Single-centre survey of the application of cardiovascular magnetic resonance in clinical routine

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Aims
Awareness of cardiovascular magnetic resonance (CMR) is growing due to increasing evidence for providing relevant functional and morphologic information. This single-centre survey aimed at providing descriptive data about the clinical application and potential impact of CMR.

Methods and results
All 2598 clinically indicated CMR exams were prospectively registered during 1 year in one single centre. Detailed data of the individual patient and procedural information of each exam were collected. In a simulation of CMR-based clinical decision-making in a subgroup of 250 cases, the influence of CMR on further diagnostic testing and answering the clinical question was estimated. Inflammatory (31%) and coronary (28%) heart disease were the most frequent indications. The exams were fast (98%, 60 min), robust (0.4% non-diagnostic image quality), and mostly used contrast media (76%). Anxiolytic sedation was required to overcome claustrophobia in 3.8%. Two per cent of all exams were terminated prematurely. No severe adverse events occurred. All moderate adverse events (0.5%) were associated with stress medication (1.7% of all stress tests) or contrast media (0.15% of all contrast enhanced studies). In the simulation, CMR influenced the individual selection of diagnostic testing and provided valuable information to establish or exclude a diagnosis.

Conclusion
This single-centre experience demonstrated a versatile application of CMR at reasonable time expense, safety, and robustness. The simulation of CMR-based decision-making indicated that CMR may influence patient management.

Keywords
Magnetic resonance • Cardiac • Clinical use • Patient management

Introduction
Diagnostic imaging has increased more rapidly than any other component of medical care.1 Cardiovascular imaging contributed substantially to this trend.2 Hence, research focusing on the clinical usage and value of imaging modalities is required.3 Cardiovascular magnetic resonance (CMR) imaging is still a minor contributor to imaging procedures,4 which is in particular attributed to issues of novelty, access, availability, training, and initial investment. However, the application of CMR is expected to grow as CMR scanners are increasingly distributed, CMR became included in the training curriculum of physicians, evidence underlining the diagnostic and prognostic significance of CMR is evolving, and finally the potential risk for radiation-induced malignancy receives upcoming awareness.5–7

At this time, only few is known about the usage of CMR in everyday clinical practice. Therefore, the present single-centre survey aimed at providing descriptive data about the clinical use of CMR in this institution. Furthermore, we aimed at analysing whether CMR may influence patient management by simulating clinical decision-making that included information from CMR in a subgroup.
Methods

Study population

Between January and December 2009, all consecutive in vivo CMR studies conducted at one single centre were enrolled in the study (Figure 1). None of these CMR examinations was included in the German pilot phase of the EuroCMR registry. All CMR exams, which were performed exclusively within investigational trials, were excluded from further analyses, as they were exclusively study related (e.g. spectroscopy in metabolic diseases) and did not replace any clinically indicated CMR exams in the same individual. Cardiovascular magnetic resonance exams that contained research sequences on top of the conventional CMR protocol were included. All subjects gave written informed consent and the ethics committee of the Charité Medical University Berlin approved the study.

CMR setting

All CMR exams were performed at one 1.5T clinical scanner (Magnetom Avanto, Siemens Healthcare, Erlangen, Germany) in one single centre. This CMR unit is integrated in the Cardiology Department of a tertiary care hospital. The CMR service is available for out- and inpatients alike. Generally, the principal referring institutions to this single CMR centre are the host department of cardiology, the related outpatient practice for internal medicine located within the hospital building, cardiologists, and general practitioners in regional practices, as well as regional secondary care hospitals. Cardiovascular magnetic resonance protocols and slice planning were performed following standardized protocols and as described in previous reports. In brief and general, steady-state free-precession was used for cine imaging at rest and stress, triple-inversion T2-weighted spin-echo to assess myocardial oedema in inflammation or ischaemia, contrast-enhanced spin-echo to assess myocardial hypaeremia in inflammation, contrast-enhanced turbo fast low-angle shot acquisition for perfusion imaging, T1-weighted inversion-recovery turbo fast low-angle shot sequence for late enhancement, two-dimensional phase contrast acquisition for flow quantification, and three-dimensional contrast-enhanced gradient echo for angiographies. Each exam and report was supervised by at least one CMR expert with level 3 certification.

Data management

Characteristics of the subjects that underwent CMR, as well as data about the CMR procedure itself were collected for each CMR exam. Information was received from the patients, extracted from medical records provided by the patient or the referring physician, as well as from the electronic hospital information system. All data were stored in a purpose-built database (Access, Microsoft, USA) on a network platform allowing for synchronous data input and supervision by several coworkers with special training in the field.

Some variables needed detailed definitions, which are outlined:

Indications: up to three different indications were registered for each CMR exam. For example, if aortic stenosis and aortic aneurysm were assessed in one exam, both indications were counted.

Scan duration: time from moving the patient into the scanner until the patient exits the scanner room at the end of the examination.

Complications: ‘severe’ in case of death, resuscitation, or any state requiring inpatient treatment for at least 24 h following the CMR exam. ‘Moderate’, if requiring monitoring for short time or immediate medical treatment. ‘Mild’, if they did not fulfil the criteria of ‘severe’ and ‘moderate’ (e.g. partial paravasation of contrast media).

Image quality: categories adopted from the EuroCMR registry. Rated by the physician who read the CMR exam. ‘Good’ meant clear-cut blood-tissue borders and the absence of relevant artefacts. ‘Moderate’ meant that image quality in total was sufficient to draw conclusions, but artefacts restricted the accuracy and certainty of the findings. ‘Good’ and ‘moderate’ were summarized as...
‘diagnostic’ image quality. ‘Non-diagnostic’ meant that the image quality forbade interpretation.

Evaluation by an external reviewer
To estimate whether CMR may influence patient management, a subgroup of all CMR exams was evaluated by an external reviewer.

In a first step, a dedicated selection process was used to identify a representative subgroup from the total sample size. All cases were randomly ordered. Beginning with case 1 of the new order, consecutive cases were selected for each indication so that the final subgroup widely matched with the total study sample regarding the distribution of indications for CMR.

In a second step, an external reviewer evaluated the value of these selected CMR exams in a simulated decision tree mimicking the approach in clinical routine. This reviewer was an external cardiologist, who was not involved in the CMR examinations or patients’ treatment and who was equally familiar with all invasive and non-invasive procedures.

Each case was evaluated in a standardized fashion: (i) the patient’s history was introduced to the reviewer by providing the patient’s original file. (ii) The reviewer decided which cardiac diagnostic tests she would order, assuming that there was equal access to all diagnostic and therapeutic modalities. (iii) After that, the reviewer received the original CMR report. (iv) Finally, the reviewer evaluated whether CMR provided useful information to answer the clinical questions and whether further testing would be required.

Statistical analysis
Continuous data are expressed as mean ± SD and categorical data as frequency or percentage. Descriptive statistics were performed using Statistica (StatSoft Inc., Tulsa, USA).

Results
Characteristics of the study sample
Within 1 year, a total of 2868 consecutive CMR examinations were performed at this single institution. After exclusion of 270 exams that were performed within investigational trials as outlined prior in the text, 2598 exams that were all done in accordance of official appropriate criteria comprised the study sample and underwent further analysis16 (Figure 1). Table 1 lists the patients’ characteristics.

Indications for CMR
The indications for CMR are listed in Table 2, and Figure 2 illustrates the percentage distribution of indication groups. The single most frequent indication for CMR was the assessment of myocarditis in 650/2598 patients (25.0%). The reasons for the referral of patients to undergo CMR for myocarditis were: ECG abnormalities (n = 31), heart rhythm disorders (n = 101), reduced exertional capacity (n = 229), chest pain (n = 27), exertional dyspnoea (n = 95), wall motion abnormality in echocardiography (n = 39), follow-up exam (n = 117), and undetermined (n = 11). The image quality allowed applying the Lake Louise Criteria17 in 98.2% (638/650) and the diagnosis of acute myocarditis was made in 70/650 (10.8%) patients. In the remaining 580 subjects without CMR evidence of acute myocarditis, CMR revealed an unknown pathology in 109/580 patients (18.8%): dilated cardiac chamber (n = 6), impaired cardiac function (n = 11), ischaemia-related scar (n = 11), cardiomyopathy (n = 20), valvular heart disease (n = 11), pleural effusion (n = 13), pericardial effusion (n = 7), tachycardia (n = 2), aortic aneurysm (n = 5), extracardiac findings (e.g. liver tumour) (n = 21), and others (n = 2).

The second most frequent indication was the assessment of myocardial ischaemia using stress tests in 531/2598 subjects (20.4%), either by adenosine first-pass perfusion imaging (451/2598), or dobutamine wall motion analysis (80/2598). Thereby, 95.9% (509/531) of the exams fulfilled the diagnostic criteria. In these, CMR ruled out ischaemia in 85.1% (433/509) and gave suspicion of ischaemia in 14.9% (76/509). Ninety three per cent (71/76) of the positive stress studies were followed by heart catheterization vs. 2.3% (10/433) with the negative result. They led to the revascularization procedures in 66.2% (47/71) and 0%, respectively.

Procedural information
Table 3 summarizes the procedural information of the examinations.
The majority of CMR studies were orderly terminated after acquiring all required images (2547/2598; 98.0%). The main reasons for prematurely stopping the CMR exam (51/2598; 2.0%) were unsatisfactory patient compliance (n = 18), claustrophobia (n = 12), critical state of health (n = 7), no diagnostic image quality achievable (n = 4), hardware error (n = 2), unpredicted presence of subcutaneous metallic material (n = 2), significant dyspnoea/ chest pain during dobutamine stress (n = 2), allergic reaction following contrast media administration (n = 2), extravasation of contrast media (n = 1), and severe obesity (n = 1).

### Anxiolytic sedation

In 98 (3.8%) of all examinations, anxiolytic sedation was administered intravenously, either prophylactic if claustrophobia was known, or while CMR was ongoing if claustrophobia occurred newly. Oral anxiolytic medication was not used.

### Complications

Adverse event rates are shown in Table 4. No severe adverse events occurred. Nine of the 12 moderate complications were associated with CMR stress studies, leading to a rate of 1.7% of all 531 CMR stress tests. These adverse events comprised asystole of 7 s (n = 1), severe chest pain or dyspnoea (n = 5), and haemodynamic instability (n = 3). The remaining 3/12 moderate complications occurred in conjunction with contrast media administration, leading to a rate of 0.15% of all 1973 contrast-enhanced CMR studies. They included an asthmatic attack (n = 1), exanthema of the face and trunk (n = 1), and swelling of the nasal mucosa (n = 1). The 17 mild complications comprised claustrophobic symptoms (n = 12) despite anxiolytic medication, and partial paravasation of contrast media (n = 5; 0.25% of all 1973 contrast-enhanced CMR studies).

### Evaluation by an external reviewer

The reviewer had to assess twice which diagnostic tests were required; initially exclusively based on the patient’s history; subsequently based on the information from the patient’s history plus the CMR report. When comparing the second with the initial requirements, the total number of needed TTE (minus 120 exams), TEE (−5), exercise ECG (−32), and aortic CT (−4) decreased, the number of heart catheterization (plus 1 exam) and stress TTE (−2) remained widely constant, and the need for 24 h ECG (plus 5 exams) and ergospirometry (±14) increased.

Yet, even though the total number of the various examinations remained in part constant (e.g. heart catheterization), there were differences on the individual patient’s level: the reviewer forewent heart catheterization in 11/36 subjects (30.6%) based on the CMR report, who were sent for catheter after initial assessment. On the other hand, the reviewer newly set the indication for heart catheterization in 12/214 (5.6%) of the patients after insight into the CMR report. Similarly, after having access to the CMR report,
the reviewer withdrew the indication for exercise ECG or stress TTE in 39/54 subjects (72.2%) and 13/19 subjects (68.4%), respectively, who should initially undergo these examinations. On the other hand, 8/196 (4.1%) and 11/231 (4.8%) subjects were newly scheduled for exercise ECG or stress TTE based on the CMR report.

From the perspective of the reviewer, the information gained by the CMR report answered the clinical question completely in 88.4% and partly in 11.2% of all cases. Thereby, CMR mainly served to rule out a suspected diagnosis (66.4%). Alternatively, CMR confirmed a suspected or known diagnosis in 14.4 and 14.8%, respectively. In 7.6%, the reviewer received unexpected new information.

**Table 3** Procedural information of all CMR examinations (n = 2598)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td></td>
</tr>
<tr>
<td>No sedation</td>
<td>2500 (96.2%)</td>
</tr>
<tr>
<td>Intravenous sedation with midazolam</td>
<td>98 (3.8%)</td>
</tr>
<tr>
<td>Contrast media</td>
<td></td>
</tr>
<tr>
<td>No contrast media</td>
<td>625 (24.1%)</td>
</tr>
<tr>
<td>Contrast-enhanced CMR</td>
<td>1973 (75.9%)</td>
</tr>
<tr>
<td>Image quality</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>2406 (92.6%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>182 (7.0%)</td>
</tr>
<tr>
<td>Non-diagnostic</td>
<td>10 (0.4%)</td>
</tr>
<tr>
<td>Study duration&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Mean study duration ± SD&lt;sup&gt;b&lt;/sup&gt; (min-max range)</td>
<td>37 ± 16 min (0–120 min)</td>
</tr>
<tr>
<td>Duration ≤ 30 min</td>
<td>804 (30.9%)</td>
</tr>
<tr>
<td>Duration ≤ 45 min</td>
<td>1322 (50.9%)</td>
</tr>
<tr>
<td>Duration ≤ 60 min</td>
<td>408 (15.7%)</td>
</tr>
<tr>
<td>Duration &gt; 60 min</td>
<td>64 (2.5%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Some CMR exams additionally contained research sequences, which might have prolonged the conventional protocol.

<sup>b</sup> SD, standard deviation.

**Table 4** Safety of CMR in the total sample (n = 2598)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of complications</td>
<td>29 (1.1%)</td>
</tr>
<tr>
<td>Severity of complications</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>17 (0.7%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>12 (0.5%)</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

**Figure 2** Indications for CMR. Frequency of indication groups for performing the CMR study in all 2598 CMR exams. Inflammatory heart disease included myocarditis, cardiotoxicity, sarcoid, and systemic disorders. Coronary heart disease included stress exams, viability assessment, and acute infarction.

The reviewer withdrew the indication for exercise ECG or stress TTE in 39/54 subjects (72.2%) and 13/19 subjects (68.4%), respectively, who should initially undergo these examinations. On the other hand, 8/196 (4.1%) and 11/231 (4.8%) subjects were newly scheduled for exercise ECG or stress TTE based on the CMR report.

From the perspective of the reviewer, the information gained by the CMR report answered the clinical question completely in 88.4% and partly in 11.2% of all cases. Thereby, CMR mainly served to rule out a suspected diagnosis (66.4%). Alternatively, CMR confirmed a suspected or known diagnosis in 14.4 and 14.8%, respectively. In 7.6%, the reviewer received unexpected new information.
Discussion

In this single-centre experience, CMR was requested in a large variety of clinical questions, which underlines the versatility of CMR. The distribution of indications in the total sample size resembled the results of the EuroCMR registry, where the assessment of ischaemic heart disease (45.5%) and myocarditis together with cardiomyopathies (31.9%) also were the most frequent primary indications.8

The reason why inflammatory heart disease was dominant over ischaemic is most probably attributable to the single-centre nature of this survey that leads to regional referral bias. The low number of patients who received the definite CMR-based diagnosis of acute myocarditis also underlines this assumption.

The assessment of ischaemic heart disease was the second most frequent indication for CMR. The present results underlie the feasibility of performing high-volume CMR stress tests in a routine clinical setting with high percentage of diagnostic image quality and low complication rates (1.7%), comparable with the EuroCMR registry8 and other stress modalities.18 Yet, it has to be emphasized that only 14.9% of all patients referred for the assessment of myocardial ischaemia finally had a suspicion of ischaemia. Hence, this represents a highly selected low-risk population for coronary artery disease that reflects this single-centre experience. The prevalence of inducible ischaemia as well as adverse event rates may be higher in patients with higher pretest probability.

The assessment of impaired cardiac function also led to a considerable proportion of all CMR examinations, even though the quantification of ejection fraction and wall motion analysis is, in principle, accurately feasible by TTE. However, it is well known that 10–15% of routine TTE have incomplete endocardial resolution that can lead to misinterpretation.19 As some clinical decisions are mainly based on ejection fraction, high accuracy during left ventricular chamber quantification is desired and can justify the use of CMR in case of inconclusive TTE findings. As this single CMR unit is part of a comprehensive non-invasive imaging facility that covers both CMR and echocardiography, the threshold to use CMR to assess cardiac function may be lowered. This also contributes to the relatively high proportion of non-contrast-enhanced CMR studies (24.1%) in this single centre compared with the EuroCMR registry (10%).20

The large variety of indications performed in this single centre and generally accessible with CMR yet also represents a challenge regarding quality control. Strong efforts have to be made to maintain profound education and guarantee standards in performing, reading, and reporting a CMR exam.15,21

The majority of CMR exams (82%) did not last longer than 45 min and 98% of all exams were finished within 60 min. Thereby, no exam was terminated prematurely due to the time schedule before all relevant information had been collected. This information underlines that CMR exams are feasible within a reasonable expenditure of time and facilitates to organize efficient time schedules.

Contrast media were administered in 76% of all examinations. This frequency is below the results from the EuroCMR registry (90%)20 and is mainly attributable to discrepancies regarding the distribution of primary indications for CMR: as outlined before, the assessment of cardiac function was included in 14.6% of all examinations; in addition, the evaluation of valvular heart disease, which generally does not require contrast enhancement, was more frequent in this single institution (7.4%) than in the EuroCMR registry (4.8%).8 Contrast administration was associated with a rate of moderate adverse events of 0.15% and mild adverse events of 0.25%. These adverse event rates are in concordance with recently published experiences of the EuroCMR registry, which described 30 acute adverse reactions in 17,767 patients resulting in an event rate of 0.17%,20 and with the incidence in the US Food and Drug Administration-approved general radiology setting (0.04–2.2%).22,23 Hence, our data provide further evidence that the off-label use of gadolinium-based contrast in CMR should be regarded as safe concerning the frequency and severity of acute events.

Claustrophobia occurs in about 2% in unselected patients undergoing general radiology MRI examinations.24 As the rate increases with head-first and supine position, the incidence of claustrophobia is expected to be even higher in CMR imaging.25 However, no such data exist up to now. We observed a rate of 3.8% of all CMR exams that required anxiolytic sedation—either prophylactic if claustrophobia was known, or while CMR was ongoing if claustrophobia occurred newly. Using this strategy, only 12/2598 (0.5%) CMR exams had to be terminated prematurely before completing the protocol due to uncontrolled claustrophobia. Hence, even though the overall risk for claustrophobia seems to be elevated in CMR compared with MRI of other body regions, a high dropout rate can be overcome by the use of anxiolytic sedation.

In accordance with the experiences of the EuroCMR registry, which reported a 98.2% rate of diagnostic images, the image quality of this single-centre survey was diagnostic in most cases. However, the visual grading of image quality may be too crude and influenced by its subjective nature. Therefore, scores, which apply well-defined variables for image quality might be helpful in future.

There is the potential for over-use and unnecessary testing in cardiovascular imaging.4 This potential is enhanced by the availability of diagnostic tests with overlapping capabilities on the one hand, and the fear to miss a relevant cardiovascular disease on the other hand.26 It is rarely possible to demonstrate that an imaging test directly leads to improved health outcomes, especially in terms of the mortality rate. Rather than outcome measures, quality might be assessed by process measures that include impact on diagnostic and therapeutic thinking.1,27 In the present subgroup analysis, CMR appeared to favourably influence diagnostic testing: it answered the clinical question in the majority of cases, which is one prerequisite to avoid further downstream testing. It promoted the targeted use of complementary tests such as tests for heart rhythm and pulmonary function. The selection of a specific test for the individual patient was influenced. Under careful consideration of the methodical limitations, these findings underscore the clinical value of CMR and are in accordance with the experiences of the EuroCMR registry,8 but need to be confirmed in larger multi-centre trials including detailed analysis of cost effectiveness.

In conclusion, this single-centre survey demonstrated that CMR was used in a wide variety of clinical indications. Based on
standardized protocols, CMR exams were done in a reasonable expenditure of time, provided robust image quality, and were safe. The results of the simulated CMR-based clinical decision-making supported the hypothesis that CMR might favourably influence individual patient management. To confirm this hypothesis, multicentre studies and cost effectiveness analysis are required.

Limitations of the study

The main limitation of this study is its single-centre nature, which constitutes a major bias regarding patient referral, selection of imaging procedures, and application of differentiated CMR protocols. Multi-centre and multi-vendor studies—as realized with the ongoing EuroCMR registry—are therefore required to confirm this single-centre experience and to evaluate the clinical use and impact of CMR. The subgroup analysis has several limitations, too, which have to be considered when interpreting its results and which classify the findings as merely hypothesis generating. (i) Even though the study suggests that CMR influences the downstream use resources, the data did not enable a cost analysis. (ii) One single physician did the external review of the CMR information. To obtain more objective data, a multi-centre and multi-reader approach is required. (iii) Since only the cases were sent to the reviewer that had a CMR, this introduced selection bias to the analysis. (iv) There is no assessment of actual outcomes to suggest that the clinical pathway chosen based on CMR findings was indeed the optimal approach.

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References