

Update on Dobutamine Stress Magnetic Resonance

Alexander Berger · Eckart Fleck · Rolf Gebker

Published online: 4 February 2012
© Springer Science+Business Media, LLC 2012

Abstract Over the past years dobutamine stress magnetic resonance imaging (DSMR) has matured into a highly valuable clinical tool for the assessment of myocardial ischemia and viability. Furthermore, the results of DSMR can be utilized to direct clinical management and to determine cardiac prognosis. This article gives an update on recently published data regarding the performance of DSMR including technical developments, diagnostic accuracy, prognosis, and the implications on clinical management in patients with coronary artery disease (CAD).

Keywords Cardiac MR · Coronary artery disease · Ischemia · Dobutamine stress testing · Prognosis

Introduction

The last 15 years have seen remarkable achievements regarding the technical development and clinical application of cardiovascular magnetic resonance (CMR) [1]. The versatility of the method has special relevance for the assessment of patients with coronary artery disease (CAD), since functional techniques like cine wall motion and perfusion imaging can be combined with each other as well as with myocardial tissue characterization utilizing late gadolinium enhancement (LGE) [2•]. Among the spectrum of available stress tests, dobutamine stress magnetic resonance (DSMR) has been established as a clinically robust imaging modality to evaluate myocardial ischemia and viability and to

determine cardiac prognosis (Fig. 1) [3, 4, 5•, 6–8]. The aim of this article is to provide the reader with an update on recent developments in the field of DSMR, which are likely to further improve our understanding in the diagnosis, prognosis, and clinical management of patients with ischemic heart disease.

CMR Techniques

One of the major benefits of CMR is the excellent endocardial border delineation inherent to cine MR sequences. Even the first DSMR studies, which applied segmented k-space turbo gradient echo (TGE) sequences, demonstrated their superior image quality compared to echocardiography [3, 6]. Steady state free precession (SSFP) is associated with yet higher contrast between blood and myocardium, especially in the long axis views and in patients with reduced left ventricular function and has become the current standard of reference for the assessment of wall motion during dobutamine stress. In combination with parallel imaging techniques like sensitivity encoding (SENSE), breath hold duration for one cine loop is 6–8 s with a temporal resolution of up to 50 phases per heart cycle at heart rates up to 220 bpm [7]. The in-plane spatial resolution of SSFP cine scans usually lies in the range of 1.8 mm×1.8 mm with a slice thickness of 8 mm. Over the past years new techniques have become available to accelerate dynamic imaging by means of reduced data acquisition based on exploiting correlations in k-space and time (k-t) [9–11]. These strategies use the quasi-periodic motion of the heart, allowing for the acquisition of a reduced data set and recovering the omitted data afterward by using a small set of training data to learn the signal correlations. Jahnke et al. [12] implemented the k-t broad-use linear acquisition speed-up technique (k-t BLAST) to acquire a three-dimensional cine

A. Berger · E. Fleck · R. Gebker (✉)
German Heart Institute, Deutsches Herzzentrum Berlin,
Augustenburger Platz 1,
13353 Berlin, Germany
e-mail: gebker@dhzb.de

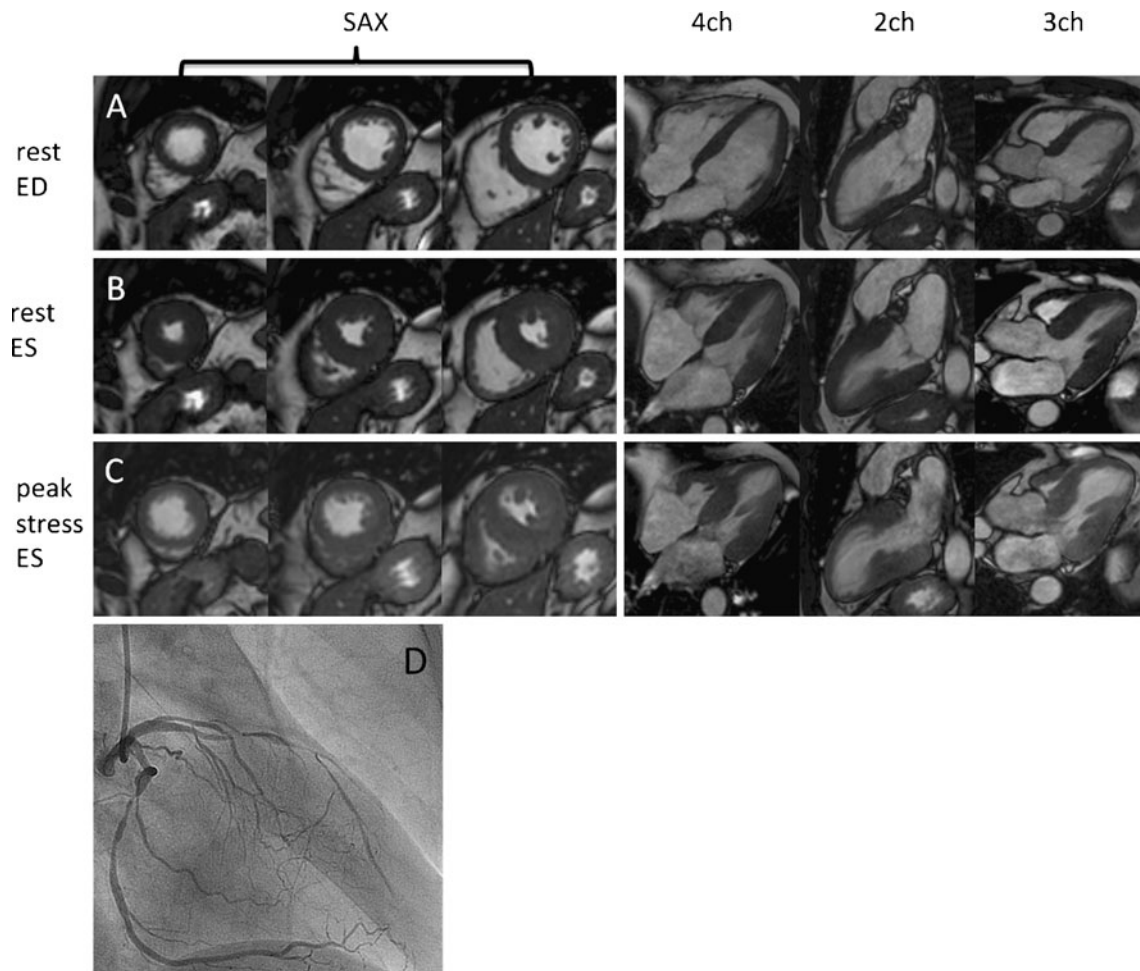


Fig. 1 DS MR with a stress-induced wall motion abnormality. Normal wall motion at rest (**a/b**). Dobutamine stress-induced akinesia of the apical and mid-anterior/anteroseptal segments (**c**). Invasive coronary

angiography showing several high-grade stenoses of the left anterior descending and left circumflex artery (**d**)

data set in a single breath hold at rest and during dobutamine stress. The potential advantage of this approach compared to multiple two-dimensional standardized views is twofold: First, complete coverage of the heart allows accurate determination of LV volumes by means of the Simpson method and evaluation of segmental wall motion at once. Second, all standard views can be reconstructed from one single three-dimensional data set, thus reducing planning effort and shortening acquisition time.

Overall, DS MR has a consistently high diagnostic accuracy at a low interobserver variability for identifying inducible left ventricular wall motion abnormalities (WMA) (Table 1) [13]. However, despite the heightened quality of CMR cine images compared to echocardiography, the qualitative identification of stress inducible WMA remains subjective and depends on the training and experience of the reader. Several studies over the last years have highlighted the application of quantitative wall motion analysis for identifying inducible ischemia by using myocardial tagging [14], harmonic phase imaging (HARP) [15], displacement encoding with stimulated echoes

(DENSE) [16, 17], and strain-encoding (SENC) [18]. The time-consuming process of quantitative evaluation of myocardial strain images has been the main limitation to routine clinical utilization of tagged cardiac MRI. Advancement in this context was the development of the HARP imaging approach, which allows automatic and near real-time analysis of tagged cardiac MR images [19]. The main drawback of HARP is its relatively low spatial resolution not allowing differentiation of strain across the wall of the heart. Although DENSE enables higher spatial resolution for evaluating regional myocardial deformation in three dimensions, data must still be analyzed offline and human studies during dobutamine have not been performed yet. More recently, SENC has been proposed for the objective evaluation of circumferential and longitudinal myocardial strain. This technique compares favorably over more conventional CMR tagging sequences in terms of temporal resolution, total scan duration, and time required for post processing of the acquired data [20]. Feature tracking, a new method of measuring strain from clinically standard CMR cine images in a manner similar to

Table 1 Sensitivity and specificity of recent studies on DSMR

Authors	Year	Patients (<i>n</i>)	Men (%)	Mean age (years)	Dobutamine dose ($\mu\text{g}/\text{kg}/\text{min}$)	Sensitivity (%)	Specificity (%)	Accuracy (%)	MRI technique	Field strength	Stenosis definition (%)
Paetsch et al. [13]	2006	150	83	61	40+atropine	78	87	83	Wall motion	1.5	≥ 50
Jahnke et al. [12]	2006	40	75	63	40+atropine	89	83	88	Wall motion	1.5	≥ 50
Gebker et al. [30]	2008	414	65	64	40+atropine	85	82	84	Wall motion	1.5	≥ 70
Gebker et al. [30]	2008	414	65	64	40+atropine	91	70	84	Wall motion + perfusion	1.5	≥ 70
Kelle et al. [22]	2008	30	24	66	40+atropine	80	86	82	Wall motion	3	≥ 50
Korosoglou et al. [46]	2009	101	71	61	40+atropine	86	92	88	Wall motion	1.5	≥ 50
Korosoglou et al. [46]	2009	101	71	61	40+atropine	98	86	94	SENC	1.5	≥ 50
Korosoglou et al. [20]	2009	65	78	64	40+atropine	70	95	87	Wall motion	1.5	≥ 50
Korosoglou et al. [20]	2009	65	78	64	40+atropine	81	96	91	Myocardial tagging	1.5	≥ 50
Korosoglou et al. [20]	2009	65	78	64	40+atropine	89	94	92	SENC	1.5	≥ 50
Manka et al. [34]	2010	41	66	64	40+atropine	92	75	85	Wall motion + perfusion	1.5	≥ 50
Gebker et al. [35•]	2010	187	79	65	40+atropine	80	83	81	Wall motion	1.5	≥ 70
Gebker et al. [35•]	2010	187	79	65	40+atropine	90	77	84	Wall motion + perfusion	1.5	≥ 70
Korosoglou et al. [45]	2010	80	72	62	20	20	97	53	Wall motion	1.5	≥ 50
Korosoglou et al. [45]	2010	80	72	62	20	76	88	81	SENC	1.5	≥ 50
Gebker et al. [31]	2010	94	72	65	40+atropine	79	90	84	Wall motion	1.5	≥ 50
Gebker et al. [31]	2010	94	72	65	40+atropine	90	85	88	Wall motion + perfusion	1.5	≥ 50
Korosoglou et al. [47•]	2011	175	74	64	40+atropine	84	94	88	Wall motion	1.5	≥ 50
Korosoglou et al. [47•]	2011	175	74	64	40+atropine	96	88	93	SENC	1.5	≥ 50
Korosoglou et al. [47•]	2011	175	74	64	40+atropine	71	92	78	Strain reserve	1.5	≥ 50
Korosoglou et al. [47•]	2011	175	74	64	40+atropine	95	92	93	Strain rate reserve	1.5	≥ 50
Gebker et al. [33]	2011	78	76	65	40+atropine	81	87	83	Wall motion	1.5	≥ 70
Gebker et al. [33]	2011	78	76	65	40+atropine	92	83	89	Wall motion + perfusion	1.5	≥ 70

echocardiographic speckle tracking, was recently presented [21]. The major advantage of feature tracking is its simplification of image acquisition with no need for additional imaging. However, further validation of this method in patients with coronary artery disease during dobutamine stress is necessary before it can be applied in clinical routine. In summary, there is great potential that quantification of abnormalities of deformation within the myocardium improves overall accuracy of dobutamine stress CMR as compared with visual assessment of wall motion.

Up to now conventional cine imaging during dobutamine stress has almost exclusively been performed at a field strength of 1.5 T. The main reason is that image quality using balanced SSFP sequences at 3 T suffers from banding

artifacts and non-uniform contrast, particularly during the high flow states observed at high doses of dobutamine and atropine. More robust image quality during high heart rates at 3 T can be achieved using TGE sequences [22]. However, the administration of a gadolinium contrast agent is necessary in order to enhance the relatively low contrast-to-noise ratio between blood and myocardium inherent to TGE cine sequences, which hinders its application in patients with severely impaired renal function. The application of new multiple RF transmit channels may allow more control of the B1 field enabling the application of SSFP cine imaging. Initial data suggest that high-dose DSMR with SSFP at 3 T using multiple transmit technology is feasible with good image quality (Fig. 2) [23]. Another obstacle that needs to

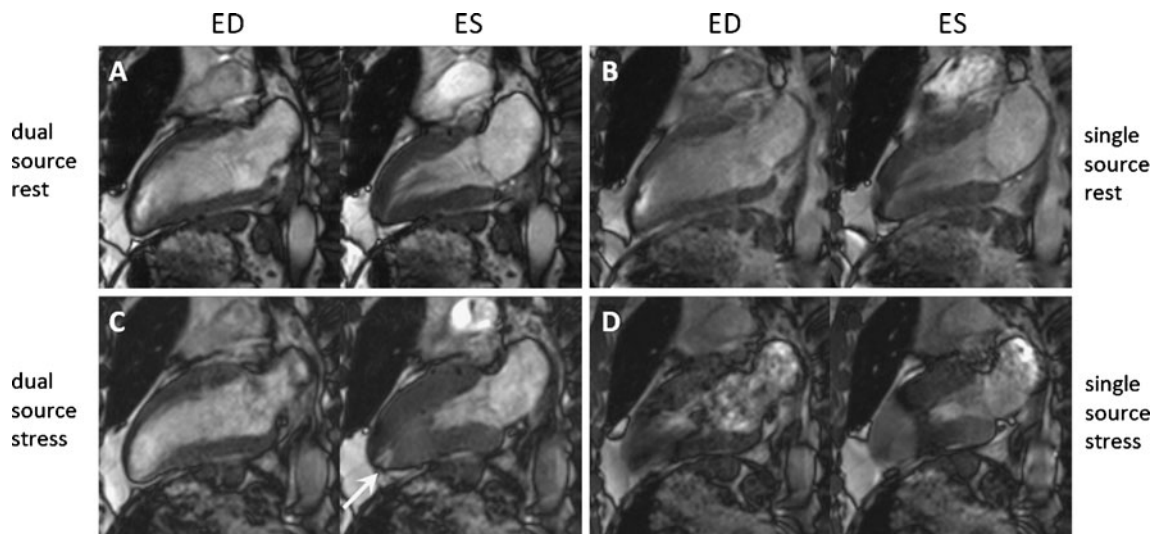


Fig. 2 DSMT at 3 Tesla using dual source transmit versus single source transmit technology. The single source transmit technology is prone to banding artifacts especially at high heart rates leading to non-

diagnostic segments as seen on image **d**. In this case a stress-induced wall motion abnormality at the apex (*white arrow*) is visible during maximum stress only using the dual source transmit technology (**c**)

be overcome under high field conditions are ECG-trigger problems related to the magneto-hydrodynamic effect, which leads to an artifactual voltage overlayed on the T-wave of the ECG causing triggering on the T-wave instead of the R-wave. This effect becomes particularly pronounced during high heart rates at higher field strengths [22].

Diagnostic Value of DSMT

DSMT in Women

Despite the fact that more women than men die of cardiac events related to CAD per year, women are generally under-reported in studies assessing the diagnostic utility of cardiovascular imaging methods [24]. In addition, both radionuclide scintigraphy and transthoracic echocardiography suffer from gender-related differences in diagnostic accuracy, which is related to more attenuation artifacts and smaller chamber size as well as poor acoustic windows, respectively [25, 26]. Thus, DSMT based on its excellent endocardial border delineation is promising to overcome the limitations of other imaging modalities. To this end, Gebker et al. [27] demonstrated in a study with 745 patients a gender-independent high diagnostic performance using DSMT for the detection of CAD. The diagnostic values (sensitivity/specificity/accuracy) were similar for men (86%/83%/85%) and women (85%/86%/85%).

DSMT-Perfusion

The traditional hallmark of myocardial ischemia during DSMT is an inducible WMA. The dependence on the

provocation of WMAs, however, may represent a general limitation of these techniques due to its relatively late appearance in the ischemic cascade [28]. Since abnormal perfusion precedes abnormal wall motion during ischemia, combining the assessment of both techniques should improve the diagnostic performance of the test (Fig. 3).

Lubbers et al. [29] assessed the additional value of first pass myocardial perfusion during peak DSMT in order to reduce the number of false-positive dobutamine stress CMR examinations. They were able to show a good correspondence between normal myocardial perfusion and absence of stress-induced wall motion abnormalities.

Gebker et al. [30] demonstrated an improvement in sensitivity (91% vs 85%, $P \leq 0.001$) by adding perfusion to the imaging protocol for the diagnosis of CAD in 414 patients. The combined protocol enabled the correct diagnosis in an additional 13% of patients with normal wall motion. In a more recent study it was shown that adding perfusion imaging to DSMT improved sensitivity in patients with intermediate (50%–70%) stenosis (87% vs 72%, $P = 0.03$), but not in those with severe ($\geq 70\%$) stenosis (93% vs 84%, $P = 0.06$), thus further corroborating the pathophysiologic concept of the ischemic cascade [31].

In both studies a decrease in specificity by adding perfusion imaging was observed. This may be attributed to an impaired coronary vasoreactivity even in the absence of a significant epicardial coronary arterial narrowing or CMR-specific artifacts, caused by limited spatial resolution of conventionally applied perfusion sequences resulting in a possible misinterpretation of dark rim artifacts as seen in other CMR perfusion studies [32]. In an effort to reduce false-positive results in this regard, Gebker et al. [33] utilized high spatial resolution perfusion imaging with an in-

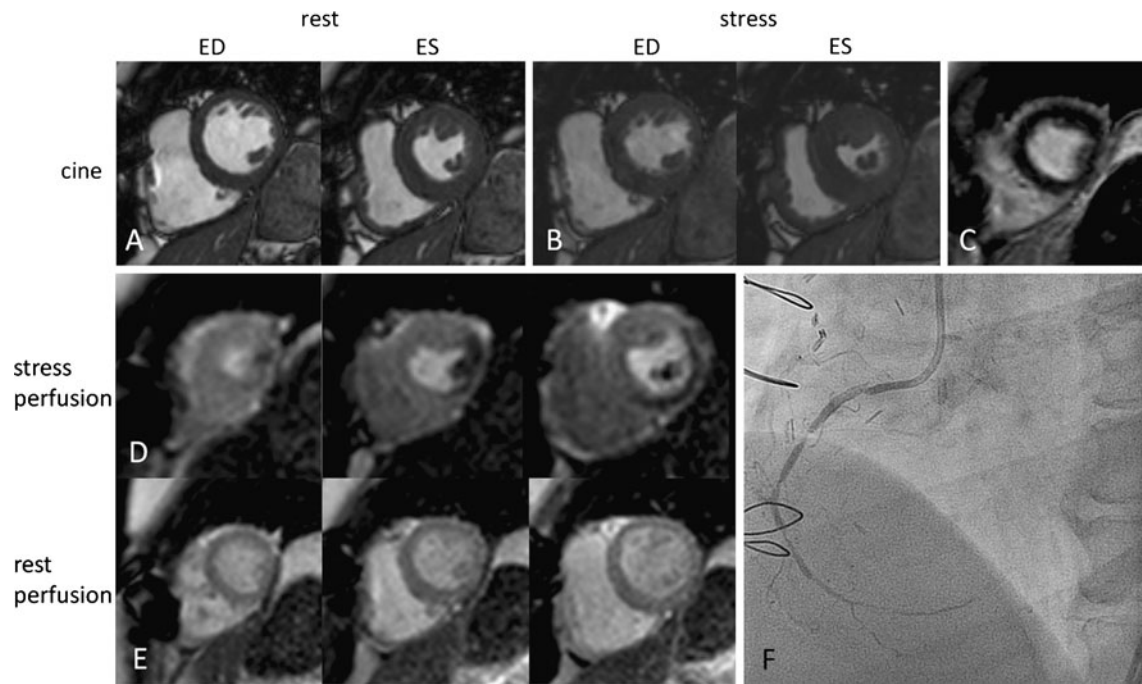


Fig. 3 Combined DSMR wall motion and perfusion. The stress-induced wall motion abnormality is limited to the basal segments of the inferior/inferolateral wall (a/b), whereas the dobutamine stress-induced perfusion deficit involves the apical, mid, and basal segments

of the inferior/inferolateral wall (d). No perfusion deficit is seen at rest perfusion. There is no scar on delayed enhancement imaging (c). Invasive coronary angiography with multiple high-grade stenoses of the RCA (f)

plane spatial resolution of $1.5 \times 1.5 \text{ mm}^2$ accomplished by accelerating imaging with k-space and time sensitivity encoding (k-t SENSE). At maximum stress level the addition of high spatial resolution perfusion to wall motion data improved sensitivity for the detection of CAD (92% vs 81%, $P=0.03$) without a relevant difference in specificity (83% vs 87%, $P=1$). Additionally, DSMR with perfusion allowed a more accurate determination of disease extent (85% vs 66% of territories, $P \leq 0.001$).

A head-to-head comparison of first-pass CMR perfusion imaging during adenosine and high-dose dobutamine/atropine stress resulted in an equally high sensitivity and specificity for stenosis detection on a per-patient basis (92% and 75% for both stressors, respectively) [34].

Left ventricular hypertrophy (LVH) can impede the identification of WMAs due to left ventricular obliteration and increased myocardial stiffness during dobutamine stress. Prior data had suggested higher sensitivity for detection of CAD using additional perfusion in patients with LVH [30]. A subsequent study highlighted the influence of different LV geometric patterns on diagnostic accuracy of wall motion and perfusion. In patients with increased LV concentricity, adding perfusion improved the diagnostic accuracy compared to wall motion alone, especially with regard to sensitivity for the detection of CAD. In contrast, the assessment of wall motion during DSMR remained an accurate test in patients with normal geometry and eccentric hypertrophy [35•].

SENC

In clinical routine the evaluation of cine scans is based on visual interpretation and therefore depends on individual experience. CMR tagging provides estimation of regional myocardial function with high accuracy; however, post-processing is relatively time-consuming. Korosoglou et al. [20] showed that tagging and SENC during high-dose dobutamine stress yielded significantly higher sensitivity of 81% and 89%, respectively ($P < 0.05$ for tagging and $P < 0.01$ for SENC vs wall motion analysis, and $P = \text{NS}$ for SENC vs tagging), while specificity was equally high (96% and 94%, respectively, $P = \text{NS}$ for all).

Another study by the same group [20] investigated the diagnostic accuracy of SENC for the detection of inducible ischemia during intermediate stress. At intermediate stress SENC demonstrated a high diagnostic performance for detection of significant CAD comparable to that provided by cine imaging during peak dobutamine stress. This may be an approach to improve patient safety and comfort for more rapid and convenient DSMR examinations.

Prognostic Value of DSMR

In recent years, the value of DSMR to predict cardiac prognosis has been evaluated extensively by several

investigators (Table 2). Hundley et al. [4] provided the first data in this context and demonstrated in a multivariate analysis that the presence of inducible ischemia or an LV ejection fraction <40% was associated with future myocardial infarction or cardiac death independent of the presence of risk factors for coronary arteriosclerosis.

CMR imaging offers the advantage of conducting myocardial perfusion and wall motion measurements at rest and under stress conditions [7]. In a unique study, 461 patients who underwent adenosine stress perfusion CMR and DSMR during a single-session examination were followed up for an average of 2.3 years [5•]. The 2-year event-free survival rates for both stress tests were similar. As with other stress imaging modalities, the authors found that the “warranty period” of noninvasive stress testing using either test may be set at a 2-year level. Interestingly, in patients with both normal adenosine stress perfusion CMR and normal DSMR results, the warranty period of event-free survival appeared to be prolonged as indicated by a constantly low event rate of 0.8% at 1-, 2-, and 3-year follow-up intervals. A large study with 1,463 patients on the long-term prognosis of DSMR further contributed to our knowledge on its value for risk stratification [36]. The authors demonstrated the independent prognostic value of DSMR in patients with suspected and known CAD over a mean follow-up time of 44±24 months. A negative DSMR carried an excellent prognosis, with an annual cardiac event rate of 1.1% over 6 years (0.8% in the first 3 years, and 1.4% between the fourth and sixth year). Thus, DSMR may not only distinguish high-risk patients in whom further interventions are necessary but also identify low-risk patients in whom additional procedures and intensive medical follow-up may not be required.

Recently, Charoenpanichkit et al. [37] identified associations of DSMR measures with future development of pulmonary edema in individuals with a preserved LVEF. In their study, a reduced augmentation of left ventricular stroke volume during dobutamine stress was associated with pulmonary edema. Importantly, this association was independent of signs of myocardial ischemia during DSMR and other risk factors for pulmonary edema. Furthermore, it appeared that measures of increased arterial stiffness contributed to the impaired ability to increase LV systolic function during stress, which may serve as a mechanism to induce pulmonary edema in the absence of ischemia.

Women

DSMR has similarly high diagnostic value in men and women [27]. Currently, most of the available prognostic data on DSMR involved men. In order to clarify whether DSMR will result in comparable prognostication of cardiac events in men and women, several investigators recently performed gender-based studies on this topic. Wallace et al. [38] included 221 consecutive women for DSMR who were followed for an average of 6.2 years. Inducible ischemia of any myocardial segment during DSMR predicted cardiac death and myocardial infarction in women, whereas women with no evidence of ischemia had a good mid-term prognosis. Importantly, the prognostic utility of DSMR stress results in women was similar to those historically reported in men. In a second study by Jahnke et al. [39], the authors compared gender-related differences regarding the predictive value of a single-session CMR examination that included both adenosine stress perfusion CMR and

Table 2 Prognostic value of DSMR

Author	Year	Patients (n)	Men (%)	Mean age (years)	Stress agent	Study performance	Follow-up	End point
Jahnke et al. [5•]	2007	461	67	61	Dobutamine and adenosine	WMA and perfusion	2.3 y	MI/mortality
Dall'Armellina et al. [40•]	2008	200	65	64	Dobutamine	WMA	5 y	MI/mortality/CHF
Wallace et al. [38]	2009	221	0	63	Dobutamine	WMA	6.2 y	MI/mortality
Walsh et al. [42]	2009	175	42	69	Dobutamine	WMA	5.5 y	MI/mortality/CHF
Charoenpanichkit et al. [43•]	2010	362	55	64	Dobutamine	WMA	6 y	MI/mortality
Korosoglou et al. [44•]	2010	1493	74	65	Dobutamine	WMA and perfusion	2 y	MI/mortality/ revascularization
Kelle et al. [36]	2011	1369	70	62	Dobutamine	WMA	44 mo	MI/mortality/ revascularization
Jahnke et al. [39]	2011	679	69	61	Dobutamine and adenosine	WMA and perfusion	5.3 y	MI/mortality/ revascularization
Korosoglou et al. [47•]	2011	320	74	64	Dobutamine	WMA and strain	28 mo	MI/mortality/ revascularization
Charoenpanichkit et al. [37]	2011	116	54	67	Dobutamine	LVEF, LV volumes, ventricular stiffness	6 y	Pulmonary edema
Gebker et al. [48•]	2011	1532	67	63	Dobutamine	WMA	2.1 y	MI/mortality

DSMR wall motion. A total of 208 women and 471 men were followed for a median time period of 5.3 years. Using multivariate analysis the presence of inducible perfusion deficits or wall motion abnormalities were identified as independent predictors of hard cardiac events for both genders with an incremental value over conventional cardiovascular risk factors. CMR adenosine perfusion imaging and DSMR wall motion testing exhibited equally high utility for cardiac risk stratification in men and women. Interestingly, in case of a negative stress test result, event-free survival was 100% in women for 4 years, while in men annual event rates increased after the second year. Hence, the previously proposed 2-year warranty period of CMR stress testing may be prolonged to a 4 year level in test negative women.

Reduced LVEF

Many patients presenting for cardiovascular care exhibit moderate to severe LV dysfunction at rest due to pre-existing coronary atherosclerosis. Recently, Dall'Armellina et al. [40•] provided insight regarding the prognostic value of DSMR in patients with reduced LVEF. They included 200 patients with a LVEF < 55% and followed them for an average of 5 years. Myocardial ischemia during DSMR offered prognostic information only in patients with mild to moderate reduction of LVEF (40%–55%), whereas in patients with a LVEF < 40% DSMR did not significantly add to predicting future cardiac events above and beyond resting function.

Left Ventricular Hypertrophy

Several studies have demonstrated that in patients with increased LV end-diastolic wall thickness and LVH sensitivity of dobutamine inducible wall motion abnormalities is low [35•, 41]. At the same time other data suggested an association between the presence of LVH or increased wall thickness and an adverse cardiac prognosis. Recently, two studies have clarified the role of DSMR to predict cardiac prognosis for these patient populations. In the first, Walsh et al. [42] included 175 consecutive participants with preserved LV ejection fraction and no inducible WMA indicative of ischemia during DSMR in their study. In a multivariate analysis that took into account Framingham and other risk factors associated with cardiac events, a cine gradient-echo derived end-diastolic wall thickness ≥ 12 mm measured at the base of the septum or lateral wall was associated independently with an increase in cardiac death and MI. In the second study by the same group, LV mass was measured directly among individuals with a range of LVEF who underwent dobutamine stress [43•]. The authors found that LVH was an independent predictor of future MI and cardiac death in patients with or without inducible

ischemia during dobutamine cardiac stress testing. Thus, increased LV wall thickness and LVH should be considered risk factors for cardiac events in individuals without stress inducible WMA during DSMR. Additionally, LVH and increased LV wall thickness should be reported in patients referred for DSMR, particularly in those without inducible ischemia, in whom otherwise one would assume a favorable cardiac prognosis.

Combined Wall Motion and Perfusion During DSMR

As demonstrated earlier, the versatility of CMR allows performing both cine wall motion and perfusion imaging during DSMR. In order to ascertain the prognostic impact of this combined protocol, Korosoglou et al. [44•] studied 1,493 patients who were followed for 2 years. A total of 53 major cardiovascular events occurred within the study population. In this relatively large, single-center study, dobutamine-induced wall motion and perfusion abnormalities predicted future adverse cardiac events after accounting for established risk factors of atherosclerotic disease. The presence of inducible WMA was of added value for the risk stratification of patients with and without inducible perfusion deficits, whereas perfusion deficits forecasted a poorer prognosis only in the absence of inducible WMA. Furthermore, the prognostic benefit of additional perfusion deficits was limited to patients with resting WMA, those with known CAD, and LVH. These patients represent subgroups in whom the detection of true positive inducible WMA may be more challenging [30, 35•]. Another important finding of this study was that stress-induced WMA predicted cardiac prognosis in individuals regardless of the pretest probability of CAD (low, intermediate, or high). However, in the absence of inducible WMA, only patients with low or intermediate risk demonstrated an excellent long-term outcome, whereas patients with high risk still yielded a significant number of subsequent hard events. Finally, this study confirmed existing data that in patients with severely impaired baseline LV function stress-inducible WMA do not add further prognostic information to the already impaired prognosis in this population [40•].

SENC

Since SENC has the capability to detect CAD with higher sensitivity and during earlier stages of inotropic stimulation than conventional cine imaging [45, 46], SENC may significantly impact clinical outcome in patients with suspected or known CAD. Korosoglou et al. [47•] thus determined the potential of SENC to predict future cardiac events in patients who underwent DSMR. They included 320 consecutive patients with suspected or known CAD applying both qualitative wall motion analysis and myocardial strain

analysis with SENC during high-dose dobutamine stress and performed follow-up over a 28-month period. They found a significant increase in sensitivity of SENC (96% vs 84%) without a relevant loss in specificity. Furthermore, the prediction of outcome improved with an increase in chi-square from 39.3 for combined clinical variables and inducible WMA to 50.7 for segmental strain maps and 52.5 for segmental strain rate reserve. Analysis of subgroups showed that the incremental value of SENC was mainly derived from patients with intermediate pre-test probability, whereas differences were minor in patients either at low or high risk.

Clinical Management

Whereas prior studies have focused on the prognostic value of DSMR in low/intermediate-risk versus high-risk patient groups as defined by conventional cardiovascular risk factors, the design of a recently published study was unique in that it addressed the impact of DSMR on clinical management in a large unselected patient population with chest pain syndromes [48]. DSMR testing was assigned an active role in clinical decision making with treatment directed either to a medical or invasive strategy in 1,532 patients. The authors found that DSMR is applicable in a clinical routine setting with a high success rate during a reasonably short examination time of less than 30 min. The study also confirmed that DSMR is safe [49], since only 3.6% of examinations had to be terminated due to limiting side effects during the administration of dobutamine/atropine without any hard cardiac events. DSMR proved useful as an arbiter for clinical decision making with regard to invasive versus medical treatment in patients with suspected and known CAD. The positive predictive value of DSMR to detect coronary luminal narrowing >50% was high (86%). A positive DSMR was a powerful predictor of future cardiac events, and a negative DSMR test result inferred a low risk for subsequent cardiac events (about 1% in the 2 years after stress testing). Notably, patients with early events had a significantly greater extent of ischemia suggesting that an early referral to invasive angiography may be advisable in this patient group. This finding corroborates results from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) nuclear substudy trial that the magnitude of residual ischemia is proportional to the risk for death or myocardial infarction [50].

Conclusions

Dobutamine stress magnetic resonance is a highly reliable and effective diagnostic tool to identify myocardial ischemia. Over and above its diagnostic value, DSMR provides prognostically relevant information and can be used to direct

patient management. There is compelling evidence that new quantitative methods assessing myocardial strain may enter the clinical arena soon. The combined assessment of wall motion, perfusion, and delayed enhancement during a single CMR session shows great promise to be the imaging method of choice to guide the clinical management of patients with known or suspected coronary artery disease.

Disclosure No potential conflicts of interest relevant to this article were reported.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance

1. Pennell DJ. Cardiovascular magnetic resonance. *Circulation*. 2010;121:692–705.
2. • Hundley WG, Bluemke DA, Finn JP, et al. ACCF/ACR/AHA/NASCI/SCMR 2010 expert consensus document on cardiovascular magnetic resonance: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. *Circulation*. 2010;121:2462–508. *A recent expert consensus document on CMR endorsed by major societies.*
3. Hundley WG, Hamilton CA, Thomas MS, et al. Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. *Circulation*. 1999;100:1697–702.
4. Hundley WG, Morgan TM, Neagle CM, et al. Magnetic resonance imaging determination of cardiac prognosis. *Circulation*. 2002;106:2328–33.
5. • 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;115:1769–76. *This study compares the prognostic value of adenosine stress perfusion and DSMR in the same patient population.*
6. Nagel E, Lehmkuhl HB, Bocksch W, et al. Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. *Circulation*. 1999;99:763–70.
7. Paetsch I, Jahnke C, Wahl A, et al. Comparison of dobutamine stress magnetic resonance, adenosine stress magnetic resonance, and adenosine stress magnetic resonance perfusion. *Circulation*. 2004;110:835–42.
8. Wellnhofer E, Olariu A, Klein C, et al. Magnetic resonance low-dose dobutamine test is superior to SCAR quantification for the prediction of functional recovery. *Circulation*. 2004;109:2172–4.
9. Kozerke S, Tsao J, Razavi R, et al. Accelerating cardiac cine 3D imaging using k-t BLAST. *Magn Reson Med*. 2004;52:19–26.
10. Tsao J, Boesiger P, Pruessmann KP. k-t BLAST and k-t SENSE: dynamic MRI with high frame rate exploiting spatiotemporal correlations. *Magn Reson Med*. 2003;50:1031–42.
11. Tsao J, Kozerke S, Boesiger P, et al. Optimizing spatiotemporal sampling for k-t BLAST and k-t SENSE: application to high-resolution real-time cardiac steady-state free precession. *Magn Reson Med*. 2005;53:1372–82.

12. Jahnke C, Paetsch I, Gebker R, et al. Accelerated 4D dobutamine stress MR imaging with k-t BLAST: feasibility and diagnostic performance. *Radiology*. 2006;241:718–28.
13. Paetsch I, Jahnke C, Ferrari VA, et al. Determination of interobserver variability for identifying inducible left ventricular wall motion abnormalities during dobutamine stress magnetic resonance imaging. *Eur Heart J*. 2006;27:1459–64.
14. Kuijpers D, Ho KY, van Dijkman PR, et al. Dobutamine cardiovascular magnetic resonance for the detection of myocardial ischemia with the use of myocardial tagging. *Circulation*. 2003;107:1592–7.
15. Garot J, Bluemke DA, Osman NF, et al. Fast determination of regional myocardial strain fields from tagged cardiac images using harmonic phase MRI. *Circulation*. 2000;101:981–8.
16. Aletras AH, Ding S, Balaban RS, et al. DENSE: displacement encoding with stimulated echoes in cardiac functional MRI. *J Magn Reson*. 1999;137:247–52.
17. Kim D, Gilson WD, Kramer CM, et al. Myocardial tissue tracking with two-dimensional cine displacement-encoded MR imaging: development and initial evaluation. *Radiology*. 2004;230:862–71.
18. Pan L, Stuber M, Kraitchman DL, et al. Real-time imaging of regional myocardial function using fast-SENC. *Magn Reson Med*. 2006;55:386–95.
19. Kraitchman DL, Sampath S, Castillo E, et al. Quantitative ischemia detection during cardiac magnetic resonance stress testing by use of FastHARP. *Circulation*. 2003;107:2025–30.
20. Korosoglou G, Futterer S, Humpert PM, et al. Strain-encoded cardiac MR during high-dose dobutamine stress testing: comparison to cine imaging and to myocardial tagging. *J Magn Reson Imaging*. 2009;29:1053–61.
21. Hor KN, Gottliebson WM, Carson C, et al. Comparison of magnetic resonance feature tracking for strain calculation with harmonic phase imaging analysis. *JACC Cardiovasc Imaging*. 2010;3:144–51.
22. Kelle S, Hamdan A, Schnackenburg B, et al. Dobutamine stress cardiovascular magnetic resonance at 3 Tesla. *J Cardiovasc Magn Reson*. 2008;10:44.
23. Strach K, Müller A, Kouwenhoven M, et al. Feasibility of high-dose dobutamine stress SSFP cine MRI at 3 Tesla with patient adaptive local RF shimming using dual-source RF transmission: initial results. *J Cardiovasc Magn Reson*. 2011:P101.
24. Mieres JH, Shaw LJ, Arai A, et al. Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: Consensus statement from the Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and Intervention, American Heart Association. *Circulation*. 2005;111:682–96.
25. Botvinick EH. Breast attenuation artifacts in Tl-201 scintigraphy. *Radiology*. 1988;168:878–9.
26. Geleijnse ML, Fioretti PM, Roelandt JR. Methodology, feasibility, safety and diagnostic accuracy of dobutamine stress echocardiography. *J Am Coll Cardiol*. 1997;30:595–606.
27. Gebker R, Jahnke C, Hucko T, et al. Dobutamine stress magnetic resonance imaging for the detection of coronary artery disease in women. *Heart*. 2010;96:616–20.
28. Nesto RW, Kowalchuk GJ. The ischemic cascade: temporal sequence of hemodynamic, electrocardiographic and symptomatic expressions of ischemia. *Am J Cardiol*. 1987;59:23C–30C.
29. Lubbers DD, Janssen CH, Kuijpers D, et al. The additional value of first pass myocardial perfusion imaging during peak dose of dobutamine stress cardiac MRI for the detection of myocardial ischemia. *Int J Cardiovasc Imaging*. 2008;24:69–76.
30. Gebker R, Jahnke C, Manka R, et al. Additional value of myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of coronary artery disease. *Circ Cardiovasc Imaging*. 2008;1:122–30.
31. Gebker R, Frick M, Jahnke C, et al. Value of additional myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of intermediate coronary artery disease. *Int J Cardiovasc Imaging*. 2010.
32. Di Bella EV, Parker DL, Sinusas AJ. On the dark rim artifact in dynamic contrast-enhanced MRI myocardial perfusion studies. *Magn Reson Med*. 2005;54:1295–9.
33. Gebker R, Jahnke C, Manka R, et al. High spatial resolution myocardial perfusion imaging during high dose dobutamine/atropine stress magnetic resonance using k-t SENSE. *Int J Cardiol*. 2011.
34. Manka R, Jahnke C, Gebker R, et al. Head-to-head comparison of first-pass MR perfusion imaging during adenosine and high-dose dobutamine/atropine stress. *Int J Cardiovasc Imaging*. 2010.
35. • Gebker R, Mirelis JG, Jahnke C, et al. Influence of left ventricular hypertrophy and geometry on diagnostic accuracy of wall motion and perfusion magnetic resonance during dobutamine stress. *Circ Cardiovasc Imaging*. 2010;3:507–14. *Demonstrates the influence of LVH and geometric patterns on the diagnostic accuracy of DSMR with and without additional perfusion imaging.*
36. Kelle S, Chiribiri A, Vierecke J, et al. Long-term prognostic value of dobutamine stress CMR. *JACC Cardiovasc Imaging*. 2011;4:161–72.
37. Charoenpanichkit C, Little WC, Mandapaka S, et al. Impaired left ventricular stroke volume reserve during clinical dobutamine stress predicts future episodes of pulmonary edema. *J Am Coll Cardiol*. 2011;57:839–48.
38. Wallace EL, Morgan TM, Walsh TF, et al. Dobutamine cardiac magnetic resonance results predict cardiac prognosis in women with known or suspected ischemic heart disease. *JACC Cardiovasc Imaging*. 2009;2:299–307.
39. Jahnke C, Furundzija V, Gebker R, et al. Gender-based prognostic value of pharmacological cardiac magnetic resonance stress testing: head-to-head comparison of adenosine perfusion and dobutamine wall motion imaging. *Int J Cardiovasc Imaging*. 2011.
40. • Dall'Armellina E, Morgan TM, Mandapaka S, et al. Prediction of cardiac events in patients with reduced left ventricular ejection fraction with dobutamine cardiovascular magnetic resonance assessment of wall motion score index. *J Am Coll Cardiol*. 2008;52:279–86. *Identifies the limitation of DSMR to predict prognosis in patients with an LVEF <40%.*
41. Smart SC, Knickelbine T, Malik F, et al. Dobutamine-atropine stress echocardiography for the detection of coronary artery disease in patients with left ventricular hypertrophy. Importance of chamber size and systolic wall stress. *Circulation*. 2000;101:258–63.
42. Walsh TF, Dall'Armellina E, Chughtai H, et al. Adverse effect of increased left ventricular wall thickness on 5 year outcomes of patients with negative dobutamine stress. *J Cardiovasc Magn Reson*. 2009;11:25.
43. • Charoenpanichkit C, Morgan TM, Hamilton CA, et al. Left ventricular hypertrophy influences cardiac prognosis in patients undergoing dobutamine cardiac stress testing. *Circ Cardiovasc Imaging*. 2010;3:392–7. *LVH was shown to be an independent prognostic marker over and above ischemia during DSMR.*
44. • Korosoglou G, Elhmidi Y, Steen H, et al. Prognostic value of high-dose dobutamine stress magnetic resonance imaging in 1,493 consecutive patients: assessment of myocardial wall motion and perfusion. *J Am Coll Cardiol*. 2010;56:1225–34. *A large single-center study on the complementary prognostic value of wall motion and perfusion imaging during DSMR.*
45. Korosoglou G, Lehrke S, Wochele A, et al. Strain-encoded CMR for the detection of inducible ischemia during intermediate stress. *JACC Cardiovasc Imaging*. 2010;3:361–71.
46. Korosoglou G, Lossnitzer D, Schellberg D, et al. Strain-encoded cardiac MRI as an adjunct for dobutamine stress testing: incremental value to conventional wall motion analysis. *Circ Cardiovasc Imaging*. 2009;2:132–40.

47. • Korosoglou G, Gitsioudis G, Voss A, et al. Strain-encoded cardiac magnetic resonance during high-dose dobutamine stress testing for the estimation of cardiac outcomes comparison to clinical parameters and conventional wall motion readings. *J Am Coll Cardiol.* 2011;58:1140–49. *This study demonstrates the added value of imaging strain during DSMR for prognostication.*
48. • Gebker R, Jahnke C, Manka R, et al. The role of dobutamine stress cardiovascular magnetic resonance in the clinical management of patients with suspected and known coronary artery disease. *J Cardiovasc Magn Reson.* 2011;13:46. *DSMR proved useful as an arbiter for clinical decision making with regard to invasive versus medical treatment.*
49. Wahl A, Paetsch I, Gollesch A, et al. Safety and feasibility of high-dose dobutamine-atropine stress cardiovascular magnetic resonance for diagnosis of myocardial ischaemia: experience in 1000 consecutive cases. *Eur Heart J.* 2004;25:1230–6.
50. Shaw LJ, Berman DS, Maron DJ, et al. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation.* 2008;117:1283–91.