

Atrio-Esophageal Fistula After AF Ablation: Pathophysiology, Prevention & Treatment

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Abstract

Atrioesophageal fistula is an extremely rare but often fatal late complication of atrial fibrillation ablation procedures resulting from massive thermal injury to the esophagus and surrounding structures. Causes of death include cerebral air embolism, massive gastrointestinal bleeding, and septic shock. Because of its exceptionally low rate of occurrence, no predictors of lesion development have been found and there has not been an uniform approach to either early diagnosis or corrective therapy. Currently, preventive strategies include empirically reducing power titration during PVI and/or while ablating the posterior left atrial wall, limiting energy delivery time and number, avoiding overlapping ablation lines as well as monitoring intraluminal esophageal temperature. In addition, it has been suggested to use conscious sedation rather than general anesthesia for better pain perception, monitoring intraprocedural esophageal position in relation to the posterior left atrium and extensive patient education regarding signs and symptoms of esophageal injury. Early diagnosis is essential to enable an aggressive treatment including stenting and/or surgical intervention to minimize the excessive morbidity and mortality associated with this condition. Unfortunately, despite application of such preventive measures, cases of complete atrio-esophageal fistula have still been reported.

Introduction

The cornerstone of AF ablation has been considered pulmonary vein (PV) isolation using RF energy or balloon-based techniques, but more extensive substrate ablation is often required in many patients with persistent AF to achieve higher success rate.¹ Although more complex and longlasting ablation procedures may be associated with relatively higher risk of major complications including cardiac perforation/tamponade, thromboembolic events, PV stenosis, and esophageal thermal lesions, a complete atrioesophageal fistula very rarely occurs. Esophageal damage, perforation, and atrio-esophageal fistula were firstly reported after posterior left atrium RF ablation procedures as a complication of open-heart surgery.² The first reports of complete atrio-esophageal fistula formation after percutaneous RF ablation were published in 2004.³⁻⁴ Subsequently, atrio-esophageal fistula has been reported worldwide as an extremely

rare (0.04%) but catastrophic complication of catheter ablation of AF.⁵⁻²² In a worldwide survey of 8,745 patients undergoing AF ablation, major complications developed in 524 patients (6%), including 4 periprocedural deaths (0.05%) from massive cerebral thromboembolism in 2, extrapericardial PV perforation in 1, and an unknown cause in one patients, but there were no cases of atrio-esophageal fistulae.⁹

Pathophysiology

The relatively frequent occurrence of esophageal thermal lesions during any AF ablation procedure using different approaches/tools without clinical sequelae and the very rare late occurrence of complete esophageal fistula formation, usually weeks after catheter ablation suggest that mechanisms and pathophysiology of such catastrophic complication are very complex and perhaps, should be individually evaluated.³⁻⁷ As a result, at present a definite relation of esophageal mucosal lesions to atrio-esophageal fistula formation remains unknown. Presumably, a progressive and sequential involvement of many cardiac and extracardiac structures by continued and/or repeated massive thermal injury is required to induce more severe lesions with different outcomes exceptionally leading to late complete fistula formation with delayed onset of typical symptoms. The esophagus lies posterior to the LA, in a groove bounded by the aorta on the left and the spine posteriorly leading a variable course relative to the LA, adjacent to the right or left PVs or the posterior

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None.

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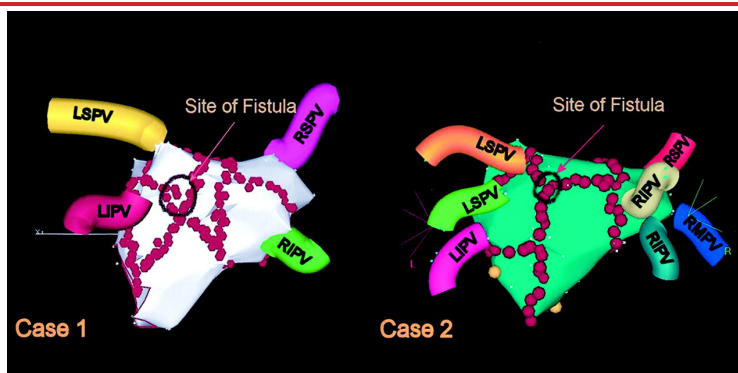


Figure 1:

Three-dimensional anatomic maps of LA and PVs from a posteroanterior view. Red tags indicate sites at which radiofrequency energy was applied, generally for a total of 20 to 30 seconds at each site. Approximate location of atrio-esophageal fistula that later occurred in cases 1 (left) and 2 (right) is circled. LIPV indicates left inferior PV; LSPV, left superior PV; RIPV, right inferior PV; RMPV, right middle PV; and RSPV, right superior PV.

wall.²³⁻³³ Therefore, there is a risk of esophageal damage when RF is delivered anywhere, particularly in the left atrium posterior wall. The posterior LA has non-uniform wall thickness and patients with AF and left atrial dilatation have larger LA-esophageal contact area and thinner fat pads with multiple anatomical structures including esophageal vessels. Once esophageal necrosis develops, mediastinitis and fistula occurs connecting esophageal lumen with pericardium. Although variable esophageal positions due to esophageal movement within patients have been reported, usually a stable position has been demonstrated. It has also reported that gastroesophageal reflux may facilitate mucosal injury playing an additional role.³⁴

Prevention

Currently, no risk factors have been reported predicting complete atrio-esophageal fistula formation. Preventive strategies may reduce the incidence of esophageal thermal lesions in many patients, but, given that catheter ablation of AF is being increasingly performed for more indications at more centers with different tools and energy forms, it is likely that esophageal fistula will continue to occur in some cases. Before considering any preventive strategy as an appropriate strategy, it should be emphasized that the rate of complete atrio-esophageal fistula is extremely low as compared with the high rate of post-ablation esophageal lesions without fistula formation. Currently, potential strategies which have been proposed to prevent

esophageal injury include: 1) empirically reducing power titration and duration of energy application while ablating the posterior LA wall; 2) avoiding overlapping ablation lines using RF; 3) monitoring intraluminal esophageal temperature, using conscious sedation rather than general anesthesia for better pain perception; 4) monitoring intraprocedural esophageal position in relation to the posterior LA; and 5) extensive patient education regarding signs and symptoms of esophageal injury. Despite application of such preventive measures in many laboratories, rare cases of atrial-esophageal fistulas have been reported.³⁵ Endoscopic evaluation post ablation reveals a high (15–48%) incidence of esophageal erosion in patients undergoing standard LA ablation protocols using both RF ablation and cryoballoon pulmonary vein isolation.³⁶⁻⁴³ Predictors of esophageal damage and potential for subsequent development of esophageal fistula have been reported using RF³⁶ and include persistent AF ablation, power >30 W, esophageal temperature rise to >40°C, intraoperative pain, and anatomic positioning of the esophagus by CT scan (proximity to LA wall). Luminal esophageal temperature also predicts esophageal lesions after second-generation cryoballoon PVI.⁴³

Real-time Esophageal Temperature Monitoring

Directly assessing heat transfer to the esophagus with continuous monitoring of the esophageal luminal temperature during ablation with special temperature sensors has been proposed to prevent esophageal thermal injury.³⁷⁻⁴⁴ However, patients under conscious sedation are less likely to tolerate nasogastric tube, temperature probe, or barium contrast and correct position of the probe is essential to detect the maximum esophageal temperature during RF applications, particularly in patients with a large esophagus in whom temperature may be underestimated. Although such strategy may be useful alerting the operator to replace the ablation tip or stop RF application, initial thermal injuries usually have a rapid resolution without major complications. The fact that esophageal fistula has been reported in a patient in which esophageal temperature did not rise during ablation,⁴⁴ clearly suggests that temperature monitoring alone is indeed insufficient to prevent esophageal thermal injuries.

Monitoring Intraprocedural Esophageal Position

Assessment of the esophagus position in the preprocedural CT/MRI scan may be useful but it is limited by the potential of the esophagus to move during the procedure.⁴⁵⁻⁵⁰ Tagging of the esophagus and real-time visualization of its course during the procedure can

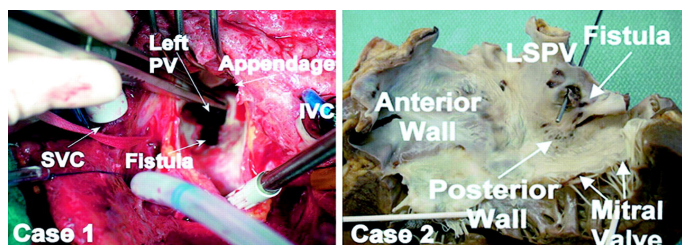


Figure 2:

Anatomic demonstration of atrio-esophageal fistulas. Left, Case 1: Intraoperative photograph taken from patient's right side with head to left, highlighting atrio-esophageal fistula arising medial to left PV ostia. Two distinct ostia cannot be seen because veins are empty and walls have collapsed. Right, Case 2: Formalin-fixed LA was incised near left superior PV and opened in book fashion, with anterior wall on left and posterior wall on right. Probe passes through fistula, which was on posterior wall near left superior PV. IVC indicates inferior vena cava; SVC, superior vena cava; and LSPV, left superior PV.

be achieved by introduction of a catheter into the esophagus and visualization in the three-dimensional electroanatomical system, by intracardiac ultrasound or by fluoroscopy.⁴⁷⁻⁴⁹ Mechanical deflection of esophagus to move it away from the tip of the ablation catheter towards either the right or left-sided PVs has been recently proposed as a new promising measure to protect the esophagus during ablation of AF.⁵¹ This strategy may prevent esophageal damage and potential fistula formation, but further larger prospective studies are required to establish its role.

Thermal Insulation of Esophagus

Thermal insulation of esophagus during ablation of AF by a balloon catheter between the left atrium and esophagus has been recommended to avoid esophageal heating in a patient whose index procedure was not completed due to esophageal heating.^{52,53}

Gastric Acid Suppression

Administration of high-dose proton pump inhibitors before and after ablation, particularly in patients with pre-existing gastroesophageal reflux has been recently recommended.⁵⁴ However, because of the very low incidence of esophageal fistula, to establish a benefit of such strategies a large number of patients are indeed required.

Limiting RF Energy Delivery

Until the mechanism of esophageal injury is fully understood, an accepted approach to minimize excessive heat transfer is to decrease the energy and temperature settings during ablation along the posterior left atrial wall. Reduction of power during energy application at the posterior left-atrial wall in close proximity to the esophagus is a simple method to limit esophageal thermal injury.⁵⁵ In our extensive experience, from 2003 to 2013 among > 25,000 patients undergoing AF ablation with 3.5 mm irrigated tip catheters esophageal fistula did not develop in any case without limiting RF energy on the posterior wall (30 W) only using short duration for each RF application (15-30 seconds) while dragging the catheter. The first 2 cases of esophageal fistulae we reported in 2004 (Figures 1-2) were associated with the use of 8 mm-tip catheters and high power settings (70-100W). A recent US-wide survey reported 6 fistulae in 20425 patients undergoing catheter ablation using 8 mm-tip catheters and high power settings.¹⁰

Atrio-Esophageal Fistula and Balloon Ablation Technologies

Many cases of atrio-esophageal fistula occurred after catheter ablation using RF since this is the most used energy to treat patients with AF. Currently, balloon-based ablation using different energies, which includes cryotherapy,⁴³ laser,⁵⁶ and ultrasound⁵⁷, represents an emerging alternative technique to RF ablation in order to improve efficacy while minimizing complications. Balloon technologies initially employed a noncompliant balloon limiting PVI proximally leading to potentially higher rates of complications such as PV stenosis and phrenic nerve damage. Unfortunately, relatively frequent esophageal ulcerations and rare cases of atrio-esophageal fistulae have been also reported using cryothermal energy. Although the modifications of the first-generation balloon (second-generation balloons) have resulted in a larger balloon surface area of optimal cooling, improved procedural efficacy has been associated with major complications with 3 cases of AE fistula early in the

second-generation-balloon experience on 16,000 procedures (FDA MAUDE database).

Treatment

Early Diagnosis of Fistula Formation for Aggressive Treatment

Table 1 summarizes incidence, symptoms, diagnostic tools and therapy of esophageal fistula development. If initial fistula formation is clinically suspected, early diagnosis with immediate intervention is required for the patient's survival because it is associated with a mortality rate of over 80% and major cerebrovascular morbidity from septic thrombi and embolic stroke.⁵⁸ Although many cases are febrile with polymicrobial bacteremia at presentation, they may respond rapidly to antibiotics and findings of both transthoracic echocardiogram and CT scan may appear unremarkable. Only when patients develop a cerebrovascular accident an additional CT scan confirms the diagnosis prompting urgent temporary stenting or immediate surgical intervention. Infectious diseases specialists must have a high index of suspicion for this diagnosis for patients who develop postablative fever, chest discomfort, unexplained neurologic deficits, and occasionally bacteremia as long as 5 weeks after the ablation procedure. Echocardiography has not been a useful diagnostic tool while thoracic or cardiac CT scanning demonstrating the presence of pneumomediastinum or intra-atrial air has been the most reliable tool for the diagnosis of esophageal fistula. CT scanning can ultimately establish the diagnosis in almost all patients. Symptoms may include mental status changes, transient ischemic attacks, stroke syndromes with hemiparesis, and seizures. Unfortunately, the neurologic deficits tend to be a late finding, occurring in the second to third week after ablation, and often leave those who survive with permanent disabilities. Other reported symptoms include chest pain, seen in about one third of patients, odynophagia, and hematemesis. The development of hematemesis often prompts esophagogastrosopy, which has disastrous consequences with rapid deterioration in clinical status and eventually death, usually as a direct complication of air embolization from the esophagogastrosopy. On the basis of these findings, invasive esophageal procedures should be contraindicated for patients suspected of having an esophageal fistula formation not to enlarge the shunt. All reported patients who did not undergo surgery died, except for one patient who was successfully treated with an esophageal stent.²⁰ Nevertheless, 40% of those who did have surgery died.

Esophageal Stenting

Esophageal stenting represents an immediate therapeutic modality to approach an atrio-esophageal fistula development rather than early surgical repair of the esophageal perforation.⁵⁸⁻⁶⁰ Surgical correction is not feasible in most cases due to inflammatory loss of mediastinal tissue planes and friability of the LA wall. The anatomic location of posterior wall esophageal fistulae requires extensive deep thoracic dissection and may not be safe in the setting of poor tissue plane visibility, and need for ongoing anticoagulation.

Surgical Options

Rapid deterioration, neurologic damage, and death ensue with any delays in surgical intervention of fully formed esophageal fistula. There are many surgical options based on presumptive and early diagnosis.⁶¹⁻⁶⁴ Recently, left thoracotomy and resection of the fistula using an extrapericardial approach without the need

Incidence	Cause	Symptoms	Imaging	Prevention	Therapy
0.03–0.25%	Energy delivery (RF or balloon-based)	Fever, Malaise, Dysphagia, Hematemesis/melena Neurological deficits, Intermittent cardiac ischemia, Septic shock	CT/MR	Monitoring of esophageal location/temperature Avoidance of micro bubble formation Low-energy delivery for short duration	Surgical correction Stenting of the esophagus

ALA= Left Atrium; PVs= Pulmonary Veins; RF= Radio-Frequency;CT/MR=Computed Tomography/Magnetic Resonance Imaging

for cardiopulmonary bypass or esophageal diversion have been proposed.⁶² More recently, 2 short surgical options have been proposed for selected patients^{63,64}: – left atrial repair with cardiopulmonary bypass followed by repair of the esophagus with an omental wrap⁶¹ and – cervical esophageal ligation and decompression⁶⁴ without cardiopulmonary bypass.

Conclusions:

Catheter ablation of AF is associated with relatively frequent esophageal thermal lesions, but with minimal or no risk of atrio-esophageal fistula, which is a catastrophic often lethal complication. Other than empirically decreasing energy and duration delivery along the posterior left atrium while dragging the catheter and/or monitoring esophageal temperature, there are no other validated approaches to minimize this exceptionally rare event. Nonetheless, its early diagnosis is essential to enable immediate therapeutic strategies to minimize the excessive morbidity and mortality associated with this condition.

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