

Detection of coronary stenosis at rest using Blood Oxygen-Level Dependent Magnetic Resonance Imaging

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In the clinical evaluation of coronary artery disease (CAD), a desirable goal is to identify functionally significant disease without recourse to physical or pharmacological stress. Previous studies utilizing myocardial contrast echocardiography have demonstrated microvascular dilation at rest in post-stenotic myocardium.(1) Blood oxygen-level dependent (BOLD) magnetic resonance imaging (MRI) is a technique which can detect myocardial ischemia.(2) The transition from diamagnetic oxyhemoglobin to paramagnetic deoxyhemoglobin induces T2 or T2* differences, thereby generating oxygen-dependent MR contrast. In diseased myocardium, BOLD signal differences relative to normal myocardium may reflect not only differences of blood oxygenation, but also of vascular volume. Increased microvascular volume, with concomitant increase in the absolute quantity of hemoglobin, is expected to alter BOLD signal. We postulated that BOLD imaging at rest could be exploited to detect functionally significant CAD without stress.

In a previously published study, we determined the diagnostic performance of stress BOLD imaging in identifying significant CAD.(3) For the present analysis, resting BOLD data from this earlier study were examined. Patient selection and study protocol are as previously described, involving BOLD and first-pass perfusion imaging at 3 Tesla.(3) Resting BOLD signal intensity (SI) was first evaluated in a derivation group comprising 20 normal volunteers and 25 patients with known CAD (single-/two-vessel disease), and then tested in a separate validation group (57 patients with suspected CAD referred for diagnostic coronary angiography). Anatomically significant CAD was defined as $\geq 50\%$ coronary stenosis, and functionally significant CAD, as ≥ 1 myocardial segment with hyperemic myocardial blood flow (MBF) $\leq 1.6 \text{ ml/min/g}$.(4)

Baseline characteristics for the study participants are as previously described.(3) Owing to marked interindividual variation in absolute segmental BOLD SI, segment-based analysis of BOLD SI failed to identify hypoperfused segments (area-under-curve 0.52 ± 0.04 , $p=0.71$). We

next evaluated whole-slice BOLD SIs by measuring the within-subject spread of resting BOLD segmental values as defined by a rest BOLD index (interquartile range of myocardial segment SIs/ median segmental SI). Rest BOLD index was greater in subjects with CAD than in volunteers (22.6%, 95% CI 17.0-28.3% versus 15.4%, 95% CI 11.1-19.7%; $p=0.038$) and ROC curve analysis defined a 16.1% threshold for identifying subjects with ischemia (area-under-curve 0.72 ± 0.08 , $p=0.0078$, 72% sensitivity and 78% specificity). Applying this threshold in the validation group, identified patients with functionally significant CAD with sensitivity 88% (95% CI 80-97%), specificity 58% (95% CI 45-71%) and diagnostic accuracy 75% (95% CI 64-86%), and for anatomically significant CAD, sensitivity 82% (95% CI 72-92%), specificity 61% (95% CI 48-74%) and diagnostic accuracy 75% (95% CI 64-86%). Nine patients had infarction in the BOLD imaging slice (mean transmuralitity $48\pm20\%$): CAD was correctly identified by rest BOLD in 7/9 patients (78%).

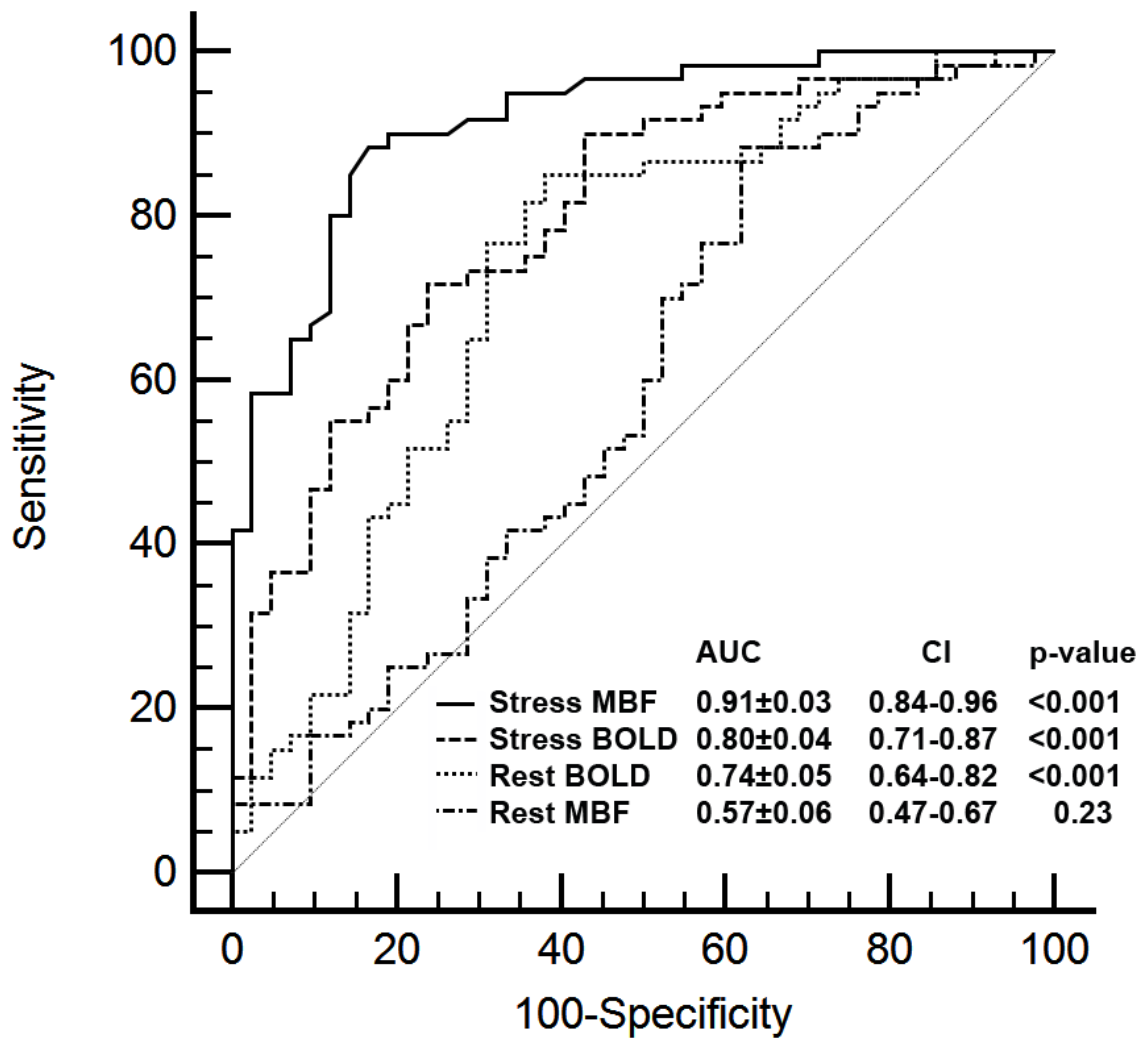
Data from both study arms were pooled to compare the discriminatory abilities of hyperemic MBF, resting MBF, stress and rest BOLD indices (Figure 1). Using QCA as the reference standard, hyperemic MBF had the highest discriminatory ability, and resting MBF, the lowest; stress and rest BOLD performed comparably (area-under-curve 0.80 ± 0.05 versus 0.74 ± 0.05 , respectively, $p=0.34$). Using hyperemic MBF as the reference standard, both BOLD indices performed comparably (area-under-curve 0.80 ± 0.04 versus 0.73 ± 0.05 , $p=0.24$).

These data indicate that BOLD imaging detects anatomically and functionally significant CAD without the need for physiological or pharmacological stress. Our findings are pertinent to alternative imaging modalities with the potential to identify microvascular heterogeneity, and advance the concept of a functional assessment of CAD being performed at rest. The inability of resting MBF to discriminate the presence of CAD indicates that the favorable diagnostic performance of resting BOLD assessment is not dependent on changes in resting MBF.

Although the observed change in resting BOLD SI is likely to reflect microvascular expansion, the underlying pathophysiological mechanism was not determined in our study: other factors may contribute to heterogeneous BOLD SI, including transit time heterogeneity, unequal hematocrit partition at bifurcations or myocardial hypertrophy leading to variations in regional demand. Similarly, coexisting microvascular pathology (e.g. diabetes, hypertension) may reduce diagnostic accuracy in CAD. Other limitations include the persistence of imaging artefact, which contributed to the limited specificity observed, and the use of a whole-slice index, which precluded assessment of the territory and extent of CAD. These issues may be addressed in future studies utilizing absolute quantification of T2* and cardiac-phase resolved imaging. Further study of resting microvascular function and oxygenation may offer valuable insights into the pathophysiology and pharmacotherapy of CAD.

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Figure 1 ROC curves for BOLD and perfusion imaging using quantitative coronary angiography as the reference standard



AUC=area-under-curve, CI=confidence interval