Workflow Optimization for CMR Adenosine Stress Perfusion in Clinical Routine

Giso v. der Recke, M.D.; David Hardung, M.D.; Heyder Omran, M.D.

St.-Marien-Hospital, Dept. of Cardiology, Bonn, Germany

Introduction

Adenosine stress perfusion cardiac magnetic resonance (CMR) has been demonstrated to provide reliable information about relevant myocardial ischemia [1, 2, 3]. In stable patients with suspected coronary artery disease, this method offers high diagnostic accuracy for identifying patients that benefit from coronary revascularisation [4]. Furthermore it has been shown that the negative predictive value for an event free follow-up is excellent [5, 6, 7]. Cardiac adverse events are extremely rare during adenosine administration. Due to the very short half-life of adenosine, stress CMR can be performed without extended patient monitoring [8].

Besides academic considerations concerning diagnostic accuracy; patient acceptance, cost and time efficiency, as well as convenience for the investigator, are also important for routine clinical application. In this outline we provide tips and tricks for improving performance of a cardiac MR unit with a focus on stress perfusion MRI based on our experience.

Logistics and patient preparation

A team of two trained technologists and one physician can efficiently operate a CMR unit in a high volume setting.

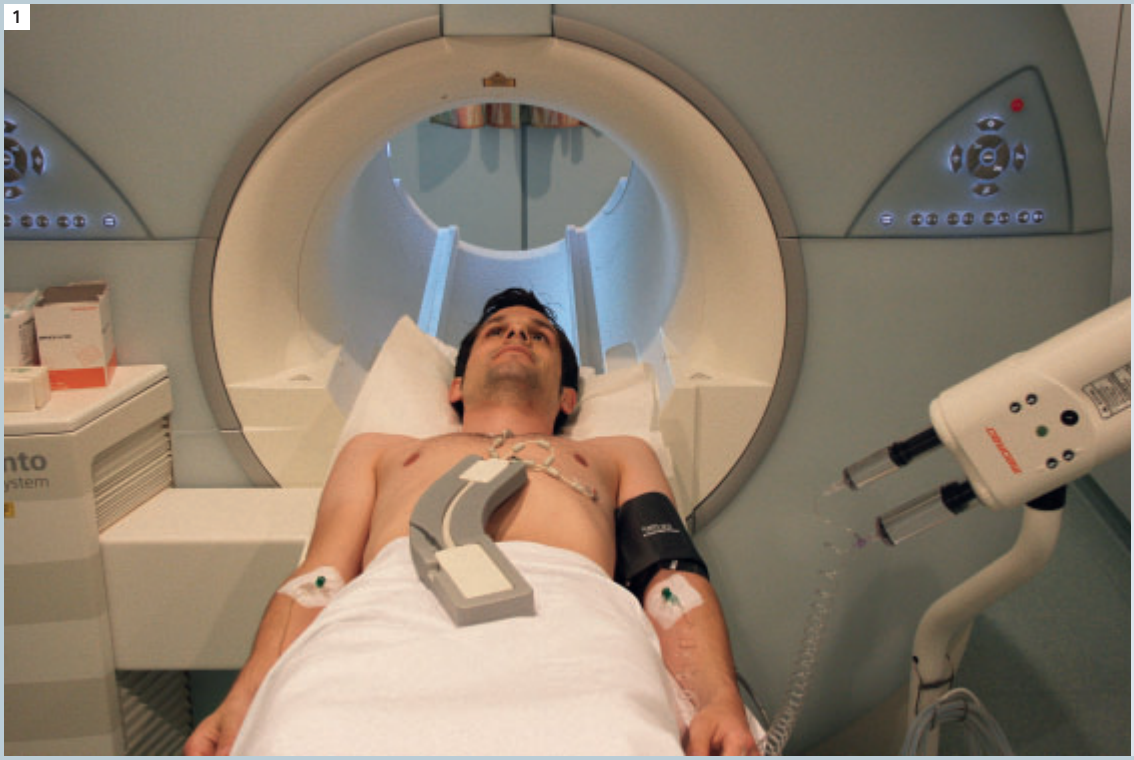
24 hours prior to the investigation patients have to refrain from caffeine (e.g. coffee, tea, cacao, energy drinks) and drugs (e.g. xanthines/theophylline, nitrates) that could alter the response to adenosine. Thus, a checklist of precautions should be handed over to the patient together with the written informed consent as early as possible.

Immediately prior to entering the magnet room, the physician explains the procedure to the patient in detail. Special emphasis should be taken on possible side effects during adenosine infusion. The patient should be informed that thoracic oppression / chest pain, dyspnoea and increased anxiousness may occur in the first 3–4 minutes. This prevents discontinuation of the procedure during or right after the stress test.

Within the scanner room, the patient is prepared by one of the technologists. Two i.v. lines should be placed in each of the antecubital veins (fig. 1). A line for contrast agent and one for adenosine are connected **separately** to avoid a bolus injection of adenosine when the contrast agent is flushed with much higher flow rate. The blood pressure cuff should be placed on the arm of the contrast injection, to avoid interference with the administration of adenosine.

ECG electrodes are placed and checked for quality. An integrated ECG display at the scanner including a 5-star quality grading visualization (new with MR B15) supports the workflow. Exclusion of tachyarrhythmia or severe ventricular arrhythmias is mandatory. Additional application of a pulse clip as an alternative trigger acts as a backup in case of ECG impairment while the patient is in the scanner. The venous access should be tested via administration of saline solution to exclude paravasation or slow gadolinium flow. In case of claustrophobia, the short acting benzodiazepines (e.g. midazolame 1.0 to 1.5 mg i.v.) can be administered. Possible effects on driving fitness should be taken into account.

Parallel to the preparation of the patient in the scanner room, the second technologist prepares



1 Patient preparation for CMR Adenosine Stress Perfusion Imaging. ECG electrodes are attached to the chest. Signals are transferred via Bluetooth™ to the scanner. Two iv lines are placed allowing for independent injection of Adenosine and contrast media. For optional monitoring of blood pressure during the exam, a blood pressure cuff is placed on the contrast agent injection side.

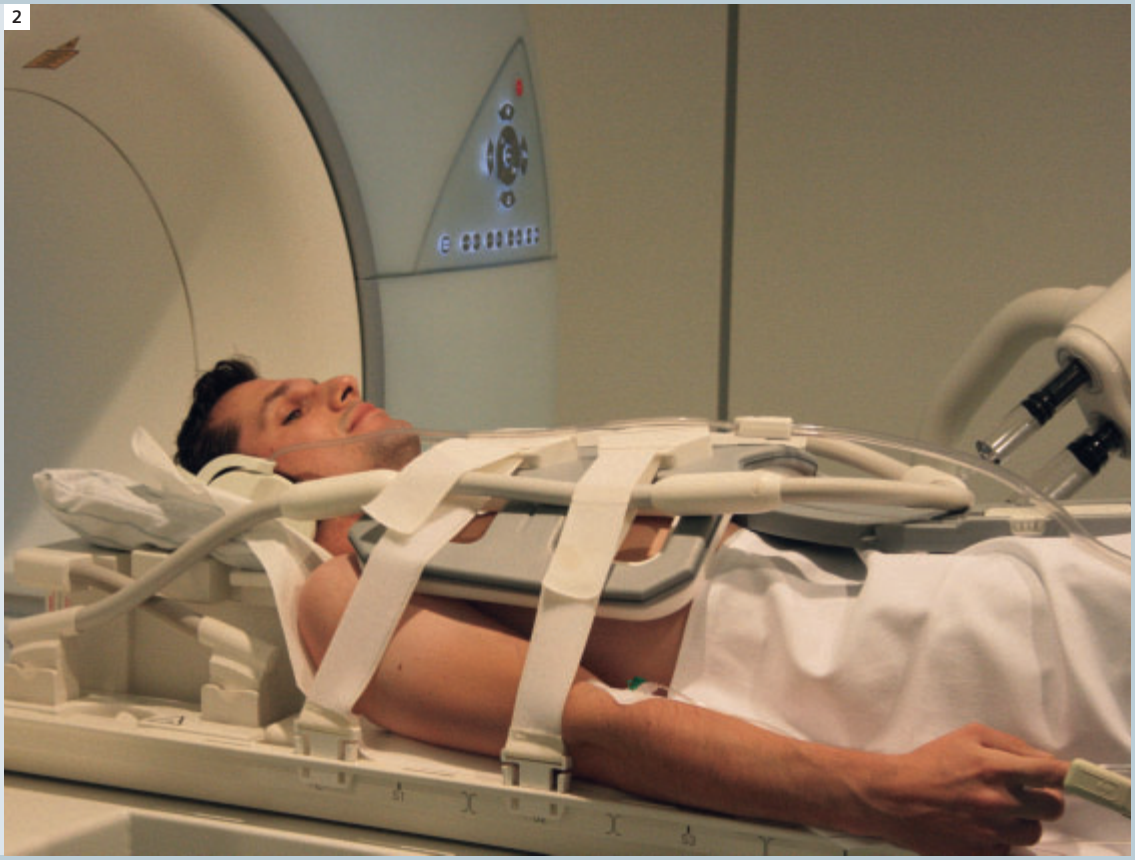
the adenosine-infusion once contraindications (e.g. severe arrhythmia, AV blockade) are excluded. We use an automatic perfusion pump for injection, which is connected to the patient by the above mentioned 6 m i.v. line. The line itself contains 12 ml of volume. The perfusion pump is positioned outside the scanner room.
The total volume of fluid filled into the pump is 48 ml. The solution consists of adenosine 140 µg/kg BW/min for three minutes plus the amount of saline needed to fill up for 48 ml. The pump is then forwarded, so that the i.v. line is completely filled. Thus, 36 ml will be given to the patient; the remaining 12 ml will stay in the 6 m i.v. line after injection.
The purpose behind this kind of preparation is for the same total amount of fluid to be injected for each patient so that the settings of the perfusion pump do not have to be adjusted. Furthermore, the adenosine is diluted, so that negative side effects due to wrong infusion rates or bolus administration can be reduced.
The total preparation time for a patient from being undressed to entering the magnet takes an average of about 8 minutes.
After patient preparation, one of the technologists performs the MRI scan. The other technologist handles the previous patient and the patient next in line. In the meantime, the physician can read the previous scan, write reports, or provide explanations for the patients.

Protocol optimization

Our protocol for adenosine stress perfusion MRI is based on study protocols used in larger trials and on our own experience. The protocol is established on a MAGNETOM Avanto 1.5 Tesla scanner (Siemens, Erlangen). For the routine indication of relevant ischemia this protocol is usually not altered. Each successive step is predefined on the scanner. This allows for a fast and standardized acquisition and reduces interobserver variability.
For other indications (e.g. myocarditis, cardiomyopathies) different selectable protocols are provided.

Function

After localizer acquisition we perform functional imaging of the left and right ventricle for assessment of global and regional wall motion abnormalities and valve function. By standard, three long axes are planned along the left ventricle, including four-chamber view (4CV), two-chamber view (2CV) and a leftventricular outflow tract (LVOT or 3-ch) view. The Siemens *syngo* acquisition work-



2 A flexible, lightweight Tim Body Matrix coil is placed on the chest. A pulse clip can be used as an alternative way for triggering image acquisition. A headphone is connected for communication with the patient – due to the very low noise level on the MAGNETOM Avanto, there is no need for special noise protection.

place is configured in such a way that a short axis localizer image remains in the middle view segment. That way, the orientation of the image plane can easily be rotated into each of the long axis views and acquisition speed can be increased. Special care is taken for the left ventricular outflow tract to exclude severe aortic stenosis as a contraindication for stress testing. Next, 2 views along the long axis of the right ventricle and a stack of up to 12 short axis slices covering both ventricles are acquired.

Stress perfusion

The module of stress perfusion consists of a test acquisition and the actual perfusion sequence. The test sequence is performed to guarantee correct slice position. Fold-over artifacts into the left ventricle should be avoided. Furthermore, care should be taken to exclude the left ventricular outflow tract from the most basal slice. The test sequence can be adjusted as often as necessary for an optimal acquisition. As soon as this is achieved, a "copy reference" is activated, which transfers all settings to the following sequences.

Accordingly, the set of short axes of the test perfusion is the reference for all following acquisitions including wall motion, perfusion, and late enhancement which enables easy comparison of the respective slices.

After informing the patient about the expected physiologic reactions, the perfusion pump for the adenosine is started. Usually, an increment in heart rate is expected within the first 30 seconds to one minute – the extent can differ from patient to patient and there is no maximum heart rate to be reached. The blood pressure is then checked [BP control is not mandatory]. For a successful study, it is important to keep talking to the patient and to reinsure her/him that the changes she/he might experience are quite usual.

30 seconds prior to the end of the adenosine infusion (after 2.5 min), the perfusion sequence is started together with a 0.075mmol / kg BW injection of Gd-DTPA at a rate of 4 ml / sec. (The applied dose of contrast is sufficient for visual analysis; it may differ from site to site, but is usually between 0.05 and 0.1 mmol/kg BW). An "online window" can give information on the correct appearance of

3 The CCTV screen, adenosine perfusion pump, injector control unit and the BP/sO_2 monitoring device are positioned next to the MR acquisition workplace to ensure optimal workflow and patient monitoring.

contrast in the heart and the "physio control window" identifies correct ECG triggering.
Afterwards, the patient is questioned again about condition. Usually, the heart rate starts to drop within 30 seconds after the end of the adenosine infusion and possible complaints disappear in parallel.
A possible amendment for this module is to include functional stress imaging during the plateau phase of heart rate increment. The plateau after reaching peak heart rate normally comprises the last minute before contrast agent injection. During this time, an SSFP (TrueFISP) cine sequence with real time acquisition can acquire three short axis slices in six heart beats. These then allow for wall motion analysis. This method has been demonstrated to have a very low sensitivity for relevant ischemia. However, the specificity of an observed wall motion abnormality for a high grade coronary artery stenosis is very high.

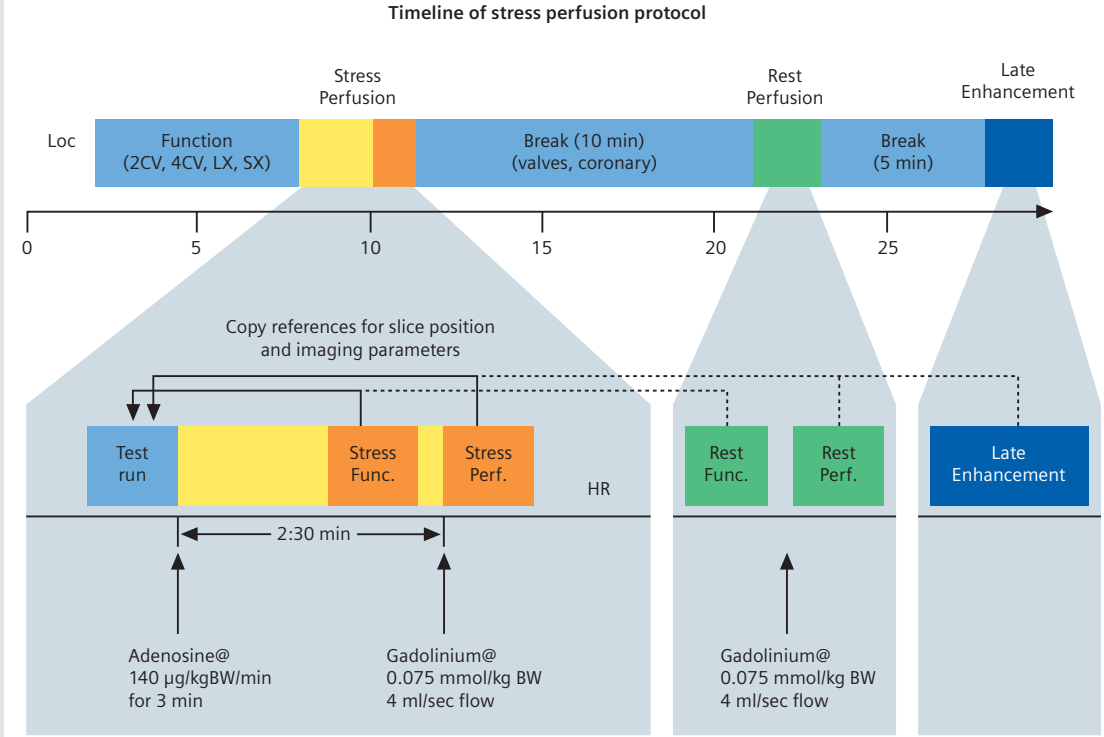
Break

To allow contrast wash-out from stress perfusion, a gap of ten minutes is planned between stress and rest perfusion. During this time, the patient stays in the magnet. Either further functional studies (e.g. valve function, phase-contrast sequences) are acquired, or simply the radio is turned on for the entertainment of the patient, during which time the physician can review the stress perfusion and function.
Alternatively, using a Whole-Heart 3D sequence with motion – adaptive diaphragmatic triggering, an approach towards coronary MR angiography can be taken during this break. But since patients do experience a considerable drop in heart rate during the first minute after stress perfusion, the accurate planning of this sequence might be challenging.

Rest Perfusion

Rest perfusion is performed using exactly the same sequence parameters and amount of contrast agent as for stress perfusion. By implementation of a "copy reference" on the stress perfusion, the sequence can be run without any further planning or adjustment. In case of a completely normal stress perfusion, the rest perfusion could be skipped. In

4 The Cardiovascular MRI team of St. Marien-Krankenhaus, Bonn; from left to right: Ms Ilka Hees (RT), Dr. Carsten Pipp (volunteer), Dr. Giso von der Recke (head of CMR team), Dr. David Hardung (cardiology resident), Ms. Christine Bäumler (RT)



5 Timeline of stress perfusion protocol
Loc = Localizer Sequence
2CV = two-chamber view
4CV = four-chamber view
LX = long axis
SX = short axis
Func = function
Perf = perfusion
HR = heart rate
BW = body weight

that case a second bolus of contrast agent should be administered to reach the required 0.15 to 0.2 mmol / kg BW for optimal late enhancement imaging. However, we recommend including rest perfusion in every patient for retrospective evaluation.

Late Enhancement

At least five minutes after the second contrast agent has been administered, the sequences for late enhancement are run. Generally, we use a phase sensitive inversion recovery (PSIR) sequence. Therefore, no adjustment for correct "Time of Inversion" is needed. Otherwise, when using a IR-GRE (e.g. IR TurboFLASH), a TI-Scout sequence is performed first. However, if we stick to the time frame of 10 minutes between stress and rest, and an additional five minutes between rest and late enhancement, the time of inversion is relatively fixed at 300 ms with our scanner. Again, these sequences are planned using copy references. First, a high resolution IR-sequence with reference on the stress perfusion slices is planned. Afterwards, a single-shot sequence with a copy reference on the stack of short axes acquired for cine imaging is used cover the whole left ventricle. In case of pathologic findings on the late enhancement, additional long axis slices are planned manually to confirm this finding. Afterwards, the patient is taken out of the scanner.

As pointed out predefined protocols using copy references facilitate the investigation. Essentially, as soon as the first set of short axes for the test perfusion is adjusted to the optimal field of view, no further planning is needed for the standard adenosine stress perfusion protocol. However, this implies that the stack of short axes for test perfusion is planned with meticulous care.

With this protocol the question of relevant myocardial ischemia is answered in less than 30 minutes scanning time.

Summary

Adenosine stress perfusion MR is a feasible and safe procedure for a high throughput setting. Inpatients as well as outpatients can easily be handled by two technologists and one physician. With the above mentioned protocol optimization and logistic guidelines, 40 minutes in the scanner room can be assigned for each patient.

For optimal logistics it is essential to use trained personnel that routinely handle patients for stress perfusion measurements and are accustomed to the specific preparation steps. Furthermore, a standardized and predefined protocol for adenosine stress perfusion guarantees time efficiency as well as low interobserver variability.

Contact
Giso v. der Recke, M.D.
St.-Marien-Hospital
Robert-Koch-Str. 1
53115 Bonn
Germany
Phone: +49-228-505-2577
recke@cardiomrt.net

References

1 Schwitter J, Nanz D, Kneifel S, et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation. 2001;103(18):2230–5.
2 Klem I, Heitner JF, Shah DJ, et al. Improved detection of coronary artery disease by stress perfusion cardiovascular magnetic resonance with the use of delayed enhancement infarction imaging. J Am Coll Cardiol. 2006;47(8):1630–8.
3 Schwitter J. MR IMPACT: First-pass MR perfusion test superior to SPECT for detection of CAD. Oral presentation. Annual meeting of European Society of Cardiology 2005, Stockholm, Sweden.
4 Pilz G, Bernhardt P, Klos M, et al. Clinical implication of adenosine-stress cardiac magnetic resonance imaging as potential gatekeeper prior to invasive examination in patients with AHA/ACC class II indication for coronary angiography. Clin Res Cardiol. 2006;95(10):531–8.
5 Ingkanisorn WP, Kwong RY, Bohme NS, et al. Prognosis of negative adenosine stress magnetic resonance in patients presenting to an emergency department with chest pain. J Am Coll Cardiol. 2006;47(7):1427–32.
6 Jahnke C, Nagel E, Gebker R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. Circulation. 2007;115(13):1769–76.
7 Hardung D, v. der Recke G. Event free survival in patients with suspected coronary artery disease and a negative test result in adenosine stress perfusion magnetic resonance imaging. Oral presentation. SCMR Ninth Annual Scientific Sessions 2006, Miami, USA.
8 Miszalski K, v. der Recke G. A prospective study in 644 consecutive patients to assess safety and feasibility of adenosine stress magnetic resonance perfusion for diagnosis of myocardial ischemia. Oral presentation. SCMR Ninth Annual Scientific Sessions 2006, Miami, USA.