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Strategies to Prevent Esophageal Injury During Catheter Ablation of Atrial Fibrillation

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Introduction

Radiofrequency (RF) catheter ablation has been introduced as a treatment to maintain sinus rhythm in patients with drug-refractory paroxysmal and persistent atrial fibrillation (AF).¹ A key element of most ablation procedures is electrical isolation of the pulmonary veins (PVs), which often trigger paroxysmal AF.² The most commonly employed strategy presently involves creation of circumferential lesions around the PV ostia or antra. Additional linear lesions may be delivered in the left atrial roof, mitral isthmus, or posterior wall, usually in patients with persistent AF. In addition, complex fractionated atrial electrograms, which are believed to identify tissue important for perpetuation of AF, may be targeted at various locations in the left atrium (LA).³

AF ablation carries a small risk of complications. One of the most serious is atrioesophageal fistula (AEF). Although the incidence is less than 0.1%, it carries a high mortality rate, over 70% in most series.^{4,5} This review will examine strategies to detect and avoid esophageal injury during catheter ablation of AF, in order to reduce the risk of AEF.

Pathophysiology

Patients with AEF typically present with delayed onset, making direct mechanical insult an unlikely cause of fistula formation. AEF formation occurs because of thermal damage to the esophagus. The insult is believed to start at the esophageal side and extend into the mediastinum and LA.⁶ Epithelial intestinal tissue is highly susceptible to RF-induced thermal injury and lesions formed by irrigated catheters are teardrop shaped, with the largest lesion projected deeper into the tissue. Heat damage results from thermal conduction in the tissue rather than direct power application. Total energy delivery is proportional to programmed power delivered and the duration of application of the RF energy, and is affected by catheter orientation and contact force.⁷ In a canine model, esophageal ulceration was produced when the esophageal temperature was greater than or equal to 50°C and was more frequent when applied closer to the esophagus.⁸

Heat may affect esophageal endothelial cells directly, or may damage anterior esophageal arteries, causing ischemia and ulceration of the mucosal layers. Morphological changes of periesophageal connective tissue and the posterior wall of the LA can be seen on endosonography after PV isolation, even in the absence of endoscopic endothelial damage.⁶ In addition, pre-existing esophagitis due to gastroesophageal reflux seems to play a role in the development of AEF, perhaps interfering with the usual repair mechanisms after esophageal injury.⁹ After esophageal tissue necrosis develops, mediastinitis and fistula formation occurs, eventually connecting the esophageal lumen with the pericardium and then left atrial blood pool via the oblique sinus.

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Clinical presentation and surgical management

Patients usually present AEF 1–4 weeks after ablation, although earlier and later onsets have been reported.¹⁰ Most early symptoms and signs are not specific, varying from fever, fatigue, and malaise to sudden-onset chest discomfort, nausea, vomiting, dysphagia, odynophagia, hematemesis, melena, and dyspnea. A high index of suspicion is recommended in patients with constitutional symptoms after AF ablation, especially high-grade fever, as well as sudden-onset chest or epigastric pain.

With any of these symptoms, white blood cell count should be obtained; this is an early and sensitive laboratory marker.¹¹ In addition, imaging should be performed emergently. Imaging can include an esophogram with thin barium or water-soluble contrast that may show extravasation from the esophagus to the LA or mediastinum. Computed tomographic (CT) scan of the chest with intravenous contrast may demonstrate pneumomediastinum or pneumopericardium, and is diagnostic if intravenous contrast enters the esophagus from the LA. Endoscopy and transesophageal echocardiography are not recommended since they could increase fistula size and the risk of food or air embolism secondary to instrumentation and insufflation.¹²

Early recognition is important, as patients often develop endocarditis with septic emboli, leading to neurological manifestations such as altered mental status, seizures, and coma within hours of symptom onset.¹¹ The symptoms reflect polymicrobial sepsis with or without mediastinitis and pericarditis. Transthoracic echocardiography may reveal pericardial effusion.

Early surgical intervention may prevent a fatal outcome. This typically involves thoracotomy with mediastinal drainage, atrial and esophageal repair, often with interposition of a muscle flap or pericardium.¹³ Some reports have described non-surgical management, including esophageal stenting¹⁴ or even conservative management under specific circumstances.¹⁵ A case report describes managing AEF with esophageal decompression and ligation at the cervical level combined with gastrostomy and jejunostomy, resulting in faster recovery than the traditional thoracotomy and esophageal repair.¹⁶

Risk factors for atri-esophageal fistula

Owing to the low incidence of AEF, esophageal endoscopic studies have been used to screen for asymptomatic endothelial injuries after ablation, with esophageal ulcerations (ESULs) serving as potential precursors of fistula formation. Several studies have examined predisposing risk factors for esophageal injury. Patients with persistent AF may be at higher risk because of larger LA size, additional linear lesions and fractionated electrogram ablation on the posterior wall, longer total RF delivery, and higher power settings. With a maximum power of 25 watts at the posterior LA wall, ESUL incidence is 2–3%, but increases with higher power settings.¹⁷ Achieving

excessive contact force using a deflectable sheath may also predispose to fistula formation.¹⁸ In a single-center study, over 260 patients were screened for ESUL 24 h after ablation; multivariate analysis showed the only independent predictor of ESUL was distance between LA and esophagus, although mitral isthmus line and coronary sinus ablation showed a trend towards significance.¹⁹ Patients with persistent AF were more likely to have LA enlargement with compression of the esophagus between the LA and the spinal cord or the aorta.

Some reports have suggested that the risk of developing ESUL is increased in those undergoing general anesthesia versus conscious sedation.²⁰ Proposed mechanisms include lack of esophageal peristalsis and swallowing during anesthesia, which might prevent physiological cooling, and use of an orogastric tube, which might cause mechanical fixation of the esophagus against the LA.

Body mass index (BMI) is also associated with risk of esophageal injury. Yamasaki et al²¹ performed endoscopic examinations 48 h after ablation in 104 patients. Procedures were done under conscious sedation with maximum energy of 20–25 watts and duration of 30 s per site at the posterior LA wall. A total of 9.6% of patients had esophageal injuries, and all were below normal body weight (BMI of 24.9 kg/m²), likely due to a shorter distance between esophagus and LA as well as paucity of intervening connective tissue.

Anatomical considerations

Understanding the anatomic relationship between the esophagus and LA is crucial during catheter ablation for AF. The esophagus lies posterior to the LA, in a groove bounded by the aorta on the left and the spine posteriorly (**Figure 1**). The esophagus leads a variable course relative to the LA, adjacent to the right or left PVs or the posterior wall.²² Hence, the risk of esophageal damage could be encountered with RF delivery anywhere in the posterior LA.

The posterior LA has non-uniform wall thickness, as does the fat-pad layer between the LA and the esophagus. Patients with AF and left atrial dilatation demonstrate thinner fat pads by CT scanning and a larger LA–esophageal contact area.^{23,24} Multiple anatomical structures were visualized in these fat pads, including lymph nodes, branches of the left vagus nerve, and esophageal vessels. Thermal damage to these structures may also have a role in inducing ischemic esophageal injury.

Although concern has been raised regarding variable esophageal position due to esophageal movement within patients, several reports have demonstrated a stable position. In one series, cine-fluoroscopic images of the esophagus during a barium swallow were recorded and the course of the esophagus was tagged on the three-dimensional (3D) map in patients going for repeat AF ablation; the esophagus was found to be in the same position relative to the PVs as during the initial procedure.²⁵ In another study the position of the

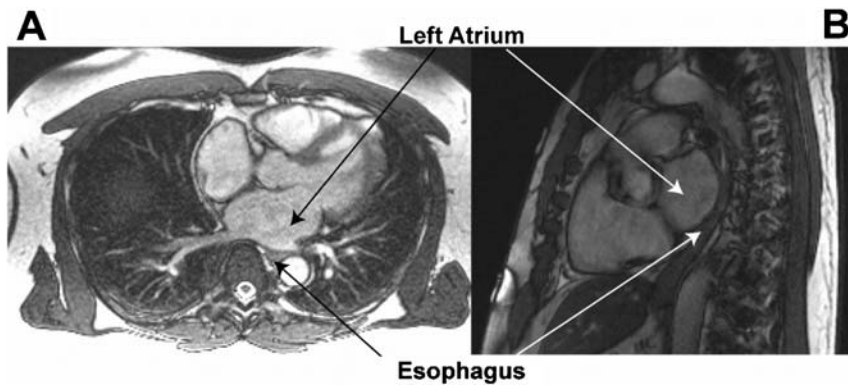


Figure 1: Magnetic resonance imaging showing close approximation of posterior left atrial wall and esophagus in axial (a) and sagittal (b) views. Radiofrequency energy delivery to posterior left atrial wall can result in thermal esophageal injury.

esophagus on pre-procedural CT corresponded to the intraoperative position when defined using an electroanatomic mapping system.²⁶

Esophageal imaging and localization

A variety of imaging techniques are available to visualize the esophagus during AF ablation procedures. Visualization allows limiting RF energy and minimizing RF application near points at which the esophagus lies in close proximity to the posterior LA wall. Some imaging techniques depend on obtaining pre-procedural images using CT or magnetic resonance contrast angiography. Visualization can be improved with swallowed barium sulfate or gadolinium diglutamate.²⁷ One potential caveat for these modalities is that a time delay before ablation could allow changes in the size and location of the esophagus, making the images less useful.

A 3D rendering of the esophagus can also be generated during the procedure using an electroanatomic mapping system (NavX, St Jude Medical, Minneapolis, MN or Carto, Biosense Webster, Diamond Bar, CA). Esophageal location can be marked by advancing a diagnostic electrophysiologic catheter into the esophagus and tagging its location.²⁸ Another method is the Carto SoundStar system, which renders the LA and adjacent structures by merging multiple two-dimensional (2D) imaging planes generated by intracardiac echocardiography.^{29,30} Recently 3D rotational angiography (3DRA) has emerged as an alternative to CT or magnetic resonance imaging (MRI) for anatomic reconstruction.^{31,32} The principle of 3DRA is similar to CT; images acquired from different angles with a rotating fluoroscopic system are used to create a 3D image. The LA and PVs are opacified by contrast injection into the LA, while the esophagus is opacified with barium paste prior to image acquisition. The LA, PVs, esophagus, and the other surrounding structures can be segmented and registered with the fluoroscopy to serve as a roadmap for ablation. While these methods display esophageal location on the day of the ablation, they do not offer true real-time visualization, since they acquire static esophageal images at the beginning of the procedure.

Real-time visualization of the esophagus can be achieved by fluoroscopy utilizing esophageal luminal markers, such as a nasogastric tube, temperature probe, or

barium contrast.³³ Relying solely on the nasogastric tube or temperature probe for esophageal localization could be misleading, as the entire lumen of the esophagus is not visualized. Barium paste allows visualization of the esophageal lumen, but does not show esophageal wall thickness. These real-time methods carry the advantage of compensating for esophageal movement during the procedure. However, patients under conscious sedation (rather than general anesthesia) are less likely to tolerate luminal esophageal markers, and barium paste will remain in the esophagus only transiently because of peristalsis.

Measures to minimize the risk of esophageal injury

Gastric acid suppression

Multiple endoscopic studies have demonstrated esophageal ulceration following AF ablation. Pre-existing gastroesophageal reflux might play a role in aggravating the esophageal insult and promote development of AEF in patients with ulceration after ablation. Prophylactic proton-pump inhibitors (PPIs) have been recommended for patients undergoing AF ablation due to potential benefit and benign side effect profile.⁹ Large clinical trials to establish efficacy may never be feasible because of the low incidence of AEF.

Esophageal temperature monitoring

Although power and duration of RF energy application are limited at the posterior LA wall, other factors also affect the risk of thermal esophageal injury, including catheter contact force and orientation, distance between ablation site and esophagus, and the presence of intervening connective tissue. Because these may be difficult to quantify and predict, another method of minimizing risk is directly assessing heat transfer to the esophagus with real-time luminal esophageal temperature monitoring. With a temperature probe in the esophagus directly adjacent to the ablation catheter, increases in luminal esophageal temperature can alert the operator to reposition the ablation catheter or interrupt RF application (**Figure 2**).

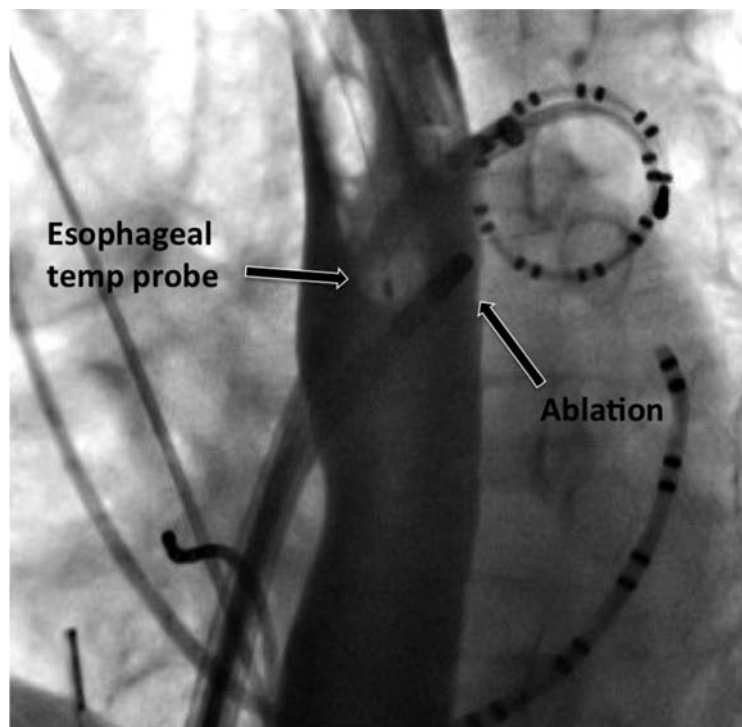


Figure 2: Left anterior oblique fluoroscopic view of esophageal temperature monitoring during atrial fibrillation ablation. The esophagus is filled with barium paste and an endoluminal probe continuously monitors esophageal temperature during ablation.

Singh et al,³⁴ in a retrospective study when esophageal temperature was monitored, showed that patients were less likely demonstrate esophageal injury after ablation. Their practice was to interrupt RF when the temperature increased to 38.5°C; the ablation catheter was then moved to a new site or power was decreased. Only 6% of patients with ablation guided by esophageal temperature monitoring developed esophageal ulcerations by endoscopy, as opposed to 36% of those without monitoring. A more recent prospective study showed that by guiding ablation with a triple-thermocouple esophageal temperature monitor (Esotherm, Florence, Italy) and limiting esophageal temperature to 40°C, only 1.6% of 184 patients had signs of thermal esophageal injury.³⁵ To determine a safe level of esophageal temperature increase, Leite et al used a deflectable catheter to monitor luminal esophageal temperature with the temperature monitor positioned as close as possible to the site of left atrial RF application.³⁶ Power on the posterior wall was limited to 25 watts and terminated when the temperature increased 2°C from baseline. Using this strategy, no patients had esophageal thermal injury on follow-up endoscopy. Taken together, these studies suggest that with careful esophageal temperature monitoring, and interrupting RF with an increase of 2°C, the risk of esophageal injury and AEF will be low.

However, correct position of the temperature probe is crucial for assuring that the maximum esophageal temperature is detected during ablation. The probe must be repositioned repeatedly within the esophagus during

the procedure in order to measure temperature as close as possible to the ablation site. If the esophagus is large or the probe is not situated directly adjacent to the LA, esophageal temperature may be underestimated.³⁷ Moreover, esophageal temperature usually continues to rise even after RF is interrupted, resulting in temperature overshoot in up to 93% of patients. Finally, esophageal luminal temperature may be significantly lower than esophageal mural temperature.³⁸ Consequently, ulcerations may occur after ablation even when the luminal esophageal temperature is assiduously monitored.²⁰ Even the most dreaded complication, AEF, has been reported in a case in which esophageal temperature did not rise during ablation.³⁹ This illustrates that esophageal temperature monitoring alone is insufficient to completely prevent esophageal thermal injuries, prompting the search for methods to actively protect the esophagus during AF ablation.

Mechanical deflection of esophagus

Since the esophagus lies in proximity to targeted sites on the posterior LA wall in nearly every patient undergoing ablation for AF,⁴⁰ an array of mechanical techniques have been devised to move the esophagus away from the tip of the ablation catheter. This is possible because the thoracic esophagus is not fixed in position by true ligaments or other significant fibrous attachments to surrounding structures. Chugh et al⁴¹ showed the feasibility of displacing the esophagus by deflecting an endoscope during

ablation. They found that it was possible to move the esophagus in 10 of 12 (83%) patients, on average 2 cm towards either the right or left-sided PVs. However, the endoscope was removed during RF application, to avoid mechanical complications and shunting of RF energy towards the endoscope. In only 22% of patients, the esophagus remained in its displaced position after endoscope removal, presumably lowering the risk of esophageal heating during ablation in only a few patients. This study did not show definitively whether the esophagus was moved or simply stretched by the endoscope. A more recent study by Koruth et al⁴² demonstrated that during RF or laser ablation of the posterior LA wall, an endotracheal stylet within a thoracic chest tube could deflect the esophagus away from the area of energy delivery in 20 patients. Leftward and rightward deflection averaged 2.8 cm each, and was maintained during ablation at the posterior wall; luminal temperature rises were limited. Postprocedural endoscopy showed ulceration in one patient (5%) and evidence of trauma from esophageal instrumentation in 63% without any clinical sequelae.

This technique did not require participation of an endoscopist during the ablation procedure. Together these studies suggest that endoluminal esophageal displacement holds promise as a method of protecting the esophagus during ablation of AF.

Thermal insulation of esophagus

Another means of protecting the esophagus during posterior LA ablation is instrumentation of the pericardial space and introduction of a balloon catheter between the LA and esophagus. This technique has been demonstrated in a case report from our center in which a balloon catheter was positioned in the oblique sinus and filled with fluid to move the esophagus away from the LA and reduce heat transfer.⁴³ This allowed complete PV isolation without esophageal heating or injury in a patient whose previous procedure could not be completed due to esophageal heating. Nakahara et al⁴⁴ studied the method systematically in an animal

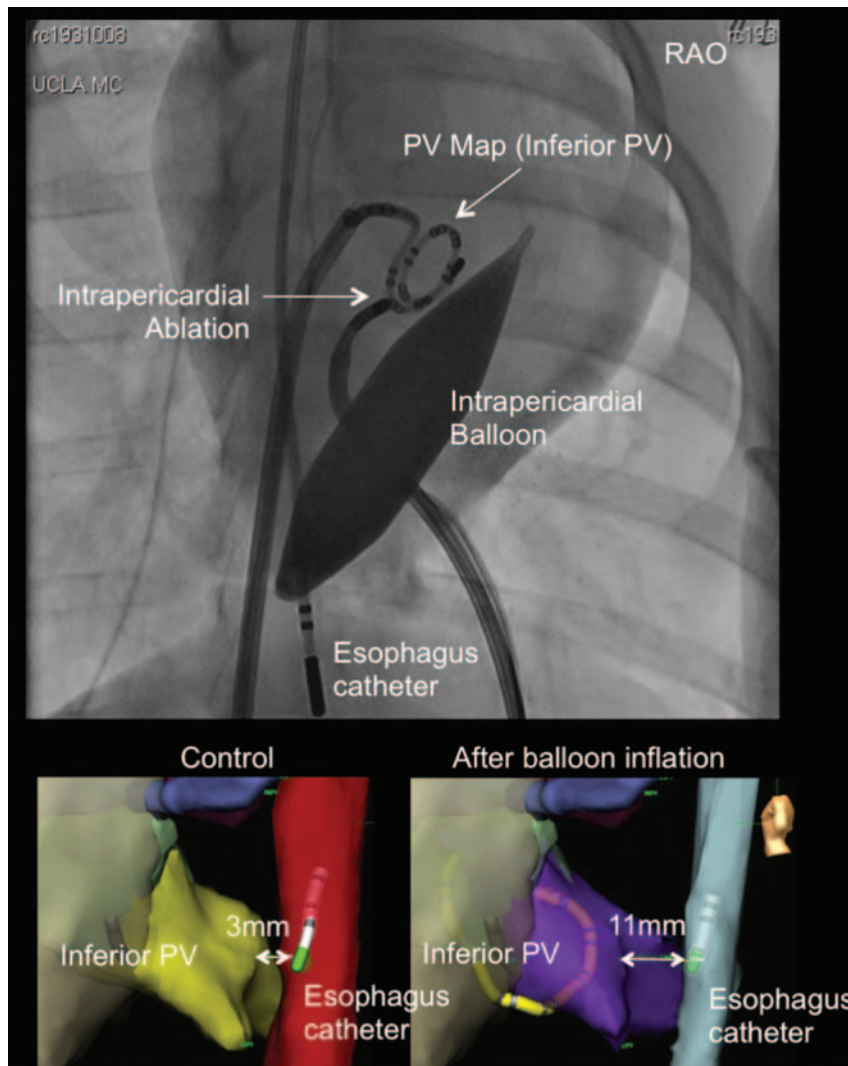


Figure 3: In an animal model, inflation of a balloon catheter in the pericardial space separated the pulmonary vein antrum from the esophagus and allowed radiofrequency delivery without esophageal heating. Courtesy of Shiro Nakahara, MD.

model and found that esophageal temperature rises could be limited introducing a pericardial balloon. In that study esophageal temperature increase was prevented by the use of the balloon in the pericardium (Figure 3) and there was no hemodynamic compromise due to the use of the balloon.

Limiting energy delivery

Titration of energy delivery plays a major role in preventing AEF. This requires a balance between effective lesion formation (procedural efficacy) and avoiding thermal injury to the esophagus (procedural safety). Titration of energy is based on risk factors such as esophageal proximity, enlarged atria, and patient BMI. Utilizing imaging modalities as described above, power can be reduced at areas where the posterior wall is in close proximity with the esophagus. Martinek et al¹⁷ demonstrated with endoscopic survey that esophageal ulceration was rare when a maximum of 25 watts is delivered with open-irrigated tip catheters at the posterior wall. However, despite real-time visualization of the esophageal course by barium contrast, ESUL was not completely avoided. Halm et al⁴⁵ reported ESUL incidence of 15% detected by endoscopy in 185 patients undergoing left atrial ablation using an open irrigated tip ablation catheter with a maximum power of 30 watts at the posterior wall, without esophageal temperature limitation. Sause et al,³⁵ in a series of 184 patients, showed when limiting power to 30 watts on the posterior LA with titration to maintain esophageal temperature below 40°C that the incidence of the ESUL was only 1.6%. No ESUL was seen in either series when the maximum esophageal temperature stayed below 41°C.

New technologies

Strategies to limit thermal injury by cooling the esophagus with a saline-irrigated balloon have been evaluated, and have successfully prevented esophageal temperature rise.^{46,47} However, in theory balloon inflation in the esophagus could mechanically displace the esophagus towards the ablation site, enhancing heat transfer to the esophagus and risk of thermal injury. Other experimental *in vitro* cooling systems using temperature-controlled fluid-circulating systems have also been investigated and may have a future role.⁴⁸

Cryoballoon PV isolation is an emerging alternative technique with a favorable safety profile that to our knowledge has not resulted in a reported case of AEF. Still, results from an experimental study by Ahmed et al suggest that cryothermal energy is associated with a significant 17% risk of ESUL.⁴⁹ This may have resulted from the cryoballoon deforming of the LA and pushing it closer to the esophagus. In another series of 38 patients, there were no cases of ESUL or AEF, perhaps due to the larger balloon used in that study, preventing freezing within the PVs and allowing more warming blood flow to reach the affected part of the esophagus.⁵⁰

The emergence of catheters with contact-force sensors, direct visualization, and real time MRI will probably play a role in the future to further minimize the risk of AEF formation.

Summary

AEF is a rare but often fatal late complication of AF ablation procedures, resulting from thermal injury to the esophagus. With careful monitoring of esophageal position and temperature, while limiting power and duration of RF application at the posterior LA, this complication will remain rare. However, esophageal ulceration is still detected at an alarming rate on endoscopic examinations, and AEF does occur. Future technologies and approaches may further reduce the incidence of this dreaded complication.

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