Esophageal Injury Following Radiofrequency Ablation for Atrial Fibrillation

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1 Introduction

Atrial fibrillation is the most common clinically significant arrhythmia, with a prevalence of 3.8% in persons 60 years or older and 9.0% in persons over the age of 80, and is a major cause of stroke. Due to the rapidly growing elderly population, it has been projected that there would be a 2.5 fold increase in the prevalence of atrial fibrillation by 2050. (Go et al., 2001) In an attempt to surgically correct the arrhythmia, the maze procedure was developed and described by Cox et al. in 1991; this procedure involved creating incisions within the left atrium in order to interrupt the reentrant circuits responsible for atrial fibrillation. (Cox, 1991; Cox, Schuessler, Lappas, & Boineau, 1996) The subsequent development of percutaneous radiofrequency ablation (RFA) to create transmural lines of electrically inactive scar within the left atrium (LA) endocardially and the right atrium epicardially significantly shortened procedure time. (Raman, Seevanayagam, Storer, & Power, 2001)

The approach to RFA changed dramatically in 1998 with the discovery by Haïssaguerre et al. (Haïssaguerre et al., 1998) demonstrating that the majority of ectopic atrial beats originate somewhere within one or more of the four pulmonary veins (PVs) along the course of muscular bands extending from the LA into the PVs. Following this, mapping and ablation of arrhythmogenic foci of both the PVs and the LA have been evaluated and have shown success rates of 60 to 90%. (Lin et al., 2003; Marrouche et al., 2002; Oral et al., 2003; Pappone et al., 2004; Pappone et al., 2001) Although RFA has been effective in treating atrial fibrillation, esophageal injury is a known complication that can occur, and, in certain circumstances, cause fatal injury.

2 Anatomic Proximity of Esophagus to Pulmonary Veins

In order to establish a better understanding of the anatomic relationship between the esophagus and the posterior LA wall, Sanchez-Quintana et al. (Sanchez-Quintana et al., 2005) found in 40% of cadaveric specimens there was less than 5 mm between the esophagus and LA endocardium. In addition to these findings, Tsao et al. (Tsao et al., 2005) described two variations of the esophageal course in relation to the PVs: Type 1, which is the most common, in which the esophagus passes along the left-sided PVs with the shortest distances being 10.1 ± 3.4 mm from the left superior PV and 2.8 ± 2.5 mm from the left inferior PV, and Type 2 in which the esophagus passes along the right-sided PVs with distances measuring 10.5 ± 5.7 mm from the right superior PV and 3.7 ± 3.4 mm from the right inferior PV. The wide variability in distance has been attributed to a thin discontinuous layer of fat pad between the adventitia of the esophagus and epicardium of the posterior LA. The thinnest layer of the fat pad has consistently been seen at the level of the inferior PVs, explaining the close proximity of the esophagus and the inferior PVs. Furthermore, anterior to the esophageal adventitia are the esophageal arteries and vagus nerve plexus, which can easily be injured with transmural ablation of the LA or PVs. Extensive RFA to the posterior PV or posterior LA could lead to damage of these structures and cause neurovascular compromise of the esophagus, which if left unchecked could cause esophageal necrosis and perforation.

3 Endoscopic Esophageal Injury Classification

Esophageal injury secondary to radiofrequency ablation was first described in 2001 following intraoperative ablation for atrial fibrillation. The patient presented 9 days following RFA with an elevated white
count and odynophagia, and was found to have a transmural esophageal perforation of the anterior wall that proved to be fatal (Gillinov, Pettersson, & Rice, 2001). Doll et al (Doll et al., 2003) later reported finding 4 (1%) out of 387 patients undergoing intraoperative RFA developed left atrial-esophageal fistulas, which were diagnosed secondary to neurologic defects from air emboli, massive hematemesis, or septic shock. Although all of these patients had unremarkable early postoperative courses, they began to develop signs of perforation 6 to 12 days following RFA.

Following these initial reports of esophageal injury with intraoperative RFA, the first report of atrial-esophageal fistula formation following percutaneous RFA were reported by Scanavacca and Pappone in 2004 (Pappone et al., 2004; Scanavacca, D’Avila, Parga, & Sosa, 2004) in which 3 patients presented with nonspecific signs and symptoms including persistent fever, dysphagia, odynophagia, sepsis, endocarditis, and neurologic ischemia. These patients presented to their physicians 10 days to 3 weeks following the ablation procedure, but esophageal injury was not initially considered in the differential diagnosis. Cummings et al (Cummings et al., 2006) reported 9 fatal cases of atrial-esophageal fistula formation in a retrospective case series based on anonymous identification in 2006. These nine patients presented 10 to 16 days post-operatively with a similar constellation of symptoms reported previously; however, only 4 patients received the correct diagnosis before death. The remaining patients were diagnosed at autopsy. Due to the considerable delay in diagnosis, DAGres et al (DAGres et al., 2006) attempted to identify criteria for rapid detection of esophageal perforation. They concluded that although the symptoms are generally non-specific, patients presented with two distinct symptoms, fever and severe chest or epigastric pain, which occurred 1 to 4 weeks following procedure.

Atrial-esophageal fistula formation appears to take at least 1 week to develop in most cases, which allows esophagogastroduodenoscopy (EGD) to be performed within 24 to 72 hours following the procedure with low likelihood of inducing air embolization. Due to the nature of RFA injury to the esophagus, only transmural lesions are visible on endoscopy. In an attempt to classify these lesions further, Keshishian et al developed an injury classification in 2012 to help risk stratify these patients. (Keshishian, Young, Hill, Saloum, & Brady, 2012) This divides esophageal thermal injury into three classes based on endoscopic appearance. These classes are illustrated in the figures below and summarized in Table 1.

### 3.1 Class I Thermal Injury

These patients have erythema or discoloration of the anterior esophageal wall with minimal mucosal disruption. These lesions should be shallow erosions without vessel involvement and should be less than 5 mm in diameter. These patients seem to have a low risk of progressing into frank perforation. They can be medically managed with proton-pump inhibitor (PPI) and sucralfate with clinical follow-up to assess for any worsening of symptoms.

### 3.2 Class II Thermal Injury

These patients have ulcers of the anterior esophageal wall with or without exudate. These lesions tend to penetrate further into the esophageal wall without extension into the muscularis externa. There should not be overlying clot or vessel involvement with these lesions. These patients appear to be at an intermediate risk for progression. In addition to medical management with PPI and sucralfate, these patients require close follow-up and repeat endoscopy to ensure lesion improvement.
3.3 Class III Thermal Injury

These patients have deep ulceration that extends into and beyond the muscularis. These lesions can have evidence of eschar formation, overlying clot, or necrosis. As a result, there is an increased probability of compromising tissue blood flow and worsening the injury. These patients are at high risk of esophageal
perforation and atrial-esophageal fistula formation. They should be made nil per os (NPO) and started on medical management. Cardiothoracic surgery consultation is warranted with CT of the chest. If findings do not require an emergent operation, then repeat imaging and endoscopy can be considered to reassess healing of ulcer.

This injury classification has not been tested in large prospective trials and thus it should only be viewed as a proposed means for risk assessment and follow-up pending further verification.

![Figure 3: Class III thermal injury](image)

<table>
<thead>
<tr>
<th>Thermal Injury</th>
<th>Endoscopic Appearance</th>
<th>Treatment</th>
<th>Recommended Follow-up</th>
<th>Perforation Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Lesion less than 5 mm in diameter with minimal mucosal disruption</td>
<td>Oral PPI with sucralfate</td>
<td>Clinical follow-up to assess for worsening symptoms</td>
<td>Low</td>
</tr>
<tr>
<td>Class II</td>
<td>Ulcers that do not extend beyond the muscularis externa with no overlying clot or visible vessel.</td>
<td>PPI and sucralfate</td>
<td>Repeat endoscopy in 2 weeks</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Class III</td>
<td>Deep ulceration extending into and beyond the muscularis with eschar formation, overlying clot, or necrosis.</td>
<td>NPO IV PPI Chest CT scan Cardiothoracic surgery consultation</td>
<td>Repeat imaging and endoscopy based on findings</td>
<td>High</td>
</tr>
</tbody>
</table>

**Table 1: Esophageal Injury Classification**
4 Endoscopic Injury Progression

Below we document serial images of a patient with Class II Thermal Injury with subsequent endoscopy performed 10 days (Figure 4) and 17 days (Figure 5) following diagnosis. No further endoscopy was performed after day 17. Initial endoscopy image was documented in Figure 2.

Figure 4: Class II thermal injury 10 days following RFA

Figure 5: Class II thermal injury 17 days following RFA
5 Incidence of Esophageal Injury

Esophageal injury is a known complication of RFA of the PVs and LA for treatment of atrial fibrillation. The etiology of the injury is multifactorial. As stated by Gillinov et al. (Gillinov et al., 2001) the goal of RFA is to achieve a series of transmural lesions in the LA, however, only the temperature and duration of energy delivered can be controlled. There is no means of controlling the lesion depth; thus it is possible to create a non-transmural lesion resulting in an unsuccessful operation, or a lesion that is too deep with consequent injury to adjacent structures. Additionally, it has been shown that intestinal tissue is far more susceptible to radiofrequency-induced thermal injury than muscle tissue, and that the convection of heat generated within the LA by the ablation probe can result in esophageal injury without direct contact of the probe to the esophagus. (Doll et al., 2003)

In order to determine the incidence of esophageal injury following RFA, Schmidt et al. (Schmidt et al., 2008) conducted the first observational study evaluating 28 patients following RFA for symptomatic and refractory atrial fibrillation. All patients underwent endoscopy within 24 hours following RFA. Esophageal wall changes were described as no change, erythema, necrosis, or atrio-esophageal fistula. If changes were seen, then patients were started on PPI and had repeat endoscopy 2 weeks later. They noted that within 24 hours of ablation 13 patients (47%) had esophageal changes with recovery seen in all patients after 2 weeks.

Following this, Halm et al. (Halm et al., 2010) performed a prospective study with 185 consecutive patients who had received RFA for symptomatic atrial fibrillation. The esophagus was intubated with a temperature probe in order to obtain intraluminal temperature monitoring in three-dimensions. All patients had endoscopy performed 1-4 days following ablation. Localized ulcer-like lesions of the esophagus were found in 27 of 185 patients (14.6%). Of these, 15 patients (8%) had lesions larger than 5 mm. In all patients with lesions, the intraluminal temperature reached at least 41˚C. Maximal intraluminal temperature was significantly higher in patients with esophageal damage than in those without esophageal lesions (42.6±1.7˚C vs 41.4±1.7˚C) with P=0.003. The study concluded that for every 1 °C increase in endoluminal temperature, the odds of an esophageal lesion increased by a factor of 1.36 (95% CI 1.07-1.74, P=0.012). No atrio-esophageal fistula or symptoms suggestive of this occurred during study.

6 Mediastinal and Submucosal Changes in Esophagus

A recent study by Zellerhoff et al. (Zellerhoff et al., 2010) demonstrated that mucosal injury of the esophagus was only the “tip of the iceberg” in terms of the thermal injury dealt to the surrounding region following RFA. This study evaluated 29 patients with both EGD as well as endosonography before and after RFA in order to detect both esophageal mucosal injury as well as injury to the esophageal submucosa and mediastinum. The study showed that 8 patients (27%) demonstrated new disruption of the regular esophageal wall layer pattern with edema and periesophageal accumulation of fluid, swelling of the posterior wall of the LA beyond site of ablation, and mediastinal adenopathy. All patients had resolution of these findings one week after RFA. Interestingly, none of these patients had mucosal injury in the form of ulcers or erythema on EGD, nor was there the development of any atrioesophageal fistulas. This study implies that the absence of esophageal lesions seen on EGD does not indicate that indirect thermal injury has not occurred to surrounding structures within the mediastinum.
7 Prevention of Esophageal Injury: Temperature Monitoring

The most commonly implemented strategy utilized to minimize esophageal injury is to limit the magnitude of power and duration the catheter is in contact with the PV or posterior wall of LA. As mentioned earlier, there is a wide variability in the distance between the adventitia of the esophagus and the epicardium of the posterior LA. For this reason, additional measures other than simply lower the magnitude of power is required because esophageal injury may still occur despite keeping the power lower in a patient whose esophagus is in close proximity to the LA. Real-time luminal esophageal temperature (LET) monitoring has been developed in order to monitor esophageal luminal temperatures. A prospective study conducted by Rillig et al. (Rillig et al., 2010) demonstrated that LET monitoring led to a reduction in esophageal injury. LET does confer three limitations however: (1) The accuracy of LET is dependent on adequate contact between the probe and esophageal wall during RFA; (2) Suboptimal orientation and positioning of the LET probe may show only a slow rise in temperature, allowing esophageal injury to occur at while showing acceptable temperatures; (3) the LET probe may fix the esophagus in a position where it may enhance contact to the LA posterior wall (Liu et al., 2012). Esophageal injury has been reported in patients following RFA in combination with LET in 6% to 26% of cases (Liu et al., 2012; Rillig et al., 2010; Singh et al., 2008) (Table 2).

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>No. of patients</th>
<th>Incidence</th>
<th>Lesions</th>
<th>Injury assessment tool</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmidt et al (Schmidt et al., 2008)</td>
<td>Observational</td>
<td>28</td>
<td>47% (24 hours)</td>
<td>Not reported</td>
<td>Endoscopy alone</td>
<td>100% (2 weeks)</td>
</tr>
<tr>
<td>Halm et al (Halm et al., 2010)</td>
<td>Prospective</td>
<td>185</td>
<td>14.6% (1-4 days)</td>
<td>Ulcer-like</td>
<td>LET 41°C</td>
<td>Not reported</td>
</tr>
<tr>
<td>Zellerhoff et al (Zellerhoff et al., 2010)</td>
<td>Before and after study</td>
<td>29</td>
<td>0% (mucosal) 27% (mural and mediastinal injury)</td>
<td>No mucosal lesions</td>
<td>EGD (mucosal) EUS (mural/mediastinal)</td>
<td>100% (1 week)</td>
</tr>
<tr>
<td>Rillig et al (Rillig et al., 2010)</td>
<td>Prospective</td>
<td>42</td>
<td>14.3% (24 hours)</td>
<td>Mucosal lesions</td>
<td>LET EGD</td>
<td>100% (2 weeks)</td>
</tr>
<tr>
<td>Sing et al (Sing et al., 2010)</td>
<td>Prospective</td>
<td>81</td>
<td>11% (1-3 days)</td>
<td>Ulcers</td>
<td>LET EGD</td>
<td>100% (1 week)</td>
</tr>
<tr>
<td>Berjano et al (Berjano &amp; Hornero, 2005)</td>
<td>Case control</td>
<td>8</td>
<td>0%</td>
<td>None</td>
<td>LET IECB</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

LET – luminal esophageal temperature  
EGD – esophagogastrroduodenoscopy  
EUS – Endoscopic ultrasound  
IECB – Intraesophageal cooling balloon

Table 2: Incidence of Esophageal Injury with RFA
8 Prevention of Esophageal Injury: Esophageal Cooling Technique

Berjano et al. (Berjano & Hornero, 2005) reported the feasibility of a cooled intraesophageal balloon reducing esophageal injury using a three-dimensional finite element model computer simulation. Their simulation demonstrated that chilling the esophagus minimizes the lesion in the esophageal wall compared to cases in which no balloon, or a non-cooled balloon was used. Following this, a pilot study was conducted on eight patients who underwent RFA for refractory atrial fibrillation using a 9-Fr esophageal balloon in combination with LET. These study patients were compared to controls that only had LET. In the control, the LET increased from 36.4±0.8 °C to 40.5±1.7 °C within 26.1±8.2 seconds, whereas the patients who received the esophageal cooling balloon went from a lower baseline of 30.2±2.9 °C to 33.5±2.9 °C within 30 seconds. No study patients were found to have esophageal injury throughout the follow-up period; thus, the authors concluded that the placement of an intraesophageal cooling balloon may help to minimize esophageal injury.

9 Prevention of Esophageal Injury: Cryoablation

RFA with temperatures exceeding 40°C has been implicated with esophageal injury; for this reason, it was believed that cryoablation may be a less damaging means of ablating patients with atrial fibrillation. Ahmed et al. (Ahmed et al., 2009) performed 67 cryoablations on patients with atrial fibrillation with concurrent LET. There were significant LET decreases noted in 62 of 67 patients, which was defined as greater than 1 °C. LET continued to decrease after termination of cryoablation, and was more pronounced in the inferior than in the superior pulmonary veins with the lowest observed temperature of 0°C. Post-cryoablation endoscopy revealed esophageal ulceration in 17% of patients, all of which healed on subsequent endoscopy. There were no patients who developed atrio-esophageal fistulas; however, the presence of esophageal ulceration in a significant percentage of these patients treated with cryoablation indicates that the potential for esophageal perforation exists. More data on esophageal injury with cryoablation is needed before it can be recommended as a safer alternative to radiofrequency ablation.

10 Conclusion

Esophageal injury following ablation for atrial fibrillation is relatively frequent, although perforation of the esophagus is uncommon. Mucosal injury and esophageal perforation as a result of ablation therapy for atrial fibrillation are important complications to be aware of. It appears that the primary risk factor for post-ablation esophageal injury is close proximity of the esophageal wall to the posterior wall of the LA and inferior pulmonary veins. Esophageal thermal injury has been noted to occur despite several interventions to monitor intraluminal temperature, decrease maximum threshold power, and use of cryotherapy. Esophageal cooling technique has proven, on a small scale, to be an effective means of preventing esophageal injury from RFA, and if not available, early upper endoscopy should be considered even in asymptomatic patients based on high incidence of esophageal injury of up to 47%. Patients who develop symptoms of odynophagia, dysphagia, heartburn, or substernal chest pain following ablation therapy should be evaluated with EGD and those with mucosal injury require close monitoring and follow up as detailed in the algorithm in Figure 6.
**Figure 6:** Diagnosis and proposed management of RFA-induced esophageal injury

**References**


