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 sub-study 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. © 2019 The Author(s) Published by S. Karger AG, Basel

**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,
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

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**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                         | 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.
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, echocardiography,

### 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  | 103 (0.79–1.12)     | 97 (0.88–1.12)          | 0.907|
| Median GFR (IQR), mL/min/1.73 m²| 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.
| Sex | Age, years | Cardiac MRI – pathological findings (segments) | Cardiac MRI – late gadolinium enhancement | CA – pathological findings (culprit lesion: yes/no) | CA – pathological findings (culprit lesion: yes/no) | LVA WMA | LVA EF | Echo – pathological findings |
|-----|------------|-----------------------------------------------|------------------------------------------|-----------------------------------------------|-----------------------------------------------|--------|--------|--------------------------------|
| M   | 71         | none                                          | none                                     | none (no)                                     | apical ballooning                              | normal | normal | none (no)                                      |
| F   | 82         | stress CM                                     | apical ballooning                         | reduced, no                                   | none                                           | normal | normal | normal                                        |
| F   | 71         | ischemic CM, hypokinesis and thinned wall (5, 7, 12, 13, 16, 17) | anterior mid-ventricular, apical (RIVA), basal inferolateral (RCX) | no                                             | none                                           | normal | normal | none (no)                                     |
| M   | 87         | ischemic CM, hypokinesis and thinned wall      | anterior mid-ventricular, apical (RIVA), basal inferolateral (RCX) | no                                             | no                                             | normal | normal | normal                                        |
| M   | 73         | none                                          | none                                     | nonischemic                                   | none                                           | normal | normal | HCM                                           |
| F   | 75         | none                                          | none                                     | RIVA and RCA stents (no)                      | none                                           | normal | normal | none                                           |
| M   | 58         | HCM                                            | none                                     | none (no)                                     | none                                           | normal | normal | none                                           |
| F   | 69         | ischemic CM, hypokinesis and thinned wall (7, 8, 13, 14) | transmural mid-ventricular to apical anterior and anterolateral | RIVA and RCA stents (no)                      | none                                           | normal | normal | none                                           |
| F   | 79         | ischemic CM, hypokinesis and thinned wall (7, 8, 13, 14) | transmural mid-ventricular to apical anterior and anterolateral | CTO in RCA,RCX with ~80% stenosis (yes)        | anterior                                       | reduced | none   | 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 interventricularis 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 research 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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