RESEARCH LETTER

Ferumoxytol-Enhanced Coronary Magnetic Resonance Angiography Compared to Invasive Coronary Angiography for Detection of Epicardial Coronary Artery Disease

To the Editor:

The prevalence of cardiac disease in patients with estimated glomerular filtration rates (eGFRs) < 30 mL/min/1.73 m^2 is estimated between 40% and 55%.[1,2] The incidence of coronary artery stenosis > 50% in proximal segments amenable to intervention was identified using invasive coronary angiography (ICA) in 28.5% of asymptomatic patients with chronic kidney disease (CKD) stage 5 requiring dialysis.[1] Use of iodinated contrast agents in patients with eGFRs < 30 mL/min/1.73 m^2, including dialysis-dependent patients with residual kidney function, is limited by the risks for contrast-induced acute kidney injury (CI-AKI).[3] It has recently been suggested that exposure to <20 g of elemental iodine may place patients at lower risk for CI-AKI.[4] Ferumoxytol is a feasible contrast agent for cardiac magnetic resonance angiography (cMRA) based on preliminary studies visualizing cardiac anatomy in patients with CKD. If offered in coordination with targeted percutaneous intervention, rather than computed tomographic coronary angiography, the risk for CI-AKI may be reduced. The performance of ferumoxytol-enhanced cMRA (fcMRA) compared with standard intraluminal imaging of the coronary arteries has not been studied.

The primary objective of the study was to assess the sensitivity and specificity of fcMRA using ICA as the reference standard in asymptomatic patients with CKD stage 4-5 at high risk for coronary artery disease. Clinical characteristics and radiologic imaging data from 13 patients who completed fcMRA were then analyzed (Fig S1; Tables S1 and S2). No women were enrolled. One patient was of African American ethnicity. Mean age of enrolled patients was 67 ± 6 years. Five patients had diabetes mellitus diagnosed. Mean weight was 88.4 ± 15.4 kg. All patients had maintained urine output, while 30.8% were receiving maintenance hemodialysis. The eGFR of patients not requiring dialysis was 14 ± 3 mL/min/1.73 m^2. The mean dose of ferumoxytol was 264 ± 46 mg. No anaphylactic reaction was reported during the imaging protocol, immediately afterward, or within 30 days following fcMRA. The mean absolute time between ICA and fcMRA was 90 ± 35 days.

A total of 144 vessel segments were evaluated among 13 patients to calculate the test accuracy of fcMRA using ICA as the reference standard (Figs 1, 2, S2, and S3). The prevalence of 1 or more stenotic sites per patient identified using fcMRA or ICA was 100% (Table S3), and 25.0% of all segments (36/144) contained a stenosis identified using ICA. Mean percentages of stenosis using fcMRA and ICA were 40% ± 24% and 31% ± 22%, respectively ($P = 0.38$). A total of 103 segments were reported as true negatives having 0% stenosis; 38 lesions identified using fcMRA were analyzed in comparison to 36 lesions identified using ICA. fcMRA sensitivity was 91.4% (95% CI, 76.9%-98.2%) and specificity was 94.5% (95% CI, 88.4%-98.0%; Table S4). Positive predictive value was 84.2% (95% CI, 70.9%-92.1%) and negative predictive value was 97.2% (95% CI, 92.1%-99.0%). Accuracy was 93.8% (95% CI, 88.5%-97.1%). Among stenoses ≥50%. there were no false negatives reported, thus increasing test sensitivity in this subcategory to 100% (95% CI, 81.5%-100%) and negative predictive value to 100%.

These findings describe the clinically relevant accuracy of fcMRA in a cohort of patients with stage 5 CKD being evaluated for kidney transplantation. They potentially have broader application to more than 1.3 million patients not yet receiving dialysis who qualify for kidney transplant evaluation in the United States.[5,6] The patient profile reported here corresponded with a population known to have 10-fold greater risk for cardiovascular events compared with patients with eGFRs > 60 mL/min/1.73 m^2.[7] This risk is further complicated by the association between cardiac disease and posttransplantation acute rejection, a relative hypercoagulable state[8] that is not currently accounted for in recent studies of asymptomatic patients pretransplantation. Despite being asymptomatic, patients had 100% prevalence of stenosis in at least 1 vessel segment evaluation. Such a high rate of stenosis directly contributed to the clinically relevant accuracy of fcMRA to ICA that was similar to noncontrasted cMRA in a cohort of nonobese Asian patients (body mass index < 25 kg/m^2) without CKD and a prevalence of stenosis of 44%.[9]

Limitations of this study reflect the current fcMRA imaging protocols that use gradient echo sequences. Ventricular contraction about the fixed axis of the aorta caused radial motion artifact, limiting visualization of stenoses in more distal segments of the coronary vessels. The use of 3-dimensional ultra-short time-to-echo sequence could potentially increase vessel resolution of midsegment and distal segments of the coronary arteries by removing susceptibility-induced signal dropout and signal contribution from flow that reduce the anatomical specificity of the magnetic resonance imaging signal in these vessels.[10]

Despite these limitations, our findings offer a potential tool to provide intraluminal coronary data in patients otherwise denied an expedient kidney transplant evaluation due to clinical management options that may involve ICA and percutaneous intervention. The utility of this technique may also apply more broadly to symptomatic patients with CKD diagnosed with an acute coronary syndrome when targeted percutaneous intervention is possible and iodinated contrast exposure is to be minimized.

Timothy Miller, Mathew S. Chin, Codi Gharagouzloo, Ayaz Aghayev, Sijie Zheng, Raymond Kwong, Aliza Anwar Memon, Andrew M. Siedlecki

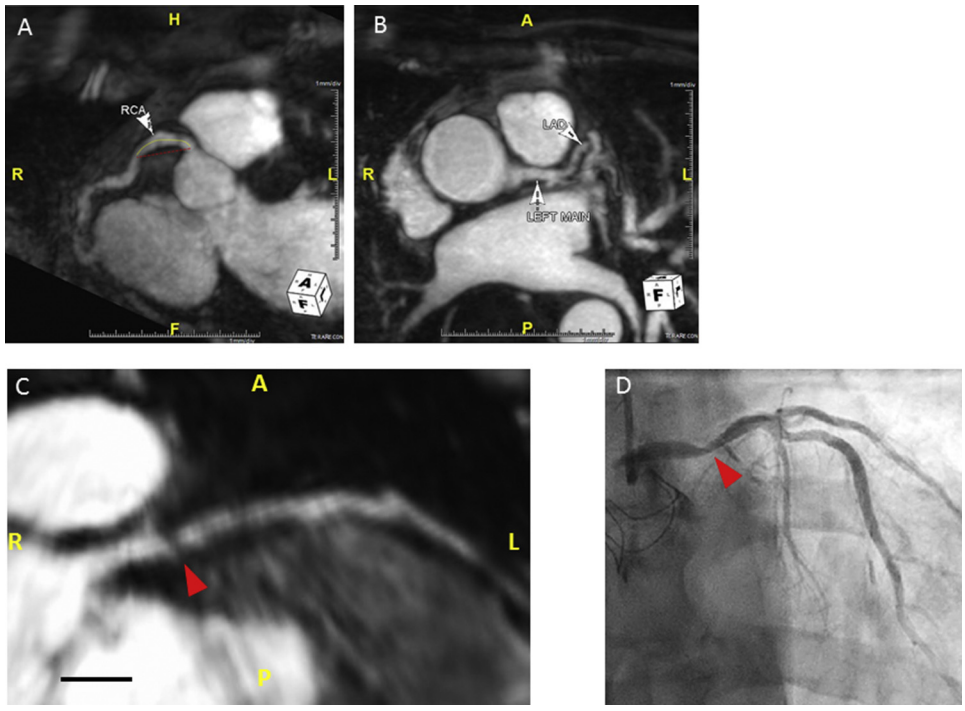

Figure 1. Ferumoxytol-enhanced magnetic resonance angiography (MRA) of the coronary artery tree (A) Right coronary artery (RCA) visualized with ferumoxytol-enhanced cardiac MRA (fcMRA) in an asymptomatic patient evaluated as a potential kidney transplant recipient. Distance from coronary ostium to the 25% stenosis of the RCA in patient 4 by axial (2.01 cm, red dotted line) and curvilinear (2.27 cm, yellow solid line) measurement. Apparent defect at 0.5 cm from origin was confirmed by both blinded radiologists to be an artifact of the reconstructed image. (B) Widely patent left main artery and left anterior descending (LAD) artery (patient 8) visualized with fcMRA. (C) fcMRA of patient 1 shows stenosis in the left main artery (red arrow; scale bar = 1 cm). (D) Corresponding x-ray coronary arteriography in the caudal right anterior oblique view shows 70% left main artery stenosis in patient 1.

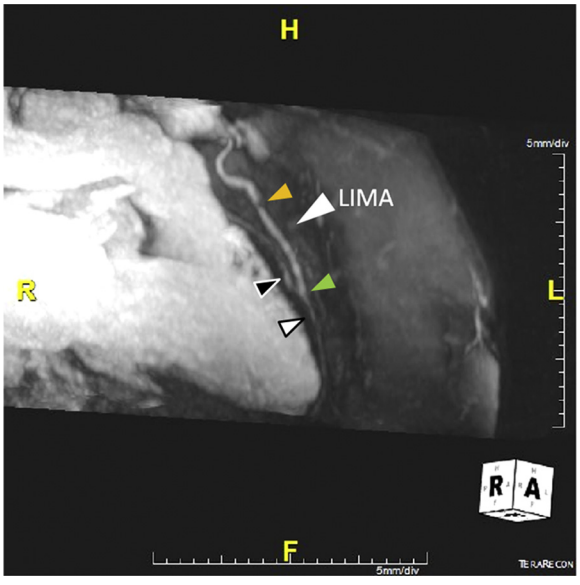

Figure 2. Ferumoxytol-enhanced cardiac magnetic resonance angiography of patient 5. Left internal mammary artery (LIMA) is visualized. There was no stenosis identified at the anastomosis with the left anterior descending artery (green arrow). Both anterograde (white arrow, black outline) and retrograde (black arrow, white outline) were visualized. Stenoses (yellow arrow) of proximal segments of bypass conduits were not included in vessel segment analysis.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Flowchart of study recruitment, enrollment, and participation.

Figure S2. Ferumoxytol-enhanced cardiac magnetic resonance angiography of patient 1.

Figure S3. Ferumoxytol-enhanced cardiac magnetic resonance angiography of patient 2.

Table S1. Imaging Protocol for Ferumoxytol-Enhanced Cardiac Magnetic Resonance Angiography

Table S2. Patient Characteristics

Table S3. Location and Distance From Anastomosis of Coronary Lesions Identified by fcMRA and ICA

Table S4. Per Segment Intraluminal Stenosis

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Timothy Miller, MD, Mathew S. Chin, MD, Codi Gharagouzloo, PhD, Ayaz Aghayev, MD, Sijie Zheng, MD, PhD, Raymond Kwong, MD, Aliza Anwar Memon, MD, and Andrew M. Siedlecki, MD.

Authors' Affiliations: Tristate Imaging Medical Group, Inc, Cincinnati, OH (TM); Geisinger Wyoming Valley Medical Center, Wilkes-Barre, PA (MSC); Imaginostics, Inc, Cambridge, MA (CG); Department of Medicine, Kaiser Permanente, Oakland, CA (AA); Department of Radiology (AA), Division of Cardiology (SZ, RK), and Division of Renal Medicine (AAM, AMS), Brigham and Women's Hospital, Boston, MA.

Address for Correspondence: Andrew M. Siedlecki, MD, 77 Ave Louis Pasteur, HIM 568B, Boston, MA 02115. E-mail: asiedlecki@bwh.harvard.edu

Authors' Contributions: Research idea and study design: AMS, TM, MC; data acquisition: TM, MC; data analysis/interpretation: AMS, TM, MC, CG, SZ, AA, RK; statistical analysis: AAM, AMS. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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