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Original Paper

Cardiac Magnetic Resonance Imaging in Patients with Acute Ischemic Stroke and Elevated Troponin: A TRoponin ELevation in Acute Ischemic Stroke (TRELAS) Sub-Study

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Keywords
Magnetic resonance imaging · Stroke · Acute coronary syndrome · Coronary angiography

Abstract
Background: Elevated high-sensitive cardiac troponin (hs-cTn) can be found in more than 50% of the patients with acute ischemic stroke. The observational TRoponin ELevation in Acute ischemic Stroke (TRELAS) study revealed that about 25% of all stroke patients with elevated troponin had a coronary angiography-detected culprit lesion affording immediate intervention, and about 50% of all patients did not have any obstructive coronary artery disease. Given the risk of procedure-related complications, the identification of stroke patients in urgent need of invasive coronary angiography is desirable. ***Methods:*** TRELAS patients were prospectively enrolled into this sub-study. In addition to conventional coronary angiography,

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a cardiac magnetic resonance imaging (MRI) at 3T was performed during the in-hospital stay after acute ischemic stroke to compare the diagnostic value of both imaging modalities. ***Results:*** Nine stroke patients (median age 73 years [range 58–87]; four females; median NIH Stroke Severity score on admission 4 [range 0–6] with elevated hs-cTnT [median 74 ng/L, interquartile range 41–247] on admission) completed cardiac MRI and underwent coronary angiography. The absence of MRI-detected wall motion abnormalities and/or late gadolinium enhancement in 5 stroke patients corresponded with the exclusion of culprit lesions or significant coronary artery disease by coronary angiography. Four patients had abnormal MRI findings, whereof 2 showed evidence of myocardial infarction and in whom coronary angiography demonstrated a >70% stenosis of a coronary artery. ***Conclusions:*** The TRELAS substudy indicates that noninvasive cardiac MRI may provide helpful information to identify stroke patients with or without acute coronary syndrome. Our findings might help to select stroke patients in urgent need of coronary angiography.

Introduction

In more than 50% of all patients with acute ischemic stroke, high-sensitive cardiac troponin (hs-cTn) is above the cutoff to rule out myocardial infarction [1]. The recently published prospective observational TRoponin ELevation in Acute ischemic Stroke (TRELAS) study revealed that patients with acute ischemic stroke and elevated hs-cTnT were significantly less likely to have coronary culprit lesions than age- and gender-matched patients with non-ST-elevation acute coronary syndrome [2]. Overall, about 25% of all TRELAS patients had a coronary culprit lesion, whereas about 50% did not have any obstructive coronary artery disease (CAD). While conventional coronary angiography is the gold standard to detect CAD, the required periprocedural application of heparin – increasing the risk of hemorrhagic transformation – exposure to radiation, procedure-related complications as well as the needed dual antiplatelet therapy after coronary intervention limit the feasibility in the acute phase of ischemic stroke. While noninvasive cardiac computed tomography could add information about underlying CAD [3], the disadvantage of exposure to radiation is also present. Subsequently, assessment of an underlying CAD is often incomplete in patients with acute ischemic stroke in clinical practice. Cardiac magnetic resonance imaging (MRI) is now considered the gold standard to assess cardiac tumors, myocarditis, cardiomyopathies, and subclinical coronary heart disease [4]. Feasibility and safety of noninvasive cardiac MRI in patients with acute ischemic stroke has already been demonstrated. However, routine use of cardiac MRI is limited due to the necessity to follow breath-hold instructions and by the restricted availability of cardiac MRI [5]. This study aimed at comparing the diagnostic value of cardiac MRI compared to coronary angiography in patients with acute ischemic stroke and elevated hs-cTn.

Materials and Methods

The design of the investigator-initiated, prospective observational TRELAS study was published previously [2, 6]. The review board of the Charité approved the TRELAS study protocol and the prospective MRI sub-study. All subsequent TRELAS patients at the Charité were asked to join the sub-study. After providing written informed consent, 24 patients admitted within 72 h after stroke onset and in-hospital hs-cTnT >50 ng/L (Roche, Mannheim, Germany) underwent diagnostic coronary angiography. Patients with creatinine ≥1.2 mg/dL,

Table 1. Baseline characteristics, stroke localization, troponin levels (hs-cTnT), and ECG findings in 9 stroke patients of the TRELAS sub-study

Sex	Age, years	Stroke localization	NIHSS admission	Cardiovascular risk factors	Known CAD	hs-cTnT admission	hs-cTnT follow-up	Pathological ECG findings on admission
M	71	multiple arteries	0	AHT, HC, smoking	no	66 ng/L	60 ng/L	none
F	82	multiple arteries	5	AF, AHT, HC	no	13 ng/L	535 ng/L	signs of ischemia
F	71	PCA left	2	AF, AHT, HC	no	510 ng/L	520 ng/L	AF
M	87	MCA/PCA right	4	AF, AHT, HC	yes	20 ng/L	76 ng/L	AF, signs of ischemia
M	73	MCA/ACA left	6	AHT	no	74 ng/L	69 ng/L	none
F	75	BA	3	AHT, HC	no	95 ng/L	128 ng/L	none
M	58	multiple arteries	4	AF, AHT, HCM	no	144 ng/L	146 ng/L	signs of ischemia, LV hypertrophy
M	69	MCA left	4	smoking	yes	61 ng/L	34 ng/L	LSB
F	79	multiple arteries	1	AF, AHT, HC, diabetes	no	347 ng/L	518 ng/L	none

AHT, arterial hypertension; HC, hypercholesterolemia; AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; LV, left ventricular; LSB, least significant bit; PCA, posterior cerebral artery; MCA, middle cerebral artery; ACA, anterior cerebral artery; BA, basilar artery.

modified Rankin scale ≥4 before admission, or ST-elevation at baseline echocardiography (ECG) were not enrolled. Nine stroke patients provided informed consent to undergo cardiac MRI at 3T (Magnetom Tim Trio; Siemens AG, Erlangen, Germany) as described previously [5]. ECG-gated images were acquired during breath hold using a phased array receiver coil (Body Matrix-coil#TATS; Siemens AG). Cine images of three long-axis as well as 14–18 short-axis views using an ECG-gated gradient-echo sequence were acquired. Approximately 10 min after intravenous administration of 0.15 mmol/kg bodyweight Gadobutrol (Gadovist®; Bayer HealthCare, Leverkusen, Germany) at a concentration of 1 mmol/mL, an inversion recovery gradient-echo sequence was acquired in corresponding long-axis and short-axis slices adjusting the inversion time to null normal myocardium. Blinded cardiac MRI reading was done by a board-certified cardiologist (C.J.) specialized in cardiac MRI. Data were summarized with absolute and relative frequencies of qualitative characteristics or medians and interquartile range (IQR) for quantitative variables.

Results

The median age of the 9 stroke patients undergoing cardiac MRI was 73 years (range 58–87), four were female. The median NIH Stroke Severity (NIHSS) score on admission was 4 (range 0–6), 3 patients had a history of CAD (Table 1). Additional information can be found in Table 2, also including data of the 15 TRELAS patients who either rejected or were unable to undergo cardiac MRI. Besides a higher median creatine kinase on admission in patients undergoing additional MRI, univariate analysis revealed no differences between both patient groups.

All 9 stroke patients completed the cardiac MRI as well as coronary angiography during the in-hospital stay. The median delay between hospital admission and cardiac MRI or coronary angiography was 83 h (IQR 68–106) or 71 h (IQR 45–89), respectively. In 5 stroke patients, combined analysis of wall motion and late gadolinium enhancement showed no substantial findings (Table 3). Correspondingly, no significant (>70%) coronary artery stenosis was detected by coronary angiography. Four stroke patients had abnormal MRI

Table 2. Baseline characteristics of TRELAS patients with or without cardiac MRI (adapted from [2])

	Cardiac MRI (n = 9)	No cardiac MRI (n = 15)	p
Median age (IQR), years	73 (70–81)	77 (64–82)	0.770
Male sex	55.6 (5)	60.0 (9)	1.0
Median NIHSS score (IQR)	3 (2–4)	3 (3–4)	0.411
Median GRACE score (IQR)	118 (98–145)	113 (83–148)	0.770
Cardiovascular risk factors			
Diabetes mellitus	22.2 (2)	26.7 (4)	1.0
Hypercholesterolemia	77.8 (7)	46.7 (7)	0.210
Hypertension	100 (9)	86.7 (13)	0.511
Previous stroke	33.3 (3)	13.3 (2)	0.326
Current smoking	22.2 (2)	13.2 (2)	0.615
Atrial fibrillation	55.6 (5)	46.7 (7)	1.0
Chronic heart failure	22.2 (2)	26.7 (4)	1.0
History of CAD	22.2 (2)	20.0 (3)	1.0
Laboratory measures at baseline			
Median hs-cTn levels (IQR), ng/L	74 (41–247)	85 (44–167)	1.0
Median creatinine kinase (IQR), mg/dL	166 (117–1540)	86 (61–147)	0.025
Median creatinine (IQR), mg/dL	1.03 (0.79–1.12)	0.97 (0.88–1.12)	0.907
Median GFR (IQR), mL/min/1.73 m^2	72 (63–76)	71 (59–85)	0.907
Killip class			0.172
1	88.9 (8)	80.0 (12)	
2	0 (0)	20.0 (3)	
3	11.1 (1)	0 (0)	
Medication before admission			
Prior antiplatelet use	44.4 (4)	53.3 (8)	1.0
Prior oral anticoagulation	11.1 (1)	6.7 (1)	1.0
Prior statin use	44.4 (4)	20.0 (3)	0.356
Prior use of beta-blockers	33.3 (3)	38.5 (5)	1.0

Values are presented as % (n), unless otherwise indicated. GRACE, Global Registry of Acute Coronary Events; GFR, glomerular filtration rate estimated according to the CKD-EPI formula.

findings, whereof 2 patients showed evidence of myocardial infarction. In both patients, coronary angiography demonstrated pathological findings, including a >70% stenosis of a corresponding coronary artery requiring stenting. Apical ballooning (stress cardiomyopathy) and a reduced cardiac ejection fraction was found in a single stroke patient by both imaging modalities. One patient showed nonischemic late gadolinium enhancement pathognomonic for hypertrophic cardiomyopathy (Table 3).

Discussion

This is the first prospective evaluation comparing the diagnostic value of 3-T cardiac MRI to coronary angiography in acute ischemic stroke patients with elevated hs-cTn. The exclusion of significant CAD by coronary angiography corresponded well with the absence of pathological MRI findings. Therefore, the assumption that cardiac MRI may help identify patients with or without need of invasive evaluation for CAD in the acute phase of ischemic stroke should be validated in a larger prospective study.

By providing information on myocardial infarction, cardiac MRI also appears to have a complementary diagnostic value to past medical history, laboratory results, echocardiog-

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Table 3. Imaging findings in 9 stroke patients undergoing cardiac MRI and coronary angiography (CA)

Sex	Age, years	Cardiac MRI – pathological findings (segments)	Cardiac MRI WMA	MRI EF	Cardiac MRI – late gadolinium enhancement	CA – pathological findings (culprit lesion: yes/no)	LVA WMA	LVA EF	Echo – pathological findings
M	71	none	none	normal	no	none (no)	none	normal	none
F	82	stress CM	apical ballooning	reduced	no	stable lesions in RIVA and RCX ~70% stenosis (no)	apical	severely reduced	EF reduced
F	71	none	none	normal	no	none (no)	none	normal	–
M	87	ischemic CM, hypokinesis and thinned wall (5, 7, 12, 13, 16, 17)	anterior mid-ventricular, apical (RIVA), basal inferolateral (RCX)	severely reduced	transmural anterior mid-ventricular and apical (RIVA), basal inferolateral (RCX)	stable lesions RIVA and RCX ~80% stenosis, CTO RCA; BG (yes)	global	severely reduced	–
M	73	none	none	normal	no	stable peripheral lesion RCX ~50% stenosis (no)	none	normal	none
F	75	none	none	normal	no	stable lesion RCA ~50% stenosis (no)	none	normal	–
M	58	HCM	none	normal	nonischemic	none (no)	none	normal	HCM
M	69	none	none	normal	no	RIVA and RCA stents (no)	none	normal	none
F	79	ischemic CM, hypokinesis and thinned wall (7, 8, 13, 14)	anterior and anterolateral (RIVA)	reduced	transmural mid-ventricular to apical anterior and anterolateral	CTO in RCA,RCX with ~80% stenosis (yes)	anterior	reduced	none

WMA, wall motion abnormalities; EF, ejection fraction: severely reduced <40%, reduced 40–65%, normal >65%; LAV, left ventricular angiography; CM, cardiomyopathy; HCM, hypertrophic cardiomyopathy; RIVA, ramus interventricuaris anterior; RCX, ramus circumflexus; RCA, right coronary artery; CTO, chronic total occlusion; BG, bypass graft.

raphy, and ECG parameters in the assessment of acute coronary syndrome in stroke patients. However, cardiac MRI requires active patient cooperation, which cannot always be achieved in the acute phase of stroke [5] (Table 2).

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Statement of Ethics

The Ethics Committee of the Charité – Universitätsmedizin Berlin approved the TRELAS study protocol and the prospective MRI sub-study.

Disclosure Statement

K.G.H. reports honoraria from Bayer Healthcare, Sanofi, Pfizer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Medtronic, Biotronik, W. L. Gore & Associates, and Edwards Lifesciences. C.J. reports lecture fees by Bayer Healthcare, Abbott Germany and Biotronik Germany, and research support by Novartis. J.F.S. reports lecture fees by W.L. Gore & Associates. J.B.F. has received honoraria from Perceptive, BioClinica, Boehringer Ingelheim, Cerevast, Brainomix, and Lundbeck. H.J.A. has received a grant from Pfizer, honoraria from Boehringer Ingelheim, Bayer Healthcare, Sanofi, Daiichi-Sankyo, Pfizer, Bristol-Myers Squibb, Novo Nordisk, and EVER Neuropharma. C.H.N. reports honoraria from Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer, Sanofi, and W.L. Gore & Associates. M.E. reports grant support and/or fees paid to the Charité from Bayer, Boehringer Ingelheim, BMS/Pfizer, Daiichi Sankyo, Amgen, Sanofi, Covidien GSK, Ever, and Novartis, all outside the submitted work. H.-C.M. reports honoraria from Bayer Healthcare, Sanofi, Pfizer, and Daiichi Sankyo.

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