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Initial Experience of Assessing Esophageal Tissue Injury and Recovery Using Delayed-Enhancement MRI After Atrial Fibrillation Ablation

Troy J. Badger, MD; Yaw A. Adjei-Poku, MD; Nathan S. Burgon, BS; Saul Kalvaitis, MD; Akram Shaaban, MBBCh; Daniel N. Sommers, MD; Joshua J.E. Blauer, BS; Eric N. Fish; Nazem Akoum, MD; Thomas S. Haslem, BS; Eugene G. Kholmovski, PhD; Rob S. MacLeod, PhD; Douglas G. Adler, MD; Nassir F. Marrouche, MD

- **Background**—Esophageal wall thermal injury after atrial fibrillation ablation is a potentially serious complication. However, no noninvasive modality has been used to describe and screen patients to examine whether esophageal wall injury has occurred. We describe a noninvasive method of using delayed-enhancement MRI to detect esophageal wall injury and subsequent recovery after atrial fibrillation ablation.
- *Methods and Results*—We analyzed the delayed-enhancement MRI scans of 41 patients before ablation and at 24 hours and 3 months after ablation to determine whether there was evidence of contrast enhancement in the esophagus after atrial fibrillation ablation. In patients with contrast enhancement, 3D segmentation of the esophagus was performed using a novel image processing method. Upper gastrointestinal endoscopy was then performed. Repeat delayedenhancement MRI and upper gastrointestinal endoscopy was performed 1 week later to track changes in lesions. The wall thickness of the anterior and posterior wall of the esophagus was measured at 3 time points: before ablation, 24 hours after ablation, and 3 months after ablation. Evaluation of preablation MRI scans demonstrated no cases of esophageal enhancement. At 24 hours, 5 patients showed contrast enhancement. Three of these patients underwent upper gastrointestinal endoscopy, which demonstrated esophageal lesions. Repeat upper gastrointestinal endoscopy and MRI 1 week later demonstrated resolution of the lesions. All 5 patients had confirmed resolution of enhancement at 3 months. All patients with esophageal tissue enhancement demonstrated left atrial wall enhancement directly adjacent to the regions of anterior wall esophageal enhancement.
- *Conclusions*—Our preliminary results indicate delayed-enhancement MRI can assess the extent and follow progression of esophageal wall injury after catheter ablation of atrial fibrillation. It appears that acute esophageal injury recovers within 1 week of the procedure. (*Circ Arrhythm Electrophysiol.* 2009;2:620-625.)

Key Words: atrial fibrillation ablation MRI upper gastrointestinal endoscopy esophageal injury

A trio-esophageal fistula is a serious and often fatal complication of intraoperative and endocardial catheter ablation of atrial fibrillation (AF).^{1–5} Fistula formation results from the collateral thermal effect of radiofrequency energy on the esophagus during ablation of the left atrium (LA).⁶ This injury is thought to occur due to a close anatomic relationship between the posterior structures of the left atrium, a target during circumferential ablation, and the anterior wall of the esophagus.^{6–9} Recent reports have also demonstrated subclinical thermal damage to the esophagus immediately postablation.¹⁰ Endoscopic evaluation in these patients demonstrated erythematous and necrotic lesions in the anterior wall of the esophagus in regions of close proximity to the LA, lesions that often self-resolve by later follow-up.¹⁰

Clinical Perspective on p 625

Given the serious nature of ablation-related complications, use of a noninvasive modality to assess the postablation esophageal response could contribute significantly to monitoring early complications, tracking lesion progression and initiating early intervention to avoid serious procedural consequences. In this report, we describe the use of delayedenhancement MRI (DE-MRI) to visualize and follow esophageal tissue injury after radiofrequency catheter ablation of AF.

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Table. Patient Demograp	ohics
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Total patients	41
Male	22
Female	19
Age, y	63.34±15.60
AF type	
Paroxysmal	23
Persistent	18
Underlying disease	
Coronary artery disease	4
Diabetes	4
Congestive heart failure	4
Hypertension	22

Methods

Study Population

Between April 2008 and August 2008, 57 consecutive patients who presented to the University of Utah for AF ablation had MRI scans at 3 time points: before ablation, within 24 hours after ablation, and at 3 months after ablation. Of these patients, 16 had an uninterpretable scan caused by patient motion and blurring, significant navigator artifact, and/or incorrect choice of inversion time. Forty-one patients were thus included in the final analysis. Written informed consent was obtained in all patients, and the study was approved by the Institutional Review Board at the University of Utah. Patients with esophageal enhancement were given the option to undergo upper gastrointestinal endoscopy (UGE) at the time of the scan. Three patients are shown in the Table.

DE-MRI

Patients underwent a DE-MRI sequence as previously described.11 Briefly, all patients underwent MRI studies on a 1.5-T Avanto clinical scanner (Siemens Medical Solutions, Erlangen, Germany) using a body surface phased array coil. A delayed enhancement sequence was used to identify injured or nonviable tissue. DE-MRI was acquired ≈ 15 minutes after contrast agent injection (0.1 mmol/ kg; Multihance, Bracco Diagnostic, Inc, Princeton, NJ) using a 3D inversion recovery, respiration-navigated, ECG-gated, gradient echo pulse sequence. The full dose of contrast was given in all patients, with an estimated glomerular filtration rate >60. Patients with estimated glomerular filtration rates between 30 and 60 were given half the contrast dose. Typical acquisition parameters were freebreathing using navigator gating, a transverse imaging volume with voxel size of $1.25 \times 1.25 \times 2.5$ mm (reconstructed to $0.625 \times$ 0.625×1.25 mm), repetition time/echo time of 5.4/2.3 ms, inversion time of 270 to 310 ms, GRAPPA with R=2, and 46 reference lines. ECG gating was used to acquire a small subset of phase encoding views during the diastolic phase of the LA cardiac cycle. The time interval between the R-peak of the ECG and the start of data acquisition was defined using the cine images of the LA. Fat saturation was used to suppress fat signal. The echo time of the scan (2.3 ms) was chosen such that fat and water are out of phase and the signal intensity of partial volume fat-tissue voxels was reduced allowing improved delineation of the LA wall boundary. The inversion time value for the DE-MRI scan was identified using a scout scan. Typical scan time for the DE-MRI study was 5 to 10 minutes, depending on subject respiration and heart rate.

Radiofrequency Catheter Ablation

All patients underwent pulmonary vein antrum isolation with posterior wall and septal debulking. The technique is briefly summarized below. After venous access, a 14-pole coronary sinus catheter was placed into the coronary sinus via the right internal jugular access (TZ Medical Inc, Portland, Ore, or BARD, Murray Hill, NJ) for use as a mapping reference. A phased-array ultrasound catheter was positioned in the mid right atrium (Siemens AG Inc, Malvern, Pa) and used to guide a double transseptal puncture, through which was placed a 10-pole Lasso catheter and an F-curve, Thermocool 3.5-mm irrigated tip ablation catheter (Biosense-Webster, Inc, Diamond Bar, Calif). Using fluoroscopy and electroanatomic mapping (CARTOMERGE, Biosense-Webster, Inc) for catheter navigation, intracardiac potentials in the pulmonary vein antra and on the posterior wall were mapped during sinus rhythm and were targeted for ablation if fractionation was seen distinct from far-field atrial potentials. Lasso-guided radiofrequency delivery was performed, using Lasso electrogram artifacts to confirm ablation catheter tip location relative to the substrate of interest. Lesions were delivered using 50 W with a 50°C temperature limit, for a duration of 10 seconds (maximum 15 seconds), with the end point being elimination of all local electrograms. When all antral and posterior wall targets had been ablated, this entire region was resurveyed for any return of electric activity, and any such regions demonstrating electric recovery were retreated. In addition, entry block in all four pulmonary veins was confirmed with the ablation catheter after debulking was accomplished.

DE-MRI–Based Esophageal Monitoring Protocol

Within 24 hours after the AF ablation procedure, all patients underwent DE-MRI to assess for acute esophageal injury. Patients with no contrast enhancement or changes in wall thickness were then assessed for esophageal injury on their MRI at their routine 3-month follow-up visit. Patients exhibiting acute injury at 24 hours underwent upper gastrointestinal endoscopy for lesion confirmation and repeat MRI within 1 week to assess for lesion progression or change.

DE-MRI Image Analysis and Processing

After acquisition of the scan, each 2D slice was evaluated in a random, blinded fashion for the presence of contrast enhancement in the esophageal wall by 2 independent experts in cardiac MRI. A positive finding required agreement between both reviewers. A κ statistic of 0.796 (P=<0.001) was calculated for inter-rater agreement. The esophageal images displaying contrast enhancement were then segmented into 3D models along with 3D generation of the LA and analyzed to see whether regions of esophageal enhancement overlapped regions of LA enhancement. Three-dimensional segmentation was accomplished by manually segmenting the contours of the LA and esophageal walls and then stacking the 2D slices into 3D models. After volume rendering of the images, a smooth table opacity and color-look-up-table were applied to better illuminate the contrast enhancement.

Esophageal Wall Measurements

The thickness of the anterior wall and posterior wall of the esophagus was measured at the same anatomic location of the DE-MRI obtained before ablation as well as 24 hours after ablation and 3 months after ablation. Slices of interest were based on images with contrast enhancement in the posterior wall or pulmonary vein antra of the LA. Anterior wall and posterior wall measurements of the esophagus were taken on at least 3 separate slices with each patient averaging 4 slices. The same measurements were then obtained at the same anatomic locations on the 2 other scans.

Upper Gastrointestinal Endoscopy

After obtaining informed consent, the endoscope was passed under direct vision with monitoring of heart rate, respiratory rate, blood pressure, and oxygen saturations continuously throughout the procedure. The endoscope was introduced through the mouth and advanced to the second portion of the duodenum. Radial endosonog-raphy was performed at 7.5 and 10.0 MHz with Doppler. Endoscopic ultrasound was used when appropriate. The images were then interpreted by the gastroenterologist who performed the procedure. Three patients underwent UGE on the same days as the acquisition of the DE-MRI scan after the ablation procedure due to detection of

esophageal wall enhancement on DE-MRI. Two patients with esophageal contrast enhancement seen on DE-MRI were offered and refused UGE.

Follow-Up

After the procedure, all patients underwent 24-hour observation on a telemetry unit. Patients continued anticoagulation therapy with warfarin (international normalized ratio, 2.0 to 3.0) for a minimum of 3 months. Patients were assessed for esophageal symptoms during the 24-hour postablation monitoring period as well at a 3-month clinic visit. All patients were discharged on an 8-week course of an oral proton-pump inhibitor.

Statistical Analysis

Continuous variables are presented as mean \pm SD. Tests for significance were performed using a repeated-measures 1-way ANOVA test. Turkey multiple comparison was used to test for significance between time points. The results of these reviewers were compared using Cohen κ statistic to assess for inter-rater agreement. Differences were considered significant at *P*<0.05. Statistical analysis was performed using SPSS 15.0 (SPSS, Inc, Chicago, III).

Results

Esophageal Contrast Enhancement

Of the preablation scans, none of 41 demonstrated esophageal enhancement. At 24 hours after ablation, 5 of 41 (12.2%) showed contrast enhancement in the anterior wall of the esophagus. Figure 1 demonstrates the MRI findings at all time points of 5 patients who had enhancement at 24 hours after ablation. All 5 patients did not have enhancement before ablation, and all patients had resolution of enhancement on their 3-month postablation scan. Three of the patients with contrast enhancement had repeat DE-MRI within 1 week, with all patients demonstrating resolution of esophageal enhancement. All areas of esophageal enhancement were adjacent to regions of LA wall enhancement targeted during the ablation. Of the 5 patients with esophageal enhancement, the closest contact point of the esophagus to the LA was the left superior pulmonary vein antra in 3 patients (Figure 1) and the posterior wall in 2 patients. Two of the 5 patients exhibited esophageal symptoms after the procedure, including 1 patient with a burning epigastric pain and the other patient with pain and irritation with swallowing.

Esophageal Wall Measurements

Esophagus Anterior Wall

Mean esophageal anterior wall thickness was 1.81 ± 0.36 mm on preablation scan, 2.16 ± 0.39 mm on 24-hour scan, and 1.88 ± 0.26 mm on the 3-month scan. A statistical significance was observed when comparing these means (*P*<0.001) using ANOVA. Post hoc testing showed significance between preablation and 24-hour postablation scans (*P*<0.001) and 24-hour and 3-month scans (*P*<0.001). There was no statistical significance between preablation and 3-month scans (*P*=0.66).

The average change in thickness of the anterior wall from before ablation to 24 hours after ablation was 0.36 ± 0.51 , -0.26 ± 0.44 from 24 hours to 3 months after ablation, and 0.23 ± 0.56 from before ablation to 3 months after ablation. ANOVA showed a statistical significance between these 3 means (*P*<0.001). Using post hoc analysis, a statistical significance between the change in thickness between prea-

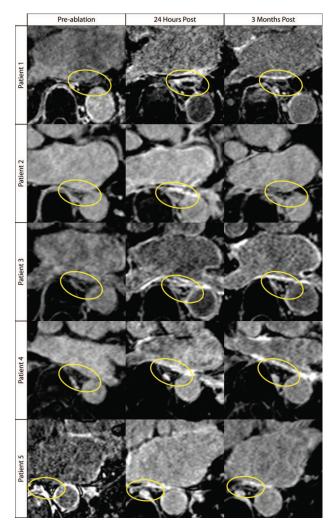


Figure 1. Acute postablation esophageal changes and recovery. Five patient examples of esophageal changes after AF ablation are shown. Preprocedure MRI (left) in all patients did not demonstrate any esophageal contrast enhancement. However, at 24 hours after ablation (middle), all 5 patients had anterior wall thickening with significant contrast enhancement primarily located in the anterior wall. This enhancement and wall thickening showed complete resolution by 3 months after the procedure (right) even though chronic LA scar remained. Regions of esophageal enhancement were in close relation to radiofrequency-induced scarring in the LA from the ablation procedure.

blation to 24 hours after ablation and 24 hours to 3 months after ablation (P<0.001) was found. Statistical significance was also found when comparing 24-hour ablation with 3 months after ablation and before ablation with 3 months after ablation (P<0.001). However, there was no significance between change in thickness from preablation to 3 months after ablation (P=0.27).

Esophagus Posterior Wall

Mean esophageal posterior wall thickness was $1.85\pm$ 0.32 mm on the preablation scan, 1.96 ± 0.28 mm on the 24-hour scan, and 1.92 ± 0.31 mm on the 3-month scan. A statistical significance was not observed when comparing these means (*P*=0.07), using an ANOVA. Post hoc testing also did not show significance between preablation and

24-hour postablation scans (P=0.06), 24-hour and 3-month scans (P=0.78), or preablation and 3-month scans (P=0.48).

The average change in thickness of the posterior wall from before ablation to 24 hours after ablation was 0.14 ± 0.33 , -0.05 ± 0.27 from 24 hours to 3 months after ablation, and 0.21 ± 0.56 from before ablation to 3 months after ablation. ANOVA showed a statistical significance between these mean values (P=0.001). Further analysis using post hoc statistics revealed a statistical significance between the change in thickness between before ablation to 24 hours after ablation and 24 hours to 3 months after ablation (P=0.02). Statistical significance was also found when comparing 24 hours with 3 months after ablation and preablation to 3 months after ablation (P=0.001). However, there was no significance between change in thickness from before ablation to 3 months after ablation (P=0.54).

UGE

Of the 5 patients who displayed esophageal enhancement on DE-MRI at 24 hours after ablation, 3 patients elected to undergo upper gastrointestinal endoscopy. Two patients refused the procedure. One patient had a superficial large erosions (1 to 2 cm) with nodular base in the lower third of the esophagus. The second patient had localized mucosal abnormality characterized by pale erythema found at 32 cm from the incisors. This was an area of approximately 1 cm in diameter, with diffuse borders. There was no ulceration or signs of bleeding. Endoscopic ultrasound demonstrated preservation of esophageal wall architecture despite the mucosal injury with no mediastinal or periesophageal adenopathy detected. The third patient had an irregular and erythematous lesion in the lower third of the anterior wall. All 3 patients had lesion size and location that correlated with the anatomic location of enhancement identified on DE-MRI based on the 3D recreations of the esophagus. Two patients had repeat endoscopy 1 week later that showed healing of the esophageal lesion. A patient example is demonstrated in Figure 2.

Discussion

In this study, we describe the feasibility and initial experience of using DE-MRI to detect acute esophageal wall injury after catheter ablation of AF. Although DE-MRI has been shown to visualize postablation LA changes resulting from the radiofrequency energy,¹¹ there have not been any reports describing esophageal wall changes using this modality. In our study, 12.2% of patients showed esophageal anterior wall injury on DE-MRI immediately after ablation in regions targeted during the procedure, with all patients showing complete lesion resolution within 1 week postablation. Endoscopic evaluation correlated the size and location of MRI enhancement patterns with intraluminal lesions detected with endoscopy.

Our findings of postablative esophageal changes are consistent with other reports detailing this phenomenon. A recent analysis by Schmidt et al¹⁰ demonstrated frequent erythematous (29%) and necrotic changes (18%) in the anterior wall of the esophagus 24 hours after AF ablation. These authors used repeat endoscopy to show complete recovery of the erythematous esophageal changes by 2 weeks after ablation and

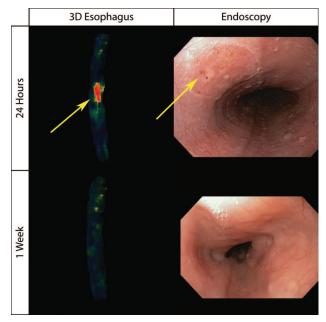


Figure 2. Evaluation of esophageal lesions with endoscopy. Three patients with enhancement seen on DE-MRI at 24 hours underwent endoscopy. The patient example below is a 62-year-old man with paroxysmal AF who had increased gadolinum uptake (yellow arrow) in the anterior wall of the esophagus on MRI at 24 hours after ablation. Endoscopic findings at that time point confirmed the presence of superficial erosion in the anterrior wall. Repeat imaging and endoscopy 1 week later showed full recovery of the esophageal lesion on MRI and UGE.

recovery of the necrotic changes by 1 month after ablation. Another recent study by Singh et al¹² demonstrated that 11% of asymptomatic patients had postablation esophageal ulcerations from radiofrequency energy.

Recovery of lesions as measured by resolution of contrast enhancement might be explained by a partial inflammatory reaction occurring in the esophagus immediately after ablation. This could be similar to the inflammatory state that has been described in the LA immediately after radiofrequency ablation.13,14 It has recently been reported that gadolinium enhancement in the LA in the immediate postablative state might represent edema/hemorrhage rather than true myocyte necrosis, because the enhancement often recedes by later follow-up.15 A similar transient inflammatory process from the radiofrequency energy with subsequent healing and recovery may also occur in the immediate postablative esophagus. The gadolinium uptake and wall thickening seen in the posterior wall of the esophagus might also represent edema rather than necrosis because this tissue is not in near contact with the ablation energy yet appears to undergo transient postablative changes as well.

Figure 3 demonstrates both LA and esophageal enhancement resolution after ablation. In this patient example, extensive enhancement is seen in the anterior wall of the esophagus and throughout a significant portion of the LA at 24 hours after ablation. Repeat imaging at 3 months demonstrates complete resolution of esophageal lesions with decrease in LA enhancement to regions solely confined to the pulmonary vein antra. The resolution of contrast enhancement and return

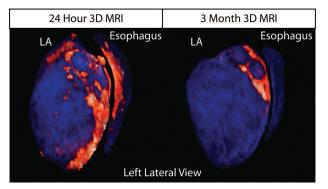


Figure 3. Recovery of contrast enhancement in the anterior wall of the esophagus. This patient example is of a 57-year-old woman presenting for catheter ablation of paroxysmal AF. Three-dimensional segmentation of the LA and esophagus at 24 hours after ablation (left) demonstrates significant contrast enhancement (orange). However, by 3 months after ablation (right), there is resolution of enhancement in the esophagus. Contrast enhancement in the LA decreases significantly to involve only portions surrounding the left pulmonary veins. Our findings indicate a possible inflammatory process that occurs in both the LA and esophagus shortly after the ablation procedure that partially or fully resolves by later follow-up. This example also demonstrates the close anatomic relationship between the LA and esophagus, primarily at the antra regions targeted during the ablation procedures.

of wall thickness to preprocedure baseline levels suggesting acute esophageal injury is often a transient phenomenon.

Evidence shows that lesions placed in the LA increase the luminal temperature of the esophagus, supporting the notion that radiofrequency energy delivery effects mediastinal structures outside the LA.6 Although our study used an ablative technique targeting the LA posterior wall, we do not believe that this caused an increase in the incidence of esophageal injury. Based on the significant anatomic overlap of the esophagus, many standard pulmonary vein antra techniques have the potential to damage the esophagus.9 This has been shown to be especially pertinent to techniques targeting the left pulmonary vein antra, as prior studies have shown this is the most common location of LA-esophageal contact.⁶ The close anatomic overlap of the esophagus to the pulmonary vein antra, primarily the left pulmonary vein antrum, is demonstrated in Figure 1. Additional studies are required to correlate the frequency and extent of esophageal tissue damage after AF ablation among the different techniques and ablation parameters used.

Esophageal fistula occurs during the acute post-AF ablation state, usually within 2 weeks of the procedure.^{2,16} Although DE-MRI findings of patients who have LAesophageal fistulas are not known, the implementation of DE-MRI as a noninvasive screening tool in the acute postprocedure stages has the potential to identify those patients at increased risk of developing this serious complication. Identification of these patients could lead to early interventions to minimize the consequences of the complication. Deciphering which patients who have acute esophageal injury who are at risk of these complications should be a topic of interest for future research.

Study Limitations

None.

Given the prospective nature of this analysis, expert MRI reviewers were not blinded to the time point of scan acquisition because MRI findings dictated further clinical management. In our study, only patients with positive MRI findings underwent endoscopy for correlation; thus, we do not have immediate 24-hour endoscopy data on patients with a normal-appearing DE-MRI. Although all patients underwent DE-MRI before the ablation and did not demonstrate any contrast enhancement in the esophagus, patients with preexisting esophageal pathology were not excluded from the study.

Conclusion

Our preliminary results indicate that DE-MRI has the ability to detect and monitor progression of esophageal lesions after catheter ablation of AF. Acute esophageal injury appears common in the immediate postablation state with resolution of the findings by later follow-up. This appears to indicate that some patients have a transient inflammatory response in the postablative esophagus that recovers without the development of serious procedure-related complications.

Disclosures

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CLINICAL PERSPECTIVE

Catheter ablation for atrial fibrillation can cause esophageal injury, and rare atrial-esophageal fistulae are a feared complication. Methods for detecting esophageal injury are of interest to help identify esophageal injury and develop methods to reduce risk, but early detection of esophageal injury has to this point required endoscopic examination. In this initial report, we demonstrate that esophageal injury can be detected as regions of esophageal delayed gadolinium enhancement on MRI. This modality has the potential to noninvasively identify patients who have esophageal injury and track healing of these lesions over time. As has been reported from endoscopic studies, we also found that esophageal lesions associated with the atrial fibrillation ablation procedure are often transient and heal without consequence. Further studies are warranted.