Magnetic Resonance Low-Dose Dobutamine Test Is Superior to Scar Quantification for the Prediction of Functional Recovery

Ernst Wellhöfer, MD; Adriana Olariu, MD; Christoph Klein, MD; Michael Gräfe, MD; Andreas Wahl, MD; Eckart Fleck, MD; Eike Nagel, MD

Background—Low-dose dobutamine challenge (DSMR) by MRI was compared with delayed enhancement imaging with Gd-DTPA (SCAR) as a predictor of improvement of wall motion after revascularization (RECOVERY).

Methods and Results—In 29 patients with coronary artery disease (68±7 years of age, 2 women, 32±8% ejection fraction), wall motion was evaluated semiquantitatively by MRI before and 3 months after revascularization. SCAR and DSMR were performed before revascularization. The transmural extent of scar was assessed semiquantitatively. Binary prediction of RECOVERY was performed by logistic regression in 288 segments with wall motion abnormalities at rest. Receiver operating characteristic-area under curve (AUC) statistics were used to compare different models. Low-dose DSMR (AUC 0.838) was superior to SCAR (AUC 0.728) in predicting RECOVERY. SCAR did not improve accuracy of prediction by DSMR. Subgroup analysis showed superiority of DSMR for 1% to 74% transmural extent of infarction.

Conclusions—Low-dose DSMR is superior to SCAR in predicting RECOVERY. This advantage is largest in segments with a delayed enhancement of 1% to 74%. (Circulation. 2004;109:2172-2174.)

Key Words: hibernation ■ revascularization ■ dobutamine ■ magnetic resonance imaging

Hibernating myocardium is defined as reversible left ventricular dysfunction due to chronic coronary artery disease that improves after revascularization. Patients with hibernating myocardium who are treated with revascularization rather than medical therapy have better outcomes. 1 Recently, quantification of the transmural extent of delayed enhancement by MRI (SCAR) has been shown to predict the likelihood of recovery of myocardial function after revascularization (RECOVERY). However, in non-transmural scars (1% to 74%), only an intermediate likelihood of RECOVERY (82% in SCAR <25% to 7% in SCAR 50% to 74%) was found. 2 The viable myocardium surrounding the scar may be normal, remodeled, hibernating, stunned, or ischemic. A dobutamine test depends on both function of viable and extent of nonviable myocardium and may therefore be superior to SCAR in predicting recovery.

Although low-dose dobutamine stimulation assessed by MRI (DSMR) has been used for many years to predict hibernating myocardium, 3,4 a direct comparison to SCAR as predictor of RECOVERY has not been performed in patients with chronic hibernation.

Methods

Patients and Study Design

A prospective blinded within-patient comparison of DSMR and SCAR was performed in 29 patients (68±7 years, 2 women, 27 with previous infarction, 13 with previous coronary artery bypass grafting, 12 with diabetes, and 28 with hyperlipidemia). Fifty patients without contraindications for MRI were screened for the following inclusion criteria: (1) chronic coronary artery disease with stable angina; (2) ejection fraction <45% (mean, 32±8%); (3) at least 2 adjacent segments with wall motion abnormalities at rest; and (4) no infarction within the last 2 months. Definite study inclusion occurred after coronary revascularization (percutaneous coronary intervention, 25 of 50; coronary artery bypass grafting, 4 of 50 patients). The primary success of revascularization was controlled by a review of all angiograms.

DSMR and SCAR were performed 1 day before revascularization. RECOVERY was verified at 3 months after revascularization. Informed consent was obtained from all patients. The local institutional review committee approved the study.

Magnetic Resonance Imaging

SCAR was evaluated 10 to 15 minutes after Gd-DTPA (0.2 mmol/kg) injection (Philips ACS, NT, 1.5-Tesla system, inversion recovery turbo gradient echo sequence, 5 pulse-delay optimized for maximal myocardial signal suppression; TE/TR/flip: 3.6/8/15). Inversion time (200 to 250 ms) was optimized for each measurement. Transmurality of SCAR was assessed on a 5-grade scale. 2 In borderline visual scoring, transmurality was determined by automatic segmentation. 6

Wall motion was assessed at rest and at the end of each dosage of dobutamine for 2-, 3-, and 4-chamber long-axis views and short-axis views at 3 levels by steady-state free precession imaging (echo time, 1.3 ms; repetition time, 2.6 ms; flip angle, 60 degrees; field of view, 350 mm; spatial resolution, 2×2×8 mm; temporal resolution, 40 ms; acquisition, 7 beats; 2 breathing cycles between 2 successive breath holds). Angulation was kept constant for short-axis and SCAR imaging to enable the use of 3D coordinates to match SCAR and wall motion images. After revascularization, only images at rest were acquired by the same technique.

Wall motion was graded as normokinesia, hypokinesia, akinesia, and dyskinesia in the 16-segment model 7 by 2 blinded

DOI: 10.1161/01.CIR.0000128862.34201.74

2172
investigators. Discordant assessments (19%) were jointly re-
viewed. An improvement of wall motion at follow-up by at least
1 grade was regarded as RECOVERY. DSMR (5 and 10 g/kg
per min for 3 minutes) was regarded as indicative of viability
when there was an improvement of 1 grade at either the 5- or the
10-g/kg per min dose. Reviewers of DSMR, SCAR, and
RECOVERY were blinded to each other.

Statistics
We analyzed 288 of 464 (29 patient X 16 segments) segments with
wall motion abnormalities at rest. Binary prediction of RECOV-
ERY was modeled by logistic regression. Different predictive
models were compared by receiver operating characteristic–area
under curve (ROC-AUC) statistics (SPSS 10.0).

Sensitivities, specificities, prevalences, and accuracy were calcu-
lated. Interobserver and intraobserver agreement was assessed in
15 patients (92 segments) for RECOVERY, DSMR, and SCAR
(Cohen’s κ, 0.7 to 0.78 interobserver, 0.80 to 0.89 intraobserver).

Results

SCAR
The logistic regression model for SCAR (25% cutoff) pre-
dicted 73% of hibernating segments correctly. RECOVERY
decreased with increasing extent of scar (Figure 1).

DSMR
DSMR predicted 85% of hibernating segments correctly. The ROC
analysis in Figure 2 and the subgroup analysis in Figure 1 demon-
strate that accuracy of the test does not depend on the transmural-
ity of scar.

SCAR and DSMR
DSMR predicted RECOVERY better than SCAR (P<0.05)
(Figure 2, A and D). The cutoff value had no impact on this
result (Figure 2D). When SCAR was performed, additional
DSMR improved accuracy of prediction, whereas the reverse
was not true (Figure 2A). The specificity of DSMR was
higher and the sensitivity comparable to SCAR.

The ROC analysis in Figure 2 (subplot C) demonstrates a
particularly low predictive value of SCAR as opposed to
DSMR in scar, with 1% to 74% transmurality.

Discussion

SCAR
Recent technical improvements and quantitative scar grading
increased the diagnostic value of delayed enhancement.5,8
The technique delineates the extent of infarction9–12 and
assesses the likelihood of RECOVERY before revasculariza-
tion.2,8,13–15 SCAR was found to be more sensitive and to
 correlate well with PET imaging, the “gold standard” for
diagnosis of viability in the past.16,17 The decreasing likeli-
hood of RECOVERY with more extensive scar found in the
present study underlines the prognostic importance of scarred
myocardium in agreement with previous studies.2,8

SCAR accurately localizes and quantifies scarred (nonvi-
able) myocardium. If a scar is not transmural (SCAR 1% to

Figure 1. Transmurality of scar: subgroup analysis. Bars refer to
the prevalence of recovery and sensitivity, specificity, and per-
centage of correct predictions by DSMR and are subgrouped
with respect to SCAR (cutoff, 25%). The specificity of DSMR
remains high irrespective of the extent of SCAR. The test retains
a high sensitivity in 25% to 49% SCAR.

Figure 2. ROC curves. The logistic
model combining SCAR and DSMR is
compared with DSMR alone and the
logistic prediction by SCAR alone. Based
on confidence intervals, the AUC values
are significantly (P<0.05) higher for
DSMR than SCAR and DSMR+SCAR
than SCAR alone in all segments (sub-
plot A, cutoff 25%) and the segments
with 1% to 74% transmurality of SCAR
(subplot C, cutoff 25%). There was no
significant difference between DSMR and
SCAR in segments without scar or SCAR
transmurality >75% (subplot B, cutoff
25%). The increase of the AUC of
DSMR+SCAR compared with DSMR
alone was not significant. Subplot D
compares DSMR and SCAR with differ-
ent cutoffs (25% and 50%) in all segments.
74%), however, this technique fails to assess the functional state of the surrounding (viable) myocardium (normal, remodeled, hibernating, stunned, and ischemic).

**DSMR**

Low-dose dobutamine may improve contractile function and cellular energetics in hypoperfused myocardium\(^1\) and perfusion by collaterals or dynamic stenoses.\(^19,20\) Thus, the test simulates effects of revascularization. The myocardial shortening and wall thickening induced by dobutamine predominantly affect the inner layers of segments with subendocardial infarcts,\(^21\) but midwall and subepicardial inotropic reserve had a prognostic impact on RECOVERY.\(^22\) Because inotropic reserve depends on the presence of sufficient viable myocardium, it was found to be confined to areas with nontransmural infarction (38±3% transmurality).\(^23\) This explains the steeply declining sensitivity of the DSMR in scars ≥50% and the high sensitivity in scars 1% to 49%.

**SCAR and DSMR**

One recent study compares DSMR to SCAR as predictors of RECOVERY after acute myocardial infarction.\(^24\) Despite protocol differences (quantitative analysis and different segmentation), the lower specificity and accuracy of SCAR compared with DSMR found in that study agrees with our results. The correlation of negative dobutamine tests with the extent of delayed enhancement by MRI demonstrated some overlap of test information. Whereas additional DSMR, which depends on the functional reserve of viable nonviable tissue, improved the diagnostic accuracy of SCAR, the reverse was not true (no functional reserve of scars). DSMR is very sensitive in SCAR <50% because of enhanced thickening of the inner layers of myocardium.\(^25\) The high specificity of the test is preserved in more transmural scars.

**Limitations**

Verification of RECOVERY at 3 months seems sufficiently late in view of the high percentages of correct predictions. Although restenosis was not controlled invasively, noninvasive follow-up was free of symptoms or signs, indicating recurrent ischemia. Visual assessment of wall motion is a limitation of the present study. Quantitative assessment of wall motion by tagging combined with rapid postprocessing algorithms may additionally enhance sensitivity of DSMR and assessment of RECOVERY (Fast-HARP).\(^25\)

**Conclusion**

Delayed enhancement and DSMR provide complementary information. Delayed enhancement localizes and quantifies scar but has impaired specificity as a predictor of RECOVERY in nontransmural scars (1% to 74%). DSMR is superior to delayed enhancement as a predictor of RECOVERY and does not depend on the transmurality of scar.

**References**

Magnetic Resonance Low-Dose Dobutamine Test Is Superior to Scar Quantification for the Prediction of Functional Recovery
Ernst Wellnhofer, Adriana Olariu, Christoph Klein, Michael Gräfe, Andreas Wahl, Eckart Fleck and Eike Nagel

Circulation. 2004;109:2172-2174; originally published online April 26, 2004;
doi: 10.1161/01.CIR.0000128862.34201.74
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/18/2172

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/