

# Diagnostic accuracy of Blood-Oxygen Level Dependent imaging and comparison with coronary angiography in patients with coronary artery disease

Hamidreza Pouraliakbar, Fallah Eshnab\*, Ali Nahardani

Department of Radiology, Shahid Rajaee Hospital, Iran University of Medical Sciences, Tehran, Iran.

**Correspondence:** Fallah Eshnab, Resident of Radiology, Radiology Department, School of Medicine, Shahid Rajaee Cardiovascular Research and Medical Center Iran University of Medical Science, Tehran, Iran. Email: falah.eshnab66@gmail.com.

## ABSTRACT

**Background:** Diagnosis of coronary artery disease (CAD) is one of the important aspects of management and treatment of these patients. The purpose of this study was to evaluate the diagnostic accuracy of Blood Oxygen Level Dependent (BOLD) cardiovascular magnetic resonance (CMR) in coronary artery disease compared with invasive angiography. **Methods:** A total of 20 patients with suspected CAD were enrolled. All patients were subjected to invasive angiography using standard and conventional methods. BOLD CMR was performed in 3 short axis slices of the heart at rest and during adenosine stress ( $140 \mu\text{g}/\text{kg}/\text{min}$ ) followed by late gadolinium enhancement (LGE) imaging ( $2\text{mmol}/\text{kg}$  gadolinium). **Results:** In this study 20 patients were studied in 11 (55%) males and 9 (45%) females with an average age of  $59.34 \pm 5.43$  years. 16 (80%) patients were diagnosed with coronary artery disease. The mean and standard deviation of delta t2 in patients with an abnormal angiogram ( $-3.49 \pm 4.40$ ) are higher than those with normal angiogram ( $2.83 \pm 0.17$ ). However, these changes were significant between the two groups ( $p = 0.006$ ). The BOLD imaging diagnostic power for coronary artery disease was shown to be 0.788 (standard deviation 0.57-0.100) for the delta t2 variable. **Conclusion:** The results of this study indicate that BOLD imaging can be a non-invasive technique suitable for diagnosing CAD compared with invasive methods.

**Keywords:** Coronary artery disease, BOLD imaging, cardiovascular magnetic resonance, angiography

## Introduction

Coronary artery disease (CAD) is a common cardiovascular disease. Each year, the disease develops in many advanced societies, especially in advanced ages. CAD due to the deposition of fat / calcium plaques along the coronary artery surface, which results in lower blood flow to the endocardium coronary arteries and reduces the amount of oxygen in the bloodstream, leading to myocardial infarction, and if the amount of oxygen is reduced, it is lower than the tolerable threshold of the heart tissue, myocytes are necrosis and

myocardial infarct occurs<sup>[1]</sup>. Considering the advancement of medical imaging technology and the emergence of different imaging techniques in this field, it is now possible to evaluate the rate of coronary artery stenosis using invasive angiography and semi invasive such as CT angiography with iodinated contrast, but each these methods have potential hazards, obvious limitations and disadvantages<sup>[2-4]</sup>. For example, angiographic imaging is a completely invasive imaging, in which events such as coronary artery dissection. Another example is the use of CT angiography, which is used in this diagnostic method of iodinated contrast agents that restricts the use of this contrast agent in some patients, such as renal failure or drug allergies. Another method is Single Photon Emission Computed Tomography (SPECT). One of the most obvious disadvantages of this method is the use of radionuclides ( $\text{Tc}99\text{m}$ ) to diagnose the disease. Here it should be noted that the absorption dose of patients in this method is relatively higher than the methods of angiography and CT angiography and have lower sensitivity and specificity in the estimation of the severity and degree of vascular aesthetic (less diagnostic accuracy)<sup>[5]</sup>. In general, the images obtained from all existing modalities, other than MRI,

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are either completely anatomical or functional, so that none of them has been able to provide a combination of these two data in a hundredths of a combination. Meanwhile, MRI is the only modality that has been able to provide highly desirable functional information for cardiovascular experts along with illustrations. In addition to the ability of MRI to obtain data anatomical and functional, this modality instead of ionizing radiation and radioactive drugs, and the combination of both magnetic field and radio waves to imaging used and no biological effects of potential so far show this attribute has led MRI to be widely accepted by cardiologists, especially the pediatric cardiology [6]. One of the new techniques of using MRI is the perfusion MRI method, which is based on gadolinium-based contrast agent injection, and provides continuous images of gadolinium entering and exiting from the heart and myocardial cavities. In this shooting, the most important sequence used is Single Shot turbo FLASH, which contains a lot of noise. Unfortunately, in a variety of perfusion imaging, contrast agents are not strongly recommended in patients with renal insufficiency. To overcome this problem, we have tried to diagnose coronary artery disease using the MRI machine using the new method called Blood-Oxygen Level Dependent imaging (BOLD). In this method, after the injection of stressor drugs, the blood acts as a contrast agent [7-9]. In this study, we intend to examine the diagnostic accuracy of BOLD imaging in patients with coronary artery disease (CAD).

## Methods

This study was performed on 20 patients with complaints of chest pain who were referred to the shahid Rajaie heart center (Tehran, Iran). Inclusion criteria: patients aged 40 to 80 years, suspected CAD (regardless of whether or not the percutaneous angiogram was performed, regardless of the history of myocardial infarction). Exclusion criteria included a history of heart surgery, CMR contraindications (such as metal implants, claustrophobia), and contraindication of adenosine administration (asthma, the first degree block of the atrioventricular). All patients were physically checked and history was collected. All patients' demographic and clinical data were collected from the patients by questionnaires. Anthropometric measurements of waist circumference (CM) and BMI (kg/m<sup>2</sup>) were measured according to the standard method. All patients received written moral consent.

### Coronary angiography:

Before CMR for detection of CAD in patients and in the 2 weeks after CMR, all subjects underwent invasive coronary angiography using standard protocol. Images of the coronary arteries were obtained in multiple projections, with avoidance of overlap of side branches and foreshortening of relevant coronary stenosis.

## MRI and BOLD imaging

MRI was performed on a 1.5-Tesla system (Avanto Siemens) with a whole-body gradient coil (switching capacity, 40 mTm-1

within 268μs). For BOLD-MRI, a single-slice interleaved T2\*-sensitized gradient-echo echo planar imaging (EPI) pulse sequence was used for BOLD with the following parameters: (FOV: 280mm, Data matrix: 128 \* 128, Flip angle: 15-degree slice thickness: 8mm, ECG gating was also used. MRI was done in rest and stress mode. Before intravenous injection of gadolinium agent and adenosine as a stressor agent, MRI sequences routine as well as T2 \* gradient echo were performed. Then to evaluate myocardial enhancement and scar areas gadolinium with dose of 0.2 mmol/kg was injected. Also adenosine was infused at a dose of 140 μg / kg / min for 4 minutes. MRI was performed in the short axis and in the basal, mid ventricular and apex of the heart. Signal intensity T2 \* was measured before and after injection of adenosine at this three levels territory of main coronary arteries (LAD, LCX, RCA). Signal changes are defined by delta signal intensity (ΔSI) and negative results for SI were considered as significant stenosis. Delta Signal Intensity T2 \* = SI stress - SI rest.

## Statistically analysis

ANOVA was used to test continuous variables. A contingency analysis with Fisher's exact test was used. All statistical analysis of the data was performed by SPSS 19) SPSS Inc, Chicago, USA) software. A P value <0.05 was considered significant. ROC analyses were used for diagnostic accuracy of BOLD imaging of CAD.

## Results

In this study, data of 20 patients were analyzed. 11 patients (55%) were male and 9 (45%) were female and the mean and standard deviation (SD) age of the patients was  $59.34 \pm 5.43$  years. The mean  $\pm$  SD of patients were  $26.54 \pm 3.24$  kg/m<sup>2</sup>. In terms of drugs, 13(65%) of patients used aspirin and 12 (60%) use statins. Also, 9 (45%) patients used beta-blockers and 8 (40%) had also consumed calcium channel blocker (CCB). 13% (65%) of patients with hypertension, 9 (45%) of diabetes, 5(25%) had previous history of ischemic heart disease (IHD), 6 (30%), hypercholesterolemia, 5 (25%) had familial history and 6(30%) smokers. In the angiographic survey, it was found that 4 (20%) of the patients did not have any angioplasty evidence of CAD. Also, in 4cases (20%), LCX, in 5 cases (25%), RCA and 7 case (35%) LAD was involvement. Also, in 8 cases (40%), one of the vessels, in 2 case (10%) two vessel, in 3 case (15%) tree vessels, and in 3 case (15%) four vessels were involved. In Figure 1, the mean and confidence interval of delta T2 is shown. As it is known, the mean  $\pm$  SD of this variable in patients with an abnormal angiography ( $-3.59 \pm 4.40$ ) are more than those with normal angiography ( $2.83 \pm 0.17$ ). These changes were significant between the two groups ( $p = 0.006$ ). In Figure 2, the mean  $\pm$  confidence intervals and delta T2 in BOLD imaging are shown in terms of coronary artery involvement. As it is known, the mean of this variable is not significantly different in terms of artery territory ( $p = 0.432$ ). Mean  $\pm$ SD in the LAD was  $0.62 \pm 3.30$ , in LCX was  $-1.50 \pm$

3.9 and in RCA was  $33.2 \pm 3.22$ , respectively. The BOLD imaging diagnostic power for CAD was shown to be 0.788 (CI 95%: 0.57-0.100) for the delta T2 variable.

## Discussion

Today, the use of non-invasive techniques to examine suspected or known patients with coronary arteries has become a challenge. Conventional cardiac patients tests, such as electrocardiography, echo or invasive angiography, have many disadvantages. But it's one of the noninvasive techniques is BOLD imaging that many studies have been done on its use in CAD patients. In this method, myocardial deoxygenation is identified by a net relative increase of de-oxygenated hemoglobin in the coronary artery and thus leads to T2\* shortening, which can be visualized by T2\* maps or by a regional signal loss in "T2\*-weighted" MR images. Also a reduce of the proportion of de-oxygenated hemoglobin causes a relative decrease of de-oxygenated hemoglobin and leads to an increase of T2\* in coronary territory and hence to an increased signal intensity in oxygenation-sensitive image [4, 8]. In our study, we investigated the BOLD imaging assessment of 20 suspected to coronary artery disease. The mean age of our patients was 59.34 years and most of them were males (60%). In the 20 patients studied, 4 patients had no evidence of CAD. The results of our study showed that the mean of delta T2 in patients with abnormal angiography was significantly higher than those with normal angiography. It was also shown that ROC under area of the BOLD imaging for CAD in our study was 0.788 (CI95%: 0.570-0.100). However, some other studies also examine the diagnostic power of this technique in CAD. Manka et al. showed that in 34 patients, the ROC area of delta T2 was 0.61 in rest and stress and 0.82 in stress for diagnosis of CAD [10]. Another study by Friedrich et al. On 25 patients that referred with chest pain showed that the ROC area for the BOLD diagnostic imaging was 0.66 and 0.63 for the SPECT [11]. Another study by Karamitsos et al, in 22 patients, reported that the ROC area for the BOLD imaging technique for CAD detecting was 0.78 [9]. These studies all rely on the uses of this method in the diagnosis of coronary artery stenosis compared with invasive methods, such as invasive angiography. The diagnostic power of our study is similar to the results of other studies. Therefore, with this technique, it is possible to detect cardiac ischemia with a desirable sensitivity and specificity. Despite of the other imaging methods, BOLD does not utilize ionizing radiation and any external contrast agents to form its contrast; thus, this technique is a safe method for young people and the patients who suffer from acute or chronic renal failure [12, 13]. Despite of the usefulness of BOLD, it suffers from a variety of limitations including the proper patient cooperation, low signal to noise ratio of the proposed sequence, slight BOLD signal changes in mild to moderate stenosis, etc. This technique benefits from the intrinsic source of contrast in the myocardium and eliminates the need for any gadolinium based agents injection to produce its contrast.

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## Disclosures

The authors declare that there is no conflict of interest.

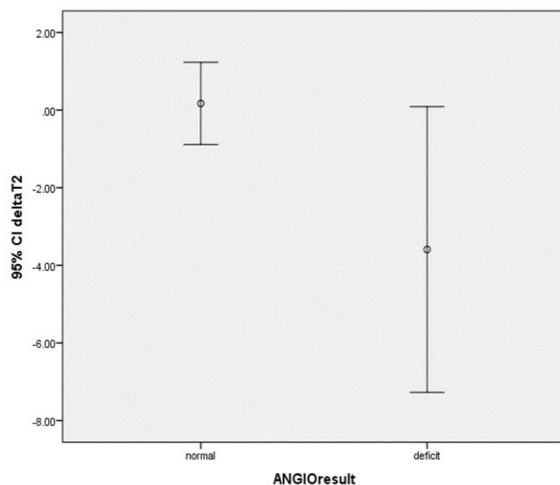
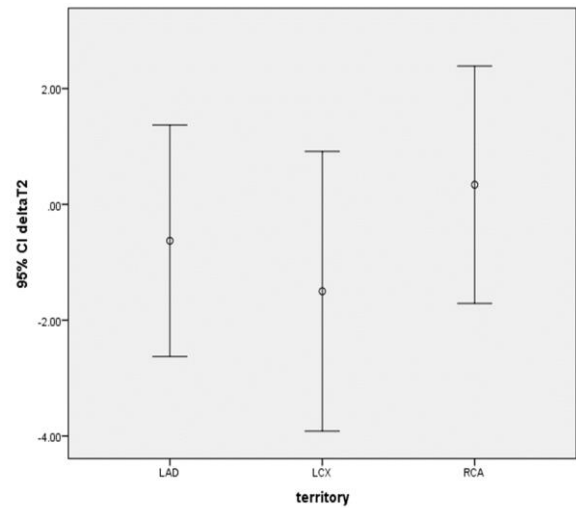
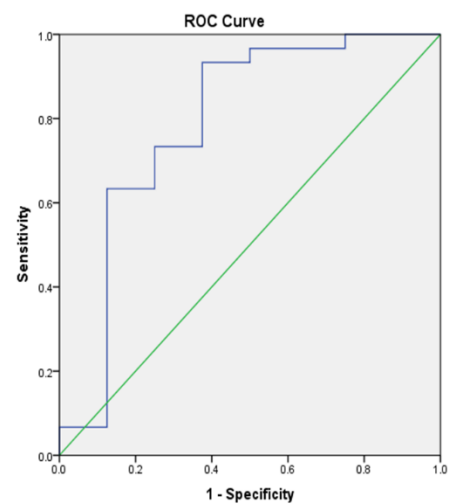
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**Table 1. Basic, clinical and angiographic characteristics of patients**

Variable	CAD Patient, n =20 N(%), mean $\pm$ SD
Sex, n (%)	
Male, n (%)	11(55%)
Female	9(45%)
Age(yrs)	59.34 $\pm$ 5.43
BMI,(kg/m <sup>2</sup> )	26.54 $\pm$ 3.24
Medication, n (%)	
Aspirin	13(65%)
Statin	12(60%)
Beta-blocker	9(45%)
Calcium blocker	8(40%)
Nitrate	7(35%)
ACE inhibitor	8(40%)
Co morbidities	
Familial history	5(25%)
Diabetes	9(45%)
Hypertension	13(65%)
Hypercholesterolemia	6(30%)
Smoking	6(30%)
IHD	5(25%)
Vessel disease	
LCX	4(20%)
RCA	5(25%)
LAD	7(35%)
Single	8(40%)
Double	2(10%)
Triple	3(15%)
Multiple	3(15%)
Without CAD	4(20%)

**Figure 1.** Mean and confidence interval of T2 according to angiography result.**Figure 2.** Mean and confidence interval of T2 according to territory result.**Figure 3.** ROC analysis showing of diagnostic performance of BOLD imaging to specify of coronary artery disease.