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Journal Subject Codes: atrial fibrillation, pulmonary vein antrum isolation, delayed-enhancement MRI, esophageal injury
Abstract:

**Background:** Esophageal wall thermal injury following atrial fibrillation (AF) 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 (DE-MRI) to detect esophageal wall injury and subsequent recovery following AF ablation.

**Methods and Results:** We analyzed the DE-MRI scans of 41 patients prior to ablation, and at 24 hours and 3 months post-ablation to determine whether there was evidence of contrast enhancement in the esophagus following AF ablation. In patients with contrast enhancement, three-dimensional segmentation of the esophagus was performed using a novel image processing method. Upper gastrointestinal endoscopy (UGE) was then performed. Repeat DE-MRI and UGE was performed one week later to track changes in lesions. The wall thickness of the anterior and posterior wall of the esophagus was measured at three time points; prior to ablation, 24 hours post, and 3 months post. Evaluation of pre-ablation MRI scans demonstrated no cases of esophageal enhancement. At twenty-four hours, 5 patients showed contrast enhancement. Three of these patients underwent UGE, which demonstrated esophageal lesions. Repeat UGE and MRI one week later demonstrated resolution of the lesions. All five patients had confirmed resolution of enhancement at 3 months. All patients with esophageal tissue enhancement demonstrated LA wall enhancement directly adjacent to the regions of anterior wall esophageal enhancement.

**Conclusion:** Our preliminary results indicate DE-MRI can assess the extent and follow progression of esophageal wall injury following catheter ablation of AF. It appears acute esophageal injury recovers within one week of the procedure.

**Key Words:** atrial fibrillation, ablation, magnetic resonance imaging, upper gastrointestinal endoscopy, esophageal injury
Introduction

Atrio-esophageal (AE) fistula is a serious and oftentimes fatal complication of intraoperative and endocardial catheter ablation of atrial fibrillation (AF).\textsuperscript{1-5} Fistula formation results from the collateral thermal effect of radiofrequency (RF) energy on the esophagus during ablation of the left atrium (LA).\textsuperscript{6} This injury is thought to occur due to a close anatomical relationship between the posterior structures of the left atrium, a target during circumferential ablation, and the anterior wall of the esophagus.\textsuperscript{6-9} Recent reports have also demonstrated subclinical thermal damage to the esophagus immediately post-ablation.\textsuperscript{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 which often self-resolve by later follow-up.\textsuperscript{10}

Given the serious nature of ablation-related complications, use of a noninvasive modality to assess the post-ablation 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 DE-MRI to visualize and follow esophageal tissue injury following radiofrequency catheter ablation of AF.

Methods

Study Population

Between April 2008 and August 2008, fifty-seven consecutive patients who presented to the University of Utah for AF ablation had MRI scans at three time points; prior to
ablation, within twenty-four hours post-ablation, and at three months post-ablation. Of these patients, sixteen had an uninterpretable scan due to 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 and informed consent was obtained in all patients and the study was approved by the IRB 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 underwent UGE. The clinical demographics of the study patients are shown in Table 1.

Delayed Enhancement MRI

Patients underwent a DE-MRI sequence as previously described. Briefly, all patients underwent MRI studies on a 1.5 Tesla 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 about 15 minutes following 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 (eGFR) > 60. Patient’s with eGFR between 30-60 were given half the contrast dose. Typical acquisition parameters were: free-breathing using navigator gating, a transverse imaging volume with voxel size = 1.25 x 1.25 x 2.5 mm (reconstructed to 0.625 x 0.625 x 1.25 mm), TR/TE = 5.4/2.3 ms, inversion time (TI) = 270-310 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 TE 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 TI value for the DE-MRI scan was identified using a scout scan. Typical scan time for the DE-MRI study was 5-10 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, OR or BARD, NJ) for use as a mapping reference. A phased-array ultrasound catheter was positioned in the mid-right atrium (Siemens AG Inc., Malvern, PA, USA) 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). Using fluoroscopy and electroanatomic mapping (CARTOMERGE, Biosense-Webster Inc.) for catheter navigation, intracardiac potentials in the PV 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 RF 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 endpoint being elimination of all local electrograms.
When all antral and posterior wall targets had been ablated, this entire region was re-surveyed for any return of electrical activity, and any such regions demonstrating electrical 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 twenty-four hours following the AF ablation procedure, all patients underwent DE-MRI in order 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 three-month follow-up visit. Patients exhibiting acute injury at 24 hours underwent upper GI endoscopy for lesion confirmation and repeat MRI within one week to assess for lesion progression or change.

**DE-MRI Image Analysis and Processing**

Follow 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 two independent experts in cardiac MRI. A positive finding required agreement between both reviewers. A kappa statistic of .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 if 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. Following 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 anatomical location of the DE-MRI obtained pre-ablation, as well as twenty-four hours and three months post-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 three separate slices with each patient averaging 4 slices. The same measurements were then obtained at the same anatomical locations on the two 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 endosonography was performed at 7.5 MHz 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 following 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**

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

**Statistical Analysis**

Continuous variables are presented as the mean plus or minus one standard deviation. Tests for significance were performed using a repeated measures One-Way ANOVA test. Turkey’s multiple comparison was used to test for significance between time points. The results of these reviewers were compared using Cohens Kappa statistic to assess for inter-rater agreement. Differences were considered significant at $p < 0.05$. Statistical analysis was performed using the SPSS 15.0 Statistical Package (SPSS Inc.; Chicago, IL).

**Results**

**Esophageal Contrast Enhancement**

Of the pre-ablation scans, 0/41 demonstrated esophageal enhancement. At twenty-four hours post-ablation, 5/41 (12.2%) showed contrast enhancement in the anterior wall of the esophagus. Figure 1 demonstrates the MRI findings at all time points of five patients who had enhancement at 24 hours post-ablation. All five patients did not have enhancement prior to ablation and all patients had resolution of enhancement on their 3 months post-ablation scan. Three of the patients with contrast enhancement had repeat DE-MRI within one 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 five patients with esophageal enhancement, the closest contact point of the esophagus to the LA was the left superior
pulmonary vein antra in three patients (Figure 1), and the posterior wall in two patients. Two out of the five patients exhibited esophageal symptoms after the procedure, including one 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 pre ablation, 2.16 ± 0.39 mm on 24 hr, and 1.88 ± 0.26 mm on three month scans. A statistical significance was observed when comparing these means (p <0.001) using analysis of variance. Post Hoc testing showed significance between pre and 24 hr post ablation scans (p <0.001). and also 24 hr and three month scans (p <0.001). There was no statistical significance between pre and three month scans (p = 0.66).

The average change in thickness of the anterior wall from pre ablation to 24 hrs post ablation was 0.36 ± 0.51, -0.26 ± 0.44 from 24 hrs to three months post ablation, and 0.23 ± 0.56 from pre to three months post ablation. Analysis of variance showed a statistical significance between these three means (p <0.001). Using post hoc analysis, a statistical significance between the change in thickness between pre to 24 hrs post ablation and 24 hrs to three months post ablation (p <0.001) was found. Statistical significance was also found when comparing 24 hrs to three months post ablation and pre to three months post ablation (p < 0.001). However, there was no significance between change in thickness from pre to three months post ablation (p = 0.27)

**Esophagus Posterior wall**
Mean esophageal posterior wall thickness was 1.85 ± 0.32 mm on pre ablation, 1.96 ± 0.28 mm on 24 hr, and 1.92 ± 0.31 mm on three month scans. A statistical significance was not observed when comparing these means (p = 0.07) using an analysis of variance. Post Hoc testing also did not show significance between pre and 24 hr post ablation scans (p = 0.06), 24 hr and three month scans (p = 0.78), or pre and three month scans (p = 0.48).

The average change in thickness of the posterior wall from pre ablation to 24 hrs post ablation was 0.14 ± 0.33, -0.05 ± 0.27 from 24 hrs to three months post ablation, and 0.21 ± 0.56 from pre to three months post ablation. Analysis of variance 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 pre to 24 hrs post ablation and 24 hrs to three months post ablation (p = 0.02). Statistical significance was also found when comparing 24 hrs to three months post ablation and pre to three months post ablation (p = 0.001). However, there was no significance between change in thickness from pre to three months post ablation (p = 0.54).

**Upper Gastrointestinal Endoscopy**

Out of the five patients who displayed esophageal enhancement on DE-MRI at 24 hours post-ablation, three patients elected to undergo upper gastrointestinal endoscopy. Two patients refused the procedure. One patient experienced a superficial large erosions (1-2 cm) with nodular base in the lower third of the esophagus. The second patient had localized mucosal abnormality characterized by pale erythema found at 32cm from the incisors. This was an area of approximately 1cm 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 revealed an irregular and erythematous lesion in the lower third of the anterior wall. All three patients had lesion size and location that correlated with the anatomical location of enhancement identified on DE-MRI based on the 3D recreations of the esophagus. Two patients had repeat endoscopy one week later, which 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 following catheter ablation of AF. Although DE-MRI has been shown to visualize post-ablation LA changes resulting from the RF energy, 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 post ablation in regions targeted during the procedure with all patients showing complete lesion resolution within one week post-ablation. Endoscopic evaluation correlated the size and location of MRI enhancement patterns with intraluminal lesions detected with endoscopy.

Our findings of post-ablative esophageal changes are consistent with other reports detailing this phenomenon. A recent analysis by Schmidt et al demonstrated frequent erythematous (29%) and necrotic changes (18%) in the anterior wall of the esophagus twenty-four hours post-AF ablation. These authors used repeat endoscopy to show complete recovery of the erythematous esophageal changes by two-weeks post-ablation.
and recovery of the necrotic changes by one-month post ablation. Another recent study by Singh et al demonstrated that 11% of asymptomatic patients experienced post-ablation esophageal ulcerations from RF energy.¹²

Recovery of lesions as measured by resolution of contrast enhancement might be explained by a partial inflammatory reaction occurring in the esophagus immediately following ablation. This could be similar to the inflammatory state that has been described in the LA immediately following RF ablation.¹³, ¹⁴ It has recently been reported that gadolinium enhancement in the LA in the immediate post-ablative state might represent edema/hemorrhage rather than true myocyte necrosis, as 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 post-ablative esophagus. The gadolinium uptake and wall thickening seen in the posterior wall of the esophagus might also represent edema rather than necrosis as this tissue is not in near contact with the ablation energy, yet appears to undergo transient post-ablative changes as well.

Figure 3 demonstrates both LA and esophageal enhancement resolution following 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 post-ablation. Repeat imaging at three months demonstrates complete resolution of esophageal lesions with decrease in LA enhancement to regions solely confined to the the pulmonary vein antra. The resolution of contrast enhancement and return of wall thickness to pre-procedure 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 RF energy delivery effects mediastinal structures outside the LA. Although our study used an ablative technique targeting the LA posterior wall, we do not feel this caused an increase in the incidence of esophageal injury. Based on the significant anatomical overlap of the esophagus, many standard pulmonary vein antra techniques have the potential to damage the esophagus. 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. The close anatomical 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 following AF ablation among the different techniques and ablation parameters utilized.

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

**Study Limitations**

Given the prospective nature of this analysis, expert MRI reviewers were not blinded to
the time point of scan acquisition, since 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 prior to the ablation and did not demonstrate any contrast enhancement in the esophagus, patients with pre-existing esophageal pathology were not excluded from the study.

Conclusions

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

Conflict of Interest Disclosures: None

References


**Table 1: Patient Demographics**

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Figure 1. Acute Post-Ablation Esophageal Changes and Recovery. This figure depicts five patient examples of esophageal changes post-AF ablation. Pre-procedure MRI (left) in all patients did not demonstrate any esophageal contrast enhancement. However, at 24 hours post-ablation (middle) all five patients had anterior wall thickening with significant contrast enhancement primarily located in the anterior wall. This enhancement and wall thickening showed complete resolution by three months post-procedure (right) even though chronic left atrial scar remained. Regions of esophageal enhancement were in close relation to radiofrequency-induced scarring in the left atrium from the ablation procedure.

Figure 2. Evaluation of Esophageal Lesions with Endoscopy. Three patients with enhancement seen on DE-MRI at twenty-four hours underwent endoscopy. The patient example below is a 62 year-old male with paroxysmal AF who experienced increased gadolinium uptake (yellow arrow) in the anterior wall of the esophagus on MRI at 24 hours post-ablation. Endoscopic findings at that time point confirmed the presence of a superficial erosion in the anterior wall. Repeat imaging and endoscopy one week later showed full recovery of the esophageal lesion on MRI and UGE.

Figure 3. Recovery of Contrast Enhancement in the Anterior wall of the Esophagus. This patient example is of a 57 year-old female presenting for catheter ablation of paroxysmal AF. Three-dimensional segmentation of the LA and esophagus at 24-hours post-ablation (left) demonstrates significant contrast enhancement (orange). However, by three months post-ablation (right) there is resolution of all 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, which partially or fully resolves by later follow up. This example also demonstrates the close anatomical relationship between the LA and esophagus, primarily at the antra regions targeted during the ablation procedures.