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MYOCARDIAL ISCHEMIA AND INFARCTION

Safety of Adenosine Stress Magnetic Resonance Imaging Using a Mobile Cardiac Magnetic Resonance System

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ABSTRACT

Background: **Contrast-enhanced magnetic resonance imaging (ceMRI) allows for the detection of ischemic heart disease. Aim of this prospective study was to show feasibility, practicability and safety of adenosine stress ceMRI in routine outpatients with a mobile scanner.** ***Methods:*** **Consecutive patients were scanned in six different cardiac outpatient centers with a 1.5 T mobile ceMRI scanner. First-pass wash-in patterns of gadolinium chelate were evaluated after three minutes of adenosine infusion. After a second bolus of gadolinium chelate myocardial late enhancement (MLE) images of the left ventricle were acquired to visualize myocardial necrosis.** ***Results:*** **Five hundred seventy-four patients were enrolled to the study. No major complications during examination and adenosine infusion were observed. One hundred seventy-three minor complications as temporary atrio-ventriculare blockade, mild chest pain or dyspnea and nausea were noticed. None of the complications led to further special treatment** ***Conclusion:*** **This ceMRI protocol is suitable for application in outpatient settings. CeMRI stress testing using a mobile scanner in an outpatient setting is feasible and safe.**

INTRODUCTION

Diagnosis and evaluation of ischemic heart disease is mandatory for guiding further treatment. Commonly used stress testings prior to invasive coronary artery (CA) angiography in routine outpatients are stress electrocardiography and echocardiography. These diagnostic methods do not provide direct information about myocardial perfusion. Positron emission and single photon emission computed tomography on the other hand suffer from attenuation artifacts and limited spatial resolution (1–3). Several studies have shown that contrast-enhanced magnetic resonance imaging (ceMRI) with pharmacologically provoked stress has a higher spatial and temporal resolution and is suitable to answer the question of myocardial perfusion with a high sensitivity and specificity (4–7). Furthermore, ceMRI provides information about myocardial viability which is necessary for further therapy decision (7–12). However, there is little knowledge about the practicability and safety of adenosine stress ceMRI in outpatients, especially regarding with examinations of patients from different centers with a single mobile ceMRI scanner.

The aim of our study was to demonstrate the feasibility, practicability and safety of stress perfusion ceMRI in a multi-center outpatient setting with one mobile ceMRI machine.

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METHODS

Study population

We prospectively enrolled consecutive patients from six German outpatient centers with suspected ischemic heart

disease over the period of 12 months. Patients with unstable angina or myocardial infarction or CA revascularization within the last six months, higher degree of heart valve disease, higher degree of atrio-ventricular blocks, acute myocarditis, internal pacemaker or defibrillator, and inability to give written informed consent were excluded from the study. Local ethical committees in Berlin and ethic committess of the medical associations responsible for the locations where CMR examinations were performed approved the study protocol. Written informed consent was obtained from all patients.

Study protocol

All patients were examined clinically and cardiovascular risk factors were assessed. A 12-lead surface ECG was obtained in each patient. Arterial blood pressure, heart rate and oxygen saturation were monitored non-invasively during adenosine infusion. All patients had to stop antianginal medication 24 hours and caffeinated food or beverages and 48 hours before examination. Mild sedation with midazolame (1 mg) was offered in case of anxiety or claustrophobia.

Magnetic resonance examination

All ceMRI studies were performed with a 1.5 Tesla whole-body system (Signa TwinSpeed, GE Medical System, Milwaukee, USA) with a 4-element phased array surface coil (Cardiac coil, GE Medical Systems) assembled on a trailer (Figs. 1 and 2) (13.65 m length, 2.6 m width, 4.00 m height, 37 t weight). All studies were performed by special trained technical assistants, and at each center, a trained cardiologist was present during the examination. Each of the cardiac outpatient centers examined their consecutive patients once a month. All of the following sequences were performed in end-expirational breath-hold. Functional imaging with steady-state free precession sequences were acquired in three long axis and in contiguous short axis orientation to cover the left ventricle from the basis to the apex (TR 5.1 ms, TE 2.2 ms, flip angle 60°, matrix 256 × 192, slice thickness 8 mm, no interslice gap, field of view 32–34 × 32–34 cm). After three minutes of adenosine-infusion at a constant rate of 140 μg/kg body-weight, gadoteric acid (Omniscan®, Amersham Health, Germany) was injected

Figure 1. Trailer transporting the MRI system.

Figure 2. Trailer interior—MRI setting.

(0.1 mmol/kg body weight) during a first pass perfusion sequence using a hybrid gradient echo/echo-planar pulse sequence (TR automatically adjusted, TE 1.3 ms, flip angle 25°, slice thickness 8 mm, matrix 128 × 96, field of view 32–34 × 24–25.5 cm, every RR-Interval), and images in 5 continuous short axis orientations were acquired. Adenosine-infusion was stopped after the perfusion sequence. Ten minutes after intravenous injection of a second bolus of 0.1 mmol/kg body-weight gadoteric acid, inversion-recovery gradient-echo sequences were acquired (TR 7.1 ms, TE 3.2 ms, flip angle 20°, TI 180–240 ms, slice thickness 8 mm, no interslice gap, matrix 256 × 160, field of view 32–34 × 32–34 cm) for myocardial late enhancement visualization. Contiguous slices in short axis orientation from the basis to the apex of the left ventricle were acquired. All side effects and complications during and one hour after adenosine infusion were recorded correspondingly.

CeMRI analysis

Two investigators examined all ceMRI studies. Analysis of the images was performed with the standard software provided by the manufacturer of the MRI system (Advantage Workstation, GE Medical System). Left ventricular ejection fraction and left ventricular mass were calculated using the short axis data of the steady-state free precession sequences (13). Qualitative assessment of the perfusion images using the 16-segments model of AHA (14) was performed. All segments were evaluated for hypoperfusion during first-pass perfusion. Areas of perfusion deficits were assigned to the corresponding coronary artery using the model of AHA (14). Analysis of myocardial late enhancement was performed visually. Bright areas, regarded as non-viable fibrotic tissue were assessed using above mentioned 16-segments mode.

RESULTS

Five hundred ninety-five patients were screened for enrollment to the study. Twelve patients were excluded due to unstable angina and 9 due to heart valve disease. All patients gave written

Table 1. Complications during adenosine infusion

	All patients (n = 574)
Temporary atrio-ventriculare blockade	64 (11%)
Mild chest pain and/or dyspnea	78 (14%)
Emesis	4 (1%)
Nausea	27 (5%)

informed consent. Five hundred seventy-four patients formed the study group. Seven patients (1.2%) had claustrophobia and were offered mild sedation. In all of latter mentioned patients, ceMRI study could be completed.

Magnetic resonance examination

Adenosine-stress ceMRI could be performed in all patients. No patient experienced a major complication. Temporary atrioventricular blockade during adenosine infusion could be observed in 64 (11%) patients, 78 (14%) patients reported of mild chest pain and/or dyspnea, and 31 (5%) patients suffered from emesis or nausea (Table 1). All minor complications resolved within a few minutes and did not lead to further special therapy.

Image quality was sufficient for further analysis in all patients. However, not all patients were able to perform breathhold for the entire first-pass perfusion sequence. Consequently, image quality in these patients was reduced but still diagnostic. Accurate assessment was not possible in one case due to reduced image quality. Interobserver agreement was very high ($\kappa = 0.94$).

Procedure length for the compiled ceMRI protocol was 27 ± 8 minutes including adenosine-stress testing.

DISCUSSION

This study is the first to report an integrated ceMRI protocol for the assessment of myocardial perfusion, and myocardial viability that has been evaluated for its practicability and safety in a multi-center outpatient setting with a mobile ceMRI scanner. Feasibility and safety of the underlying protocol was demonstrated in 574 outpatients. No major complications and only few minor complications resolving within minutes after examination were observed.

Aim of our study was not demonstrate the ability of ceMRI to visualize extent and location of hypoperfusion and/or nonviable myocardial tissue as these diagnostic aspects have been answered extensively by previous studies. Advantages of ceMRI over all other available techniques are high spatial and temporal resolution without anatomical limitations and the ability to cover the entire left ventricle in reproducible slice orientations (1–3, 5, 13). Measurement of MLE with a fixed instead of an individually adjusted inversion time as in our protocol has been also published to be suitable to detect fibrosis safely but with slightly reduced image quality in previous studies (15–18).

Feasibility and practicability of ceMRI in an outpatient setting was proven in only one recently published study demonstrating a practicable ceMRI approach in an outpatient setting showing ceMRI to be a competitive method to radionuclide ventriculography and echocardiography in terms of procedure length and reproducibility (19). Efficiency of their ceMRI clinic was demonstrated in 64 patients with heart failure and concluded that ceMRI can provide a rapid and reproducible assessment of cardiac function in those patients. However, in their study only cardiac function was assessed and procedure time still was 42 ± 4 min compared to 27 ± 8 minutes in our study. Myocardial perfusion and viability were not assessed.

In contrast, our study focused on the detection of inducible ischemia in patients with suspected or known ischemic heart disease. Our study protocol allows for the assessment of multiple aspects of ischemic heart disease in outpatients in one single compiled examination. Information about cardiac function, myocardial perfusion and viability was given in all patients which is necessary for guiding further treatment in these patients.

CONCLUSIONS

Our compiled protocol for diagnosis of ischemic heart disease with a mobile ceMRI scanner in a multi-center outpatient population is a practicable and safe approach. Adenosine-stress ceMRI could be thus used in outpatient centers complementary or as a surrogate for other stress testings without complications.

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ABBREVIATIONS

CA Coronary Artery
ceMRI Contrast-enhanced Magnetic Resonance Imaging

REFERENCES

1. Hendel RC, Berman DS, Cullom SJ Follansbee W, Heller GV, Kiat H, Groch MW, Mahmarian JJ. Multicenter clinical trial to evaluate the efficacy of correction for photon attenuation and scatter in SPECT myocardial perfusion imaging. Circulation 1999;99:2742–49.
2. Kuhle WG, Porenta G, Huang SC, Buxton D, Gambhir SS, Hansen H, Phelps ME, Schelbert HR. Quantification of regional myocardial blood flow using 13N-ammonia and reoriented dynamic positron emission tomography imaging. Circulation 1992;86:1004–17.
3. Hutchins GD, Schwaiger M, Rosenspire KC, Krivokapich J, Schelbert H, Kuhl DE. Noninvasive quantification of regional blood flow in the human heart using N-13 ammonia and dynamic positron emission tomography imaging. J Am Coll Cardiol 1990;15:1032–42.
4. Keijer JT, van Rossum AC, Wilke N, van Eenige MJ, Jerosch-Herold M, Bronzwaer JG, Visser CA. Magnetic resonance imaging of myocardial perfusion in single-vessel coronary artery disease: implications for transmural assessment of myocardial perfusion. J Cardiovasc Magn Reson 2000;2:189–200.
5. Schwitter J, Nanz D, Kneifel S, Bertschinger K, Buchi M, Knusel PR, Marincek B, Luscher TF, von Schulthess GK. Perfusion in coronary artery disease by magnetic resonance: a comparison

with positron emission tomography and coronary angiography. Circulation 2001;103:2230–5.
6. Ishida N, Sakuma H, Motoyasu M, Okinaka T, Isaka N, Nakano T, Takeda K. Noninfarcted myocardium: correlation between dynamic first-pass contrast-enhanced myocardial MR imaging and quantitative coronary angiography. Radiology 2003;229:209–16.
7. Chiu CW, So NM, Lam WW, Chan KY, Sanderson JE. Combined first-pass perfusion and viability study at MR imaging in patients with non-ST segment-elevation acute coronary syndromes: feasibility study. Radiology 2003;226:717–22.
8. Klein C, Nekolla SG, Bengel FM, Momose M, Sammer A, Haas F, Schnackenburg B, Delius W, Mudra H, Wofram D, Schwaiger M. Assessment of myocardial viability with contrast-enhanced magnetic resonance imaging: comparison with positron emission tomography. Circulation 2002;105:162–7.
9. Wagner A, Marholdt H, Holly TA, Elliott MD, Regenfus M, Parker M, Klocke FJ, Bonow RO, Kim RJ, Judd RM. Contrast-enhanced MRI and routine single photon emission computed tomography (SPECT) perfusion imaging for detection of subendocardial myocardial infarcts: an imaging study. Lancet 2003;361:374–9.
10. Kim RJ, Fieno DS, Parish TB, Harris K, Chen EL, Simonetti O, Bundy J, Finn JP, Klocke FJ, Judd RM. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002.
11. Wu E, Judd RM, Vargas JD, Klocke FJ, Bonow RO, Kim RJ. Visualisation of presence, location, and transmural extent of healed Q-wave and non-Q-wave myocardial infarction. Lancet 2001;357:21–8.
12. Rehwald WG, Fieno DS, Chen EL, Kim RJ, Judd RM. Myocardial magnetic resonance imaging contrast agent concentrations after reversible and irreversible ischemic injury. Circulation 2002;105:224–9.
13. Bellenger NG, Burgess MI, Ray SG, Lahiri A, Coats AJS, Cleland JGF, Pennell DJ. Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance. Eur Heart J 2000;21:1381–96.
14. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105: 539–42.
15. Petersen SE, Mohrs OK, Horstick G, Oberholzer K, Abegunewardene N, Ruetzel K, Selvanayagam JB, Robson MD, Neubauer S, Thelen M, Meyer J, Kreitner KF. Influence of contrast agent dose and image acquisition timing on the quantitative determination of nonviable myocardial tissue using delayed contrast-enhanced magnetic resonance imaging. J Cardiovasc Magn Reson 2004;6:541–8.
16. Kramer CM, Rogers WJ, Mankad S, Theobald TM, Pakstis DL, Hu YL. Contractile reserve and contrast uptake pattern by magnetic resonance imaging and functional recovery after reperfused myocardial infarction. J Am Coll Cardiol 2000;36:1835–40.
17. Ansari M, Araoz PA, Gerard SK, Watzinger N, Lund GK, Massie BM, Higins CB, Saloner DA. Comparison of late enhancement cardiovascular magnetic resonance and thallium SPECT in patients with coronary disease and left ventricular dysfunction. J Cardiovasc Magn Reson 2004;6:549–56.
18. Grebe O, Paetsch I, Kestler HA, Herkommer B, Schnackenburg B, Hombach V, Fleck E, Nagel E. Optimal acquisition parameters for contrast enhanced magnetic resonance imaging after chronic myocardial infarction. J Cardiovasc Magn Reson 2003;5:575–87.
19. Bellenger NG, Francis JM, Davies CL, Coats AJ, Pennell DJ. Establishment and performance of a magnetic resonance cardiac function clinic. J Cardiovasc Magn Reson 2000;2:15–22.