MRI Evaluation of Coronary Versus Systemic Endothelial Function in Healthy Subjects and Patients with Coronary Artery Disease

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Target audience: Cardiologists and radiologists with interest/expertise in coronary vascular imaging.

Purpose: Endothelial-dependent coronary artery vasoreactivity is an important indicator of vascular function and predicts cardiovascular events. The coronary vasculature differs from systemic vascular beds in terms of its paradoxical vasoconstrictor response to endothelial-dependent stressors and a recent noninvasive 3T MRI approach combined with isometric handgrip exercise (IHE) for quantifying coronary endothelial function (cor endo fx) was reported.[1,2] The internal mammary artery (IMA) differs from many systemic vascular beds in that it almost never develops atherosclerosis (and thus is often used in coronary bypass surgery) and could serve as an index of systemic vascular function, in the absence of atherosclerosis. Therefore we proposed that both cor endo fx and systemic endo fx can be assessed in the same MRI acquisition and we tested the hypothesis that cor endo fx is impaired compared to systemic endo fx (as measured by IMA vasoreactivity) in the same CAD patients.
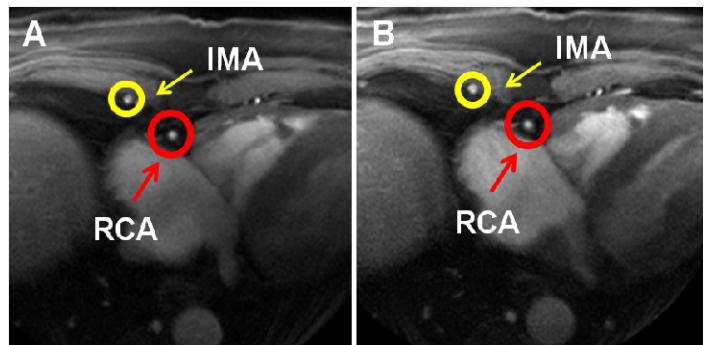
Methods: We studied seven patients with known coronary artery disease (mean age±SEM=65.4±0.9 years, 3 women) and seven healthy volunteers (38.6±3.7 years, 4 women). Each subject was placed in the prone position in a commercial 3T MRI scanner (Achieva, Phillips, Best, NL) using a 32-element cardiac coil for signal reception. For the assessment of endo fx, the temporal/spatial resolution for the anatomical images was 15ms/0.89x0.89x8.0mm^3. The radiofrequency (RF) excitation angle was 20°, 17 spiral interleaves were acquired and all scans were prospectively triggered. Both the right coronary artery (RCA) and an IMA were imaged in cross-section in the same cine sequence. Baseline images were acquired at rest for cross-sectional coronary artery and IMA area measurements, followed by repeat imaging during 4 minutes of IHE at 30% of maximum grip strength (**Figure 1**). Images were analyzed for RCA and IMA cross-sectional area using semi-automated software (Cine version 3.15.17, General Electric, Milwaukee, WI) and change in area from rest to stress was quantified.

Results: During IHE in healthy subjects, mean RCA area increased (mean ±SEM, baseline RCA area 10.3±0.9mm^2 vs. stress 11.6±1.4mm^2, p=0.07) and mean IMA area also increased (baseline IMA 8.5±0.9mm^2 vs. stress IMA 9.6±1.1mm^2, p=0.006). There was no significant difference in % area change with stress for the RCA compared to IMA in healthy subjects (p=0.61). In the CAD subjects, mean RCA area did not however increase with IHE (baseline RCA 14.5±1.8 mm^2 vs. stress area 14.7±1.9mm^2, p=0.59), whereas IMA area did increase significantly with stress (baseline IMA 10.4±1.4mm^2 vs. stress 11.6 ± 1.7, p=0.019). There was a difference in response in the CAD group between the RCA % area change and IMA % area change with stress that was of borderline statistical significance (p=0.05), **Figure 2**. There was no significant difference between IMA % area change with IHE between the healthy and CAD group (P=0.48).

Discussion: Using 3T MRI combined with IHE to quantify endothelial-dependent vasoreactivity, we confirmed earlier findings that coronary vasodilatation does not occur in CAD patients during IHE and report for the first time that the IMA exhibits a greater degree of vasodilation than the RCA in CAD patients. There was no significant difference in coronary and systemic endothelial response in the healthy subjects. These findings demonstrate that it is now possible to non-invasively evaluate both coronary and systemic endothelial function concurrently in a single MRI acquisition and this may offer important insights into the pathobiology of atherosclerosis in different atherosclerotic and atherosclerosis-free vascular beds.

Conclusion: 3T MRI with IHE provides a novel non-invasive method to assess the vascular endothelial response in two physiologically different vascular beds (coronary and systemic) in the same person, and in some situations, within the same MRI acquisition. This technique may guide future intervention studies and allow for safe and repeated measures of endothelial response over time.

Figure 1. Example of a cross section of an RCA (right coronary artery) and IMA (internal mammary artery) at baseline (A) and during isometric handgrip stress (B) in a CAD patient. In this patient there was an increase in IMA area with stress, but no significant increase in RCA area with stress using semi-automated software analysis.
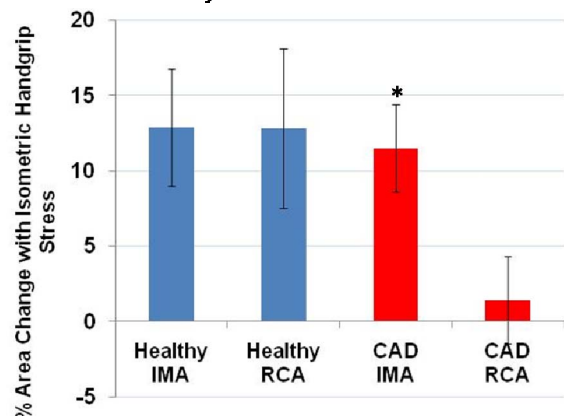
Figure 2. Percent change in coronary cross sectional area (RCA, right coronary artery) and change in cross sectional IMA (internal mammary artery) area with isometric handgrip stress in healthy subjects (blue bars) and CAD patients (red bars). There was a borderline statistically significant difference in IMA Vs. RCA area change in CAD patients (*P=0.05).

References: 1. Hays AG, Hirsch GA, Kelle S, Gerstenblith G, Weiss RG, Stuber M. Noninvasive visualization of coronary artery endothelial function in healthy subjects and in patients with coronary artery disease. *J Am Coll Cardiol*. 2010;56:1657-1665
2. Hays AG, Kelle S, Hirsch GA, Soleimanifard S, Yu J, Agarwal HK, Gerstenblith G, Schar M, Stuber M, Weiss RG. Regional coronary endothelial function is closely related to local early coronary atherosclerosis in patients with mild coronary artery disease: Pilot study. *Circ Cardiovasc Imaging*. 2012;5:341-348