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Ferumoxytol MRA for Transcatheter Aortic Valve Replacement Planning with Renal Insufficiency

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Abstract

Background—Computed tomography angiography (CTA) is the test of choice for pre-procedure imaging of transcatheter aortic valve replacement (TAVR) candidates. The iodinated contrast required, however, increases the risk of renal dysfunction in patients with pre-existing renal failure. Ferumoxytol is a magnetic resonance imaging (MRI) contrast agent that can be used with renal failure. Its long vascular resonance time allows gated MRA sequences that approach CTA in image quality. We present respiratory and cardiac gated MRA enabled by ferumoxytol that can be post-processed in an analogous fashion to CTA.

Methods—Seven patients with renal failure presenting for TAVR were imaged with respiratory and cardiac gated MRA at 3T using ferumoxtyol for contrast. Aortic annulus, root and peripheral access dimensions were calculated in a fashion identical to that used for CTA. Of these, 6 patients underwent a TAVR procedure and 5 had intraoperative valve assessment with transesophageal echocardiograph (TEE) using standard clinical protocols that employed both two- and three-dimensional techniques.

Results—Good correlation between MRA aortic annulus measurements and those from TEE were shown in 5 patients with mean annulus area of 392.4 mm^2 (290–470 range) versus 374.1 mm^2 (285–440 range), with a pairwise correlation coefficient of 0.92, p=0.029. All patients received Sapien valve implants (one 20 mm, three 23 mm, and two 26 mm valves). Access decisions were guided by MRA with no complications. Annulus sizing resulted in no greater than trace/mild aortic regurgitation in all patients.

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Conclusions—Ferumoxytol MRA is a safe alternative to CTA in patients with renal failure for pre-TAVR analysis of the aortic root and peripheral access.

Introduction

Computed tomography angiography (CTA) has emerged as the imaging test of choice for pre-procedure imaging of transcatheter aortic valve replacement (TAVR) candidates.[1] With sub-millimeter 3-dimensional spatial resolution, it is able to simultaneously assess the aortic valve annulus, coronary artery ostia and peripheral access. The iodinated contrast that is required for CTA, however, increases the risk of renal dysfunction in patients with pre-existing renal failure. Magnetic resonance angiography (MRA) is a potential alternative, but gadolinium, like iodinated contrast is restricted in patients with renal dysfunction.

Ferumoxytol is an MRI contrast agent that can be used with renal failure.[2] It is an intravenous iron preparation used for treatment of iron deficiency associated with chronic kidney disease. It has proven to be an attractive MRI contrast agent, although currently it is an off-label indication for such use. Unlike typical gadolinium-based contrast agents that are extracellular, ferumoxytol is a blood pool agent, meaning that it remains intravascular for many hours. Practical advantages of this prolonged intravascular resonance time are that rapid injection of contrast and bolus timing are not needed, and repeat contrast imaging is possible. The extended vascular resonance time also allows for longer, gated MRA sequences that can approach CTA in image quality. We present the use of both respiratory and cardiac gated MRA enabled by the use of ferumoxytol that can be post-processed in an analogous fashion to CTA.

Methods and Results

We evaluated seven patients who underwent ferumoxytol-enhanced MRA for TAVR planning. All seven patients had significantly reduced renal function, with mean serum creatinine of 2.04±0.51 and estimated glomerular filtration rates (eGFR) ranging from 20–45 mL/min/1.73m^2. Society of Thoracic Surgeons (STS) scores ranged from 13.5 to 39.5%. Informed consent was obtained for the use of ferumoxytol as an MRI contrast agent. A waiver of informed consent was issued by the institutional review board for the retrospective data analysis performed for this study. MRI studies were performed on 3 Tesla (General Electric and Siemens) scanners. Ferumoxytol was given prior to imaging at a dose of 3 mg/kg via slow intravenous administration in the pre-procedural holding area with nurse monitoring. MRI protocols included both ECG and respiratory gating for the chest, with conventional MRA for the abdomen and pelvis. Imaging took between 7 and 10 minutes, depending on heart rate and the efficiency of the respiratory gating. Cross-sectional analysis of the aortic valve annulus and root, including the height of coronary arteries from the annulus, was performed in a fashion identical that used for CTA (Figure 1A). Five patients also underwent intraoperative trans-esophageal echocardiography (TEE) using standard clinical protocols that employed both two- and three-dimensional techniques for confirmation of aortic annular sizing.

Ferumoxytol MRA and TEE sizing of the aortic annulus corresponded to the same TAVR valve size in all five patients who underwent both examinations, with valve area measurements (mm^2) ranging from 290 to 470 (mean 392.4) by MRA and 285 to 440 (mean 374.1) by TEE, with a pairwise correlation coefficient of 0.92, p=0.029. Three sizes of TAVR valves were placed (20, 23 and 26 mm) depending on aortic annular sizing. All five patients who underwent both MRA and TEE were alive 30-days after the procedure with trace to mild aortic insufficiency. A sixth patient underwent surgical aortic valve replacement due to the identification of a low origin of the right coronary artery on the ferumoxtyol MRA. The seventh patient underwent pre-procedure TAVR planning using the ferumoxtyol MRA alone and underwent successful TAVR implant. Ferumoxytol MRA aortic annulus areas, intraoperative TEE aortic annulus areas, actual valve sizes used, and patient outcomes are summarized in Table 1.

Ferumoxytol-MRA was used to evaluate the feasibility of peripheral access via the lower extremities in all seven patients (Figure 1B). The peripheral access recommendations based on MRA were used in all patients who underwent TAVR, without any complications. In one case, MRA identified severely stenotic peripheral access bilaterally, and bilateral iliac artery stenting was performed prior to TAVR. Transaortic access was performed in two cases, one due to the presence of diminutive peripheral access identified by MRA, and a second because of the presence of bilateral iliac grafts.

Discussion

Ferumoxtyol MRA is feasible for pre-procedure TAVR planning, both for evaluation of the aortic annulus and peripheral access. MRA accurately predicted aortic annulus sizing at TEE in five out of five cases. There were no aortic or access complications in our cohort within 30-days of TAVR. Furthermore, the approach to intervention was significantly altered in three of seven patients due to anatomic limitations identified by MRA. As renal dysfunction is a common comorbidity in patients considered for TAVR, the option of ferumoxtyol MRA is an attractive alternative to CTA for TAVR planning.

Other imaging modalities and MR sequences have been proposed for pre-procedure imaging prior to TAVR including noncontrast MRI and MRA, noncontrast CT, and 3D TEE. In a comparison of cardiac MR, CT, and 3D TEE for the assessment of the aortic annulus ex vivo, cardiac MR was found to have the highest accuracy and least variability[3]. Previous studies have examined the feasibility of using steady-state free procession (SSFP) cine MRI acquisitions for measurement of the aortic annulus prior to TAVR.[4, 5] This approach, however, requires a technician to correctly place the imaging plane perpendicular to the aortic annulus at the time of imaging. Ferumoxytol MRA, on the other hand, is a three-dimensional (3D) approach that allows precise localization of the aortic annulus during post-processing in a manner analogous to CTA.

Non-contrast whole heart MR has recently been proposed for assessment of the aortic annulus prior to TAVR, and demonstrated good agreement with CTA[6, 7]. A limitation of this technique is the long image acquisition time (average of 14 minutes per Ruile et al.) for analysis of the aortic annulus alone, suggesting that prolonged imaging would be required

for the combined evaluation of annulus and peripheral access that we present with ferumoxytol MRA. In our pilot group, gated scanning of the aortic annulus was achieved within 5 to 8 minutes, with combined assessment of the annulus and peripheral access in less than 10 minutes. A second limitation of non-contrast MRA is that the technique is prone to flow related artifacts[8] and motion related blurring[9], particularly when assessing the peripheral access due to long imaging times, which can result in poor and even non-diagnostic image quality in some studies[6].

In patients with heavily calcified peripheral vascular access, the extent of calcification may be underestimated by MRA. A non-contrast CT roadmap can be obtained to assess the calcium burden in combination with the MRA to determine the suitability of the peripheral access in patients with known or suspected peripheral arterial disease. Fusion of non-contrast CT with ferumoxytol MRA for TAVR planning has been shown to be feasible in a small series[10].

Limitations

Our sample size for this pilot study was small. Continued analysis of outcomes in patients with pre-operative ferumoxytol MRA for TAVR planning is needed to demonstrate the safety and utility of this approach. Comparison of ferumoxtyol MRA measurements with the contemporary gold standard of CTA was not possible given the degree of renal failure in our cohort. This pilot study shows the feasibility of ferumoxytol MRA for pre-TAVR planning in patients with renal failure, and paves the way for further investigation into this application of ferumoxytol MRA.

Ferumoxtyol is associated with risk of severe allergic reactions, with risk of anaphylaxis in approximately 1 out of 10,000 patients. The most common side effects, however, are mild and transient, and include diarrhea, nausea, dizziness, and hypotension. We took recommended safety precautions, including the slow infusion of ferumoxtyol in holding area with nurse monitoring prior to imaging, to minimize the risk of allergic reaction.[11]

Conclusion

Ferumoxytol MRA is a safe alternative to CTA in patients with renal failure for pre-TAVR analysis of the aortic root and peripheral access. Further investigation is needed to evaluate the relative strengths and limitations of ferumoxytol MRA compared to emerging non-contrast approaches to pre-procedural TAVR imaging.[12–17]

Acknowledgments

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Highlights

1. Ferumoxytol MRA is a safe alternative to CTA in patients with renal failure for pre-TAVR analysis.
2. Ferumoxtyol serves as an excellent blood pool MRI contrast agent.
3. Its long vascular resonance time allows gated MRA sequences that approach CTA in image quality.
4. Good correlation between MRA aortic annulus measurements and those from TEE were shown.
5. Peripheral access decisions were guided by MRA with no complications.

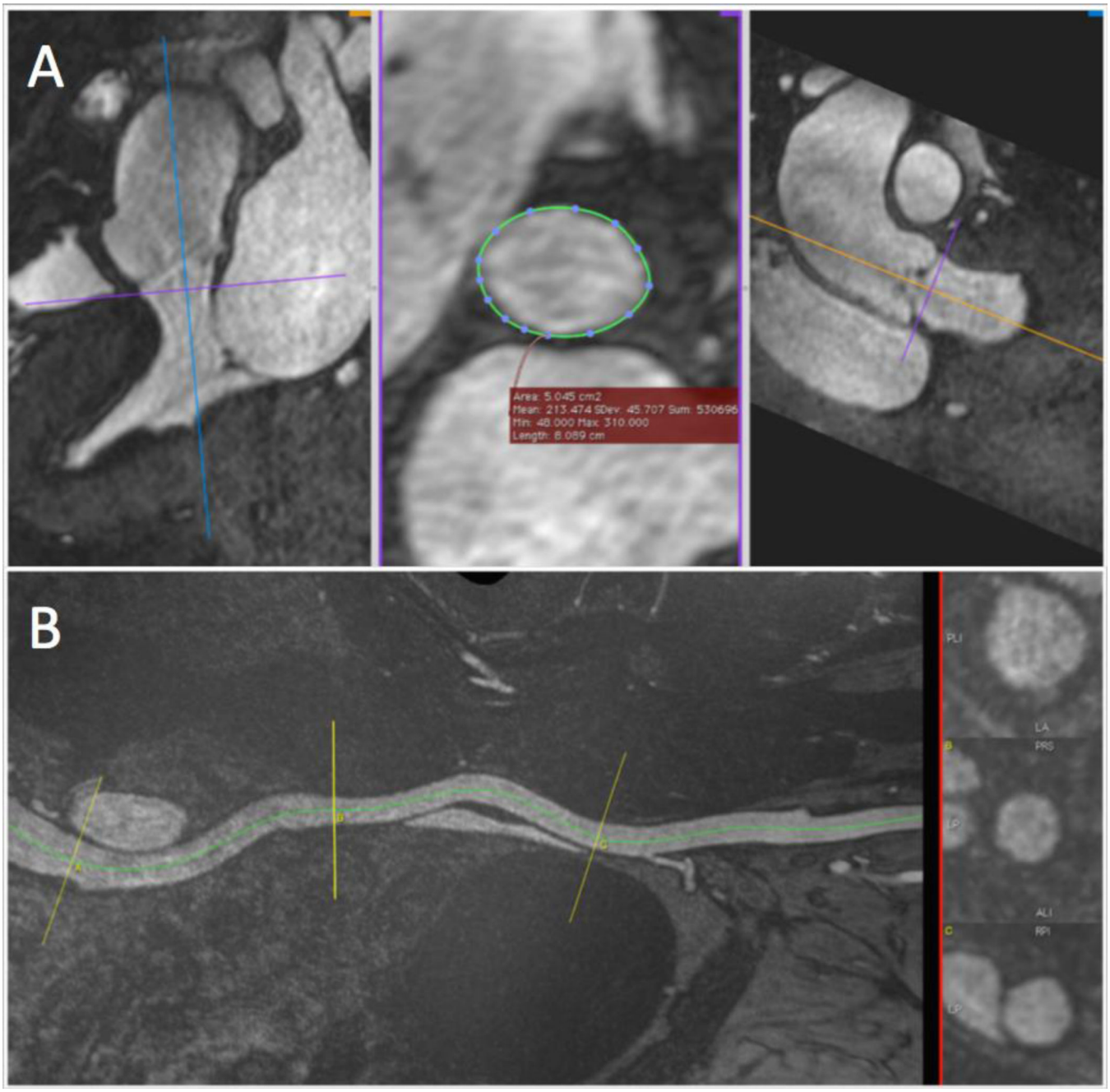

Figure.

Example of annulus measurement (**A**). A double-oblique approach is used to localize the aortic valve annulus at the base of the valve leaflets in three-dimensions (3D). Delineation of the annulus area is aided by the excellent conspicuity of the annulus compared to the surrounding tissues. Example of peripheral access evaluation (**B**). Centerline analysis of the peripheral access with cross-sectional imaging planes at the three representative levels marked.

Table

Aortic Annulus Measurements with Ferumoxytol MRA Compared to Transesophageal Echocardiography with Outcomes

Case	Age	Gender	MRA Annulus Area (mm2)	TEE Valve Size (mm2)	Actual Valve Used	30 Day mortality	Post-op AR	Comment
A	79	M	403	420	23mm Sapien S3	Alive	Trace	
B	84	F	395	360	23mm Sapien S3	Alive	Trace	
C	77	M	404	365	23mm Sapien S3	Alive	Trace	
D	76	M	470	425–440	26mm Sapien S3	Alive	Trace	
E	93	M	290	285–298	20mm Sapien XT	Alive	Trace/mild	
F	51	F	430	-	23mm Open AVR	Alive	None	Low RCA
G	70	M	487	-	26mm Sapien S3	Alive	Mild	

TAVR valve sizing is based on measurement of aortic annulus area. The manufacturer's guidelines for the Sapien S3 are: 23mm valve for annulus area of 338–430 mm^2; 26mm valve for annulus area of 430–546 mm^2. (http://www.edwards.com/)