the presence of any thrombi or vegetations.

CT Chest : Was performed to exclude pulmonary embolism & chest diseases

Approval code: MD10-4-2022

Statistical analysis

Statistical analysis was done by SPSS v28 (IBM©, Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD). Qualitative variables were presented as frequency and percentage (%). Agreement between quantitative variables was evaluated by Bland-Altman analysis. A two tailed P value < 0.05 was considered statistically significant.

Results

CMR identified cardiac abnormalities in 24% of patients. Specifically, 4% had left atrial appendage thrombus, and 8% exhibited patent foramen ovale, Additionally, 12% had left ventricular thrombi or tumors. These abnormalities were significantly associated with an

increased risk of recurrent embolic events, with a 50% higher likelihood of subsequent stroke or TIA.

Shows demographic data, and comorbidities of the studied patients. Table 1

Shows cardiological evaluation of the patients studied by MRI and Prevalence of Cardiac causes of stroke. Table 2

Shows MRI findings of the studied patients By MRI examination, the LVSVI

ranged from 40 to 48 mL/m² with a mean of 43.96 ± 2.37 mL/m². The RVSVI ranged from 35 to 54 mL/m² with a mean of 49.3 ± 4.54 mL/m². Table 3

Shows Agreement between CT and MRI of the brain of the patients. There was a significant weak (fair) agreement between CT and MRI. Table 4

Table 1: Demographic data, comorbidities of the studied patients

		Total (n=100)
Age (years)	Mean± SD	63.8 ± 13.1
Sex	Male	64 (64%)
	Female	36 (36%)
Comorbidities		
DM		56 (56%)
HTN		52 (52%)
Dyslipidemia		36 (36%)
Stroke		76 (76%)
TIA		24 (24%)

DM: diabetes mellitus, HTN: hypertension, TIA: transient ischemic attack.

Table2: Cardiological evaluation of the studied patients by MRI and Prevalence of Cardiac causes of stroke.

	Total (n=100)
Dilated LA	36 (36%)
LAA thrombus	4 (4%)
Diastolic Function Impairment	48 (48%)
LV tumor	4 (4%)
LV thrombus	8 (8%)
PFO	8 (8%)
Prevalence of Cardiac causes of stroke	24 (24%)

LA: left atrium, LAA: left atrial appendage, DD: diastolic dysfunction, LV: left ventricle, PFO: patent foramen ovale.

Table 3: MRI findings of the studied patients.

	Total (n=100)
LVSVI (mL/m ²)	43.96 ± 2.37
RVSVI (mL/m ²)	49.3 ± 4.54
LA volume (mL)	55.2 ± 5.6

MRI: magnetic resonant imaging, LVSVI: left ventricular stroke volume index, RVSVI: right ventricular stroke volume index.

Table 4: Agreement between CT and MRI brain of the patients

	Agreement
Kappa	0.342
P value	<0.001*
SE	0.072

CT: computed tomography, MRI: magnetic resonant imaging, SE: standard error, *: statistically significant as p value <0.05.

Case no 1:

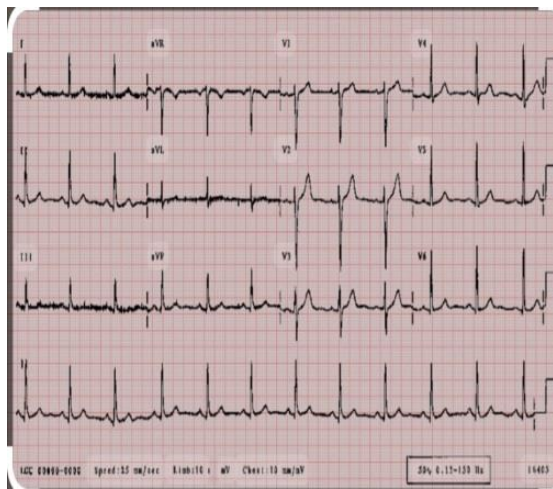
A 21-year-old female patient presented with a recent onset of right-sided weakness lasting 1 day. Initial diagnostic workup included: (A) a 12-lead surface ECG, which was performed to assess for arrhythmias; (B) CT and MRI of the brain to identify any acute ischemic lesions; (C) Cardiac MRI to evaluate for potential

cardiac sources of emboli; (D) Carotid duplex ultrasonography to rule out significant carotid artery disease; (E) Echocardiography to check for cardiac thrombi or structural abnormalities; and (F) CT chest to exclude pulmonary embolism or other thoracic pathologies.

Figure 1

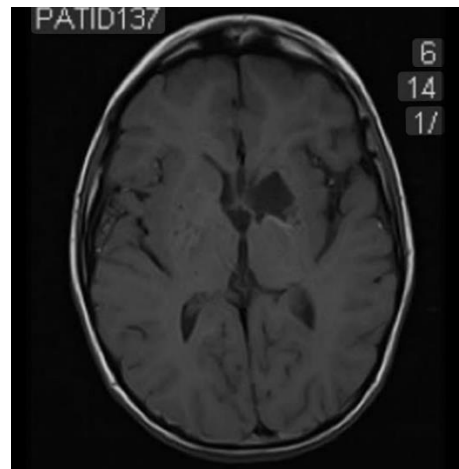
Case no1. (Figure 1)

A. 12 lead surface ECG: -



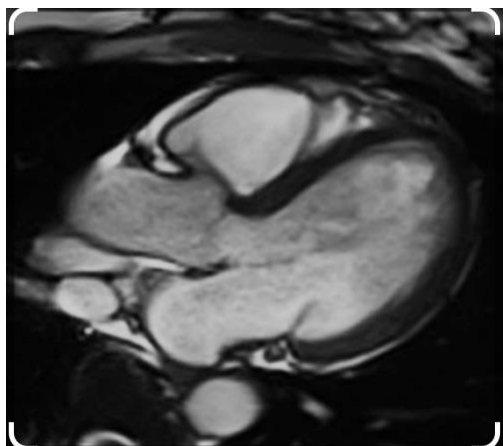
Revealed regular sinus, no ST segment deviation.

B. MRI brain



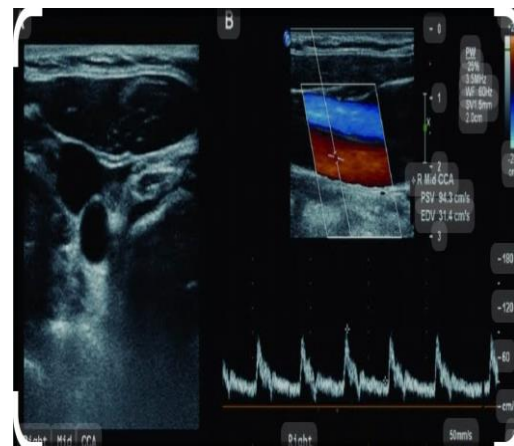
Revealed left sided hypodense area denoting stroke with no intracerebral hemorrhage

C. Cardiac MRI:-



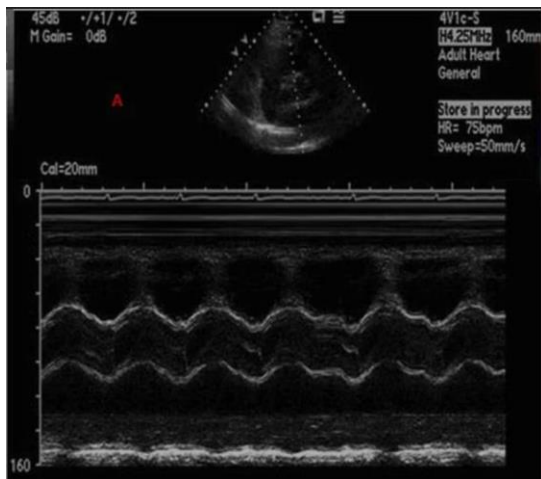
Revealed PFO with left to right shunt, LVEF= 55% , LVEDVI=70 ml/cm2, LVESVI=31 ml/cm2, RV EF= 60% ,RVEDVI=65 ml/cm2, RVESVI=34ml/cm2 , dilated LA = 4.2 cm , no SWMA.

D. Carotid duplex ultrasonography: -



Done bilateral & revealed normal flow with non-significant lesions.

E. Transthoracic Echocardiography: -



Full echo-doppler examination was performed and showed normal LV volumes (LVESV=53ml and LVEDV=95ml, EF = 60%) by Simpson method, no SWMA, normal diastolic function, mildly dilated LA = 4.1 cm.

F. CT CHEST: -



Shown normal findings.

Case no 2:

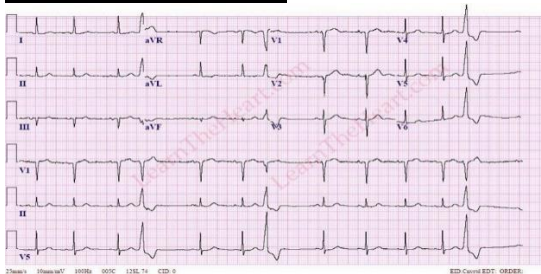
a 60-year-old male patient presented with left-sided motor weakness & sensory loss of eight hours duration with absent reflexes, normal function of the cranial nerves, and a normal state of consciousness, normal heart sounds and peripheral pulsations, he has uncontrolled diabetes & dyslipidemic, Initial diagnostic workup included: (A) a 12-lead surface ECG, which was performed to assess for

arrhythmias; (B) CT and MRI of the brain to identify any acute ischemic lesions; (C) Cardiac MRI to evaluate for potential cardiac sources of emboli; (D) Carotid duplex ultrasonography to rule out significant carotid artery disease; (E) Echocardiography to check for cardiac thrombi or structural abnormalities; and (F) CT chest to exclude pulmonary embolism or other thoracic pathologies.

Figure 2

Case no 2. (Figure 2)

A. 12 lead surface ECG:-



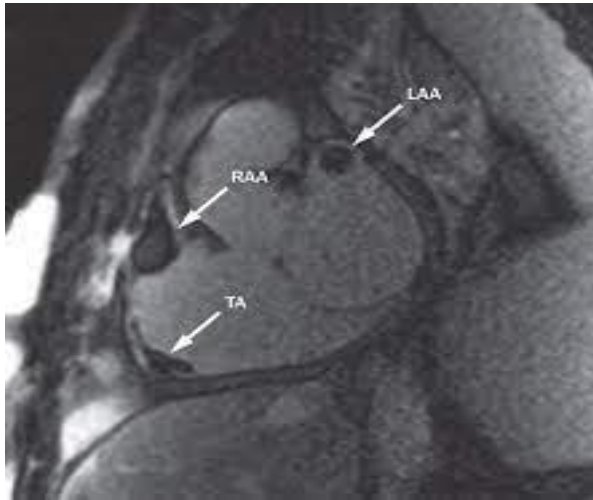
It had a steady sinus rhythm and multiple PVCs.

B. MRI brain



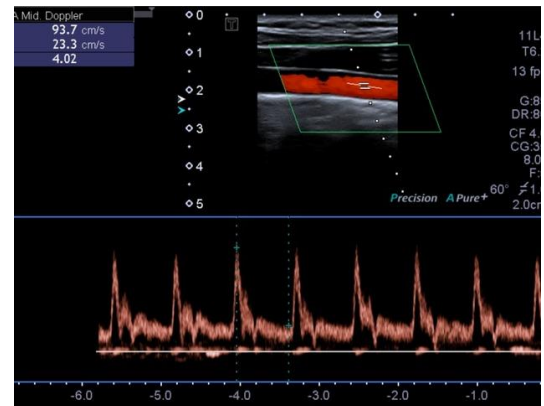
Shown RT sided hypodense area denoting stroke with no intracerebral hemorrhage.

C. Cardiac MRI: -



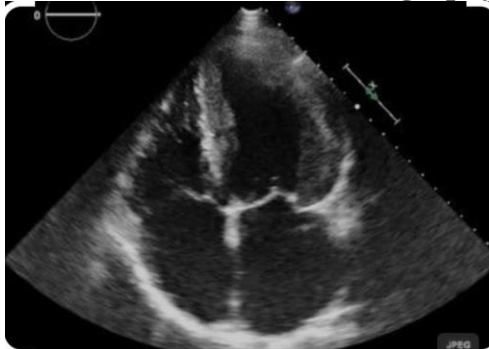
Shown dilated left atrium =4.5 cm, thrombus in LAA measuring 1.5 x1.3 cm , LVEF = 56% , LVEDVI=101 ml/cm² , LVESVI = 44 ml/cm² , RVEF = 60% , RVEDVI=64 ml/cm² , RVESVI=31 ml/cm² & LV desynchrony

D. Carotid duplex ultrasonography: -



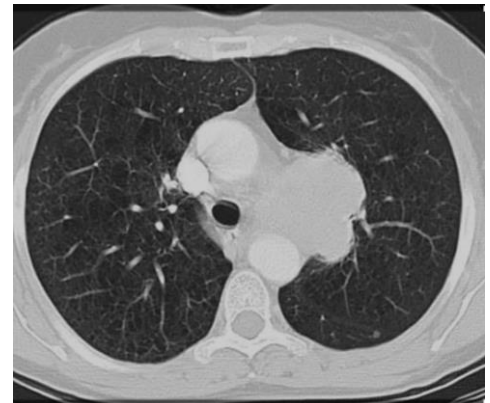
Done bilateral & revealed normal flow with non- significant lesions.

E. Transthoracic Echocardiography: -



Full echo-doppler examination was performed and showed normal LV volumes (LVESV =47 ml & LVEDV = 98 ml , EF= 56% BY Simpson method , no SWMA , Diastolic dysfunction grade I , dilated LA = 4.3 cm.

F. CT CHEST: -



Shown normal findings.

Discussion

Regarding the demographic data of the studied patients, we included 64 (64%) males and 36 (36%) females, their age ranged less than 30 to more than 60 years with a mean of 63.8 ± 13.1 years.

Similarly, Alanah et al., performed a study to assess the ischemic stroke risk factors and scales and included 359 patients and found that patients had a mean (standard

deviation) age of 67.8 (12.2) years and male predominance (56.2%)⁽⁶⁾.

In our study, the associated comorbidities among the studied patients, where 56 (56%) patients were diabetics, 52 (52%) patients were hypertensive, 36 (36%) patients had dyslipidemia, 76 (76%) patients had stroke and 24 (24%) patients had TIA.

In close proximity, Soliman et al. performed a study to assess the prevalence

of stroke risk factors and the possible relation between such risk factors and the disease severity at presentation in a sample of stroke patients presented to Beni-Suef University Hospital, north Upper Egypt including 167 patients of acute ischemic stroke and found that hypertension was detected in 104 patients (62.3%), dyslipidemia was detected in 79 patients (58.1%) and diabetes mellitus was detected in 58 patients (34.7%) with high prevalence of cardio-embolic risk factor ⁽⁷⁾.

In our study, the MRI assessment of left ventricular function showed that the LVEF ranged from 44 to 63 % with a mean of 54.6 ± 3.91 %. The LVEDVI ranged from 64 to 101 mL/m² with a mean of 82.6 ± 10.38 mL/m². The LVESVI ranged from 27 to 54 mL/m² with a mean of 37.8 ± 9.08 mL/m².

LVEF is particularly critical as it directly reflects ventricular function, with abnormal values indicating potential heart failure or cardiomyopathy, conditions known to elevate the risk of stroke and cardiovascular mortality. Similarly, LVEDVI and LVESVI offer insights into ventricular size and health, where elevated values may suggest pathological changes such as ventricular dilation or hypertrophy—common findings in chronic hypertension and valvular heart disease. Together, these indices enable clinicians to stratify patient risk, tailor treatments more effectively, and monitor disease progression or response to therapy, thereby serving as indispensable tools in the management of patients at risk for or recovering from ischemic events ⁽⁸⁾.

MRI assessment of right ventricular function showed that the RVEF ranged from 51 to 66% with a mean of 57.7 ± 3.83 %. The RVEDVI ranged from 60 to 84 mL/m² with a mean of 66.1 ± 6.4 mL/m². The RVESVI ranged from 22 to 35 mL/m² with a mean of 31.96 ± 3.15 mL/m².

RVEF indices are particularly significant in the clinical setting as they provide

insights into the volume load and pressure load conditions of the right ventricle. Increased volumes may indicate an adaptive response to increased pulmonary pressures or volume overload conditions such as tricuspid regurgitation or atrial septal defects ⁽⁹⁾.

In our study, 36 (36%) patients had dilated LA and 48 (48%) patients had DD impairment. The cardiac causes in the current study represented 24% of the studied cases; of them 4 (4%) patients had LAA thrombus, 4 (4%) patients had LV tumor, 8 (8%) patients had LV thrombus, and 8 (8%) patients had PFO.

Cardiological evaluation plays a crucial role in the comprehensive assessment of patients following ischemic stroke or transient ischemic attack (TIA). Conditions such as dilated left atrium (LA), left atrial appendage (LAA) thrombus, left ventricular (LV) tumors, LV thrombus, and patent foramen ovale (PFO) are particularly significant due to their potential to contribute to cardioembolic stroke ⁽¹⁰⁾.

Regarding the detected LV abnormalities, LV desynchrony was observed in 32 (32%) patients, LV dyskinesia was observed in 12 (12%) patients, LV akinesia was observed in 16 (16%) patients and LV scar was found in 16 (16%) patients.

Left ventricular (LV) abnormalities such as desynchrony, dyskinesia, akinesia, and scarring are closely associated with an increased risk of ischemic stroke. Studies have shown that these conditions can lead to impaired cardiac output and promote the formation of intracardiac thrombi due to abnormal myocardial motion and stasis of blood, particularly in areas adjacent to scar tissue or dysfunctional myocardium. For instance, LV desynchrony can exacerbate heart failure, which is known to reduce cerebral blood flow and contribute to the risk of cerebrovascular events ⁽¹¹⁾.

In our study, CT stroke was observed in 52 (52%) patients, and MRI stroke was observed in 84 (84%) patients.

MRI superiority in stroke detection can be attributed to its enhanced ability to visualize soft tissues and its sensitivity to changes in brain water content, which becomes altered early in ischemia. This makes MRI particularly effective in diagnosing acute and subacute strokes, and in providing detailed imaging of brain structures. Consequently, MRI is invaluable not only in confirming the diagnosis of stroke but also in determining the age of the stroke, which is essential for clinical decision-making, especially when considering interventions such as thrombolytic therapy⁽¹²⁾.

In our study, by MRI examination, the LVSVI ranged from 40 to 48 mL/m² with a mean of 43.96 ± 2.37 mL/m². The RVSVI ranged from 35 to 54 mL/m² with a mean of 49.3 ± 4.54 mL/m².

The MRI-derived ventricular volume indices such as LVSVI and RVSVI provide valuable insights into the mechanical efficiency of the heart. Evaluating these indices in stroke patients can help determine if a cardioembolic source is contributing to the stroke pathology, particularly in cases where the stroke's origin remains unclear. This approach underscores the necessity of integrating detailed cardiac assessment with neuroimaging in the comprehensive care of stroke patients, as cardiovascular health significantly impacts cerebral circulation and overall stroke risk⁽¹³⁾.

In our study, there was a significant weak (fair) agreement between CT and MRI.

MRI is a diagnostic tool sensitive enough to detect abnormalities in brain tissue and its environs. MRI has greater sensitivity and specificity in diagnosing acute ischemic stroke than CT scan. Approximately 80% of infarcts are detected within 24 hours. MRI can detect ischemic stroke within the first few hours of onset. MRI can differentiate between brain tissue at risk for infarction and brain tissue that has been damaged. Lacunar infarcts and brainstem infarcts can be identified by MRI, whereas CT scans have

difficulty due to the surrounding bone. The MRI examines the underlying pathology and is sensitive to small infarcts. Compared to CT scans, the use of MRI is still relatively uncommon at present. This is because MRI is not available in all medical facilities and the MRI examination is more time-consuming than CT scan⁽¹⁴⁾.

Conclusion

Our study utilized cardiac magnetic resonance imaging (CMR) to investigate the underlying cardiac sources in patients suffering from acute ischemic stroke or transient ischemic attack with unknown etiology. The data revealed various cardiac abnormalities such as left atrial enlargement, left atrial appendage thrombus, diastolic dysfunction, left ventricular tumors, thrombi, and patent foramen ovale, indicating a substantial prevalence of cardiac conditions that might contribute to stroke mechanisms. These findings underscore the importance of comprehensive cardiac evaluation in this patient population to better understand the cardioembolic sources of stroke, potentially leading to more targeted and effective treatment strategies.

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Author contribution

Authors contributed equally to the study.

Conflicts of interest

No conflicts of interest

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