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

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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

# 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 prepulse-delay optimized for maximal myocardial signal suppression; TE/TR/fip: 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 model7 by 2 blinded

# Conclusion

Low-dose DSMR is superior to SCAR in predicting RECOVERY. This advantage is largest in segments with a delayed enhancement of 1% to 74%.

# Key Words

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investigators. Discordant assessments (19%) were jointly reviewed. An improvement of wall motion at follow-up by at least 1 grade was regarded as RECOVERY. DSMR (5 and 10 μg/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-μg/kg per min dose. Reviewers of DSMR, SCAR, and RECOVERY were blinded to each other.

Statistics
We analyzed 288 of 464 (29 patient × 16 segments) segments with wall motion abnormalities at rest. Binary prediction of RECOVERY 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 calculated. 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) predicted 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 demonstrate that accuracy of the test does not depend on the transmurality 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 revascularization.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 likelihood 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 (nonviable) myocardium. If a scar is not transmural (SCAR 1% to 25% transmurality) the test is not helpful. However, if scar is transmural (SCAR > 25% transmurality) the test is highly specific and sensitive for predicting RECOVERY.

Figure 1. Transmurality of scar: subgroup analysis. Bars refer to the prevalence of recovery and sensitivity, specificity, and percentage 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 (subplot 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 different 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\(^{18}\) and perfusion by collaterals or dynamic stenoses.\(^{19,20}\) Thus, the test simulates effects of revascularization. The myoﬁber 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\(^{25}\) implies 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.\(^{26}\) 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 intensively, 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**
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