Esophageal Protection During Catheter Ablation for Atrial Fibrillation

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Atrial fibrillation (AF) is the most prevalent arrhythmia in the U.S., affecting over 6 million Americans. AF constitutes a major health concern worldwide owing to its association with impaired quality of life, stroke, heart failure, dementia, and increased mortality.[1-3] The ever-growing understanding of the disease allied to constant technical and technological advances has triggered a progressive expansion in the number of AF ablation procedures. As a result, guidelines are being continuously updated to broaden procedural indications based on growing safety data and consistently improved outcomes.[4-6] Nevertheless, AF ablation is not risk-free, and ablation-related esophageal thermal injury (ETI) is yet a concern. ETI seems to be more prevalent than previously thought, as "silent" lesions have been found in asymptomatic patients undergoing active post-procedural screening.[7] Atrial-esophageal fistula (AEF) remains the most dreaded complication in AF ablation procedures, and although rare, it is associated with high mortality.[8]

Procedure-related factors and individual patient characteristics have been associated with a higher risk of ETI. As the number of AF ablation procedures increases, several esophageal protective strategies have been suggested over the years; however, there is no solid evidence to individually support any of them as a definitive strategy to eliminate the risk of esophageal injury.

Anatomical and Pathophysiologic Backgrounds

The pathogenesis of ETI is complex, multifactorial, and not fully comprehended. The proximity of the esophagus to the LA posterior wall, and the amount of energy delivered locally, which in turn results from an interplay of power, time, and contact-force, seems to play a major role in the process of esophageal lesion formation.

The close proximity between the anterior wall of the esophagus and the posterior wall of the left atrium (LA) and ostia of pulmonary veins (PV) is the central substrate for ETI. The thin LA wall, especially at the posterior-inferior wall and at the level of the pulmonary vein ostia, facilitates energy transfer between the atrial endocardium (ablation site) and the esophageal surface. At the level of the inferior PVs, the LA wall thickness can be as low as 2.8 ± 2.5 mm (LIPV), when seating on the left aspect of the LA posterior wall (87%), and 3.7 ± 3.4 mm (RIPV) when located towards the right (13%).[9] Not surprisingly, extensive ablation of the LA posterior wall often results in some degree of ETI, especially in the proximity of LIPV.

Energy delivery to the esophageal surface throughout the LA wall triggers a cascade of local thermal injury, spreading from the outer to inner layers, which results in gradual but progressive damage owing to local ischemia and inflammation. Since multiple factors are involved, ETI may manifest in different forms and within a wide time range after the procedure. By virtue of this, ETI can manifest without perforation, and AEF may manifest weeks after the procedure. Fistula formation appears to progress from the esophagus towards the atrium, which would explain pericardial-esophageal fistulas preceding AEF (Figure 1).[10]

AEF is found in less than 0.1% to 0.6% of patients, and stroke (air embolism), septicemia, and gastrointestinal (GI) bleeding are the leading factors contributing to mortality rates ranging from 40% to 100%.[11]

Beyond direct thermal damage, particular effects may indirectly contribute to ETI. Outside the esophagus, damage to the periesophageal vagal innervation may result in reduction of the lower esophageal sphincter tonus, and thus, gastroesophageal reflux. Local pH reduction impairs appropriate healing, contributing to ETI[12]; inside the esophagus, recent data suggests that esophageal intraluminal content may also affect heat transfer/dissipation through the esophageal wall, and therefore, may also be implicated in the genesis of ETI.[13,14]

Risk Factors and Protective Strategies

Although the pathophysiology of ETI is not completely understood, multiple factors have been associated with an increased risk of ETI (Table 1). Among those, understanding the interaction between individual anatomical characteristics and ablation settings appears to be critical while adopting strategies to minimize the risk of esophageal lesion formation. High-power and long-duration radiofrequency ablation (RFA) are well recognized as important risk drivers, especially when using non-irrigated catheters. Intraluminal esophageal temperature (IET) monitoring is widely employed as a protective strategy, although the actual benefit derived from its systematic application is still uncertain. Variables such as the type of temperature probe (solid shaft vs acoustascope)[15], number of temperature electrodes/sensors, response time (sensitivity), and mainly TP positioning are crucial for accurate feedback, each of which carry the potential to affect the real-time temperature readout. Undervaluation of the IET can mislead the operator, contributing to otherwise preventable ETI. This may explain why esophageal lesions are still found despite temperature-guided, power-limited procedures, and AEF is yet described with a rise in intraluminal esophageal temperature (IET) of less than 1°C.[15] Moreover, a low incidence of esophageal ulceration despite the absence of temperature

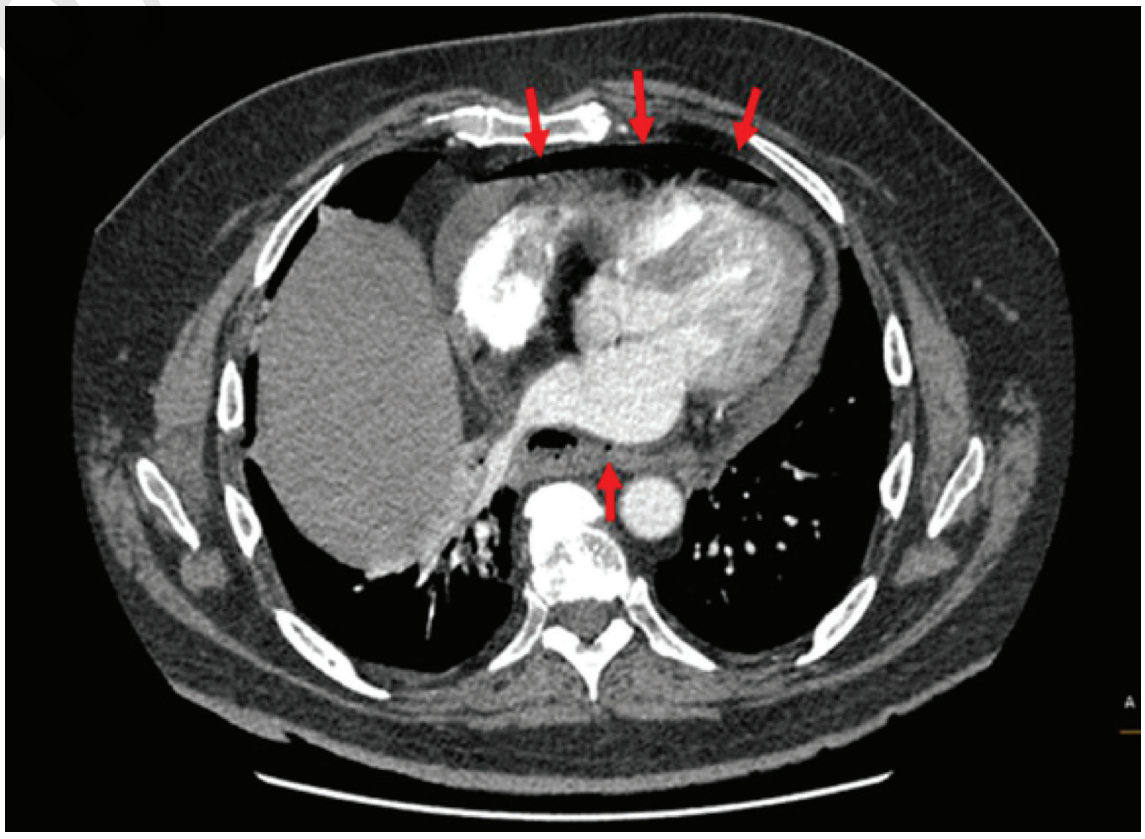

Figure 1. **Esophageal-pericardial fistula preceding atrio-esophageal formation.**

Table 1. Factors associated with risk of esophageal thermal injury ***(Adapted from Assis FR[11]).***

General anesthesia[16,26,27]
Usage of nasogastric tube
Barium swallow
High power output (>25-30W), long application duration (>20-30s), and contact force >15-20g)
Non-irrigated catheter
LA enlargement
Reduced distance between:
- spine and LA (computed tomography)
- spine and Ao
- temperature probe and LA
Low BMI:
<24.9kg/m^2
<26 kg/m^2
Remote-controlled magnetic PVI
Max temperature rise:
>38.5°C
>39°C
>40°C
>41°C
>42°C
Δ >2°C
Δ >1.5°C + ≥39°C
<-15°C (cryo)
Number of ablations lesions in the posterior wall of LA
LIPV ablation
Non-brushing ablation technique at LA posterior wall
Acid reflux

Ao = aortic wall; LA = left atrium; BMI = body mass index; PVI = pulmonary vein isolation; LIPV = left inferior pulmonary vein

control was reported by Martinek and colleagues in two large studies.[17,18] A meta-analysis including 411 patients failed to demonstrate significant difference in ETI when comparing patients with and without IET monitoring during RF ablation procedures.[19] Most recently, a randomized study showed that IET was not able to prevent ETI assessed by esophagogastroduodenoscopy after RF pulmonary vein isolation.[20] Neither power titration nor IET control alone seems to eliminate the risk of ETI.

ETI risk management during AF ablation mainly relies on appropriate monitoring (passive) and energy modulation (active). As mentioned, IET monitoring is a common practice; however, a definitive strategy has not yet been reported. Energy modulation entails the type of energy employed as well as its titration towards a safer yet more efficient ablation. In RF ablation procedures, lower power settings (25-30W), shorter duration (<20-30s), adequate contact force (<10-15g), and open-irrigated catheters are associated with a more favorable safety profile without compromising procedural antiarrhythmic outcomes.[21] Alternative approaches such as RFA using high-power (50-90W) with short-duration (4-5s) and low-irrigation rates (2 ml/min instead of 17 ml/min) have been reported as safe, with non-inferior antiarrhythmic outcomes.[22,23] Nevertheless, a recent meta-analysis including 2467 patients demonstrated similar ETI rates when comparing high-power, short-duration ablation versus low-power, long-duration ablation.[24] Different RF delivery and IET control strategies have been reported and are summarized in a recent review by our group on ETI associated with catheter ablation.[11]

Although distinct energy sources may have different roles in the process of lesion formation, ETI has been documented with both cryoablation and RF ablation. Although cryoballoon ablation has been associated with low AEF incidence,[25] a recent study including 95 patients showed endoscopic signs of ETI in 22% of patients undergoing cryoballoon ablation. No AEF was reported.[26] More recently, pulsed field ablation (PFA) has been found to reduce the risk of esophageal complications. PFA is non-thermal, tissue-specific ablative modality that utilizes an ultrafast, high-voltage electrical pulse to create micropores on cell membrane (electroporation), and therefore, disrupt cellular ionic homeostasis and cause cell death. Recently, Reddy et al reported the long-term results of PFA in patients with paroxysmal AF including 121 patients from 3 multicenter clinical trials (IMPULSE, PEFCAT, and PEFCAT II), showing durable pulmonary vein isolation rates up to 96% after 3 months. No esophageal complications given by dysmotility and AEF were reported.[27]

Luminal Esophageal Protective Strategies

Besides IET monitoring, multiple adjunctive strategies have been suggested to mitigate the risk of ETI during CA by changing the anatomical

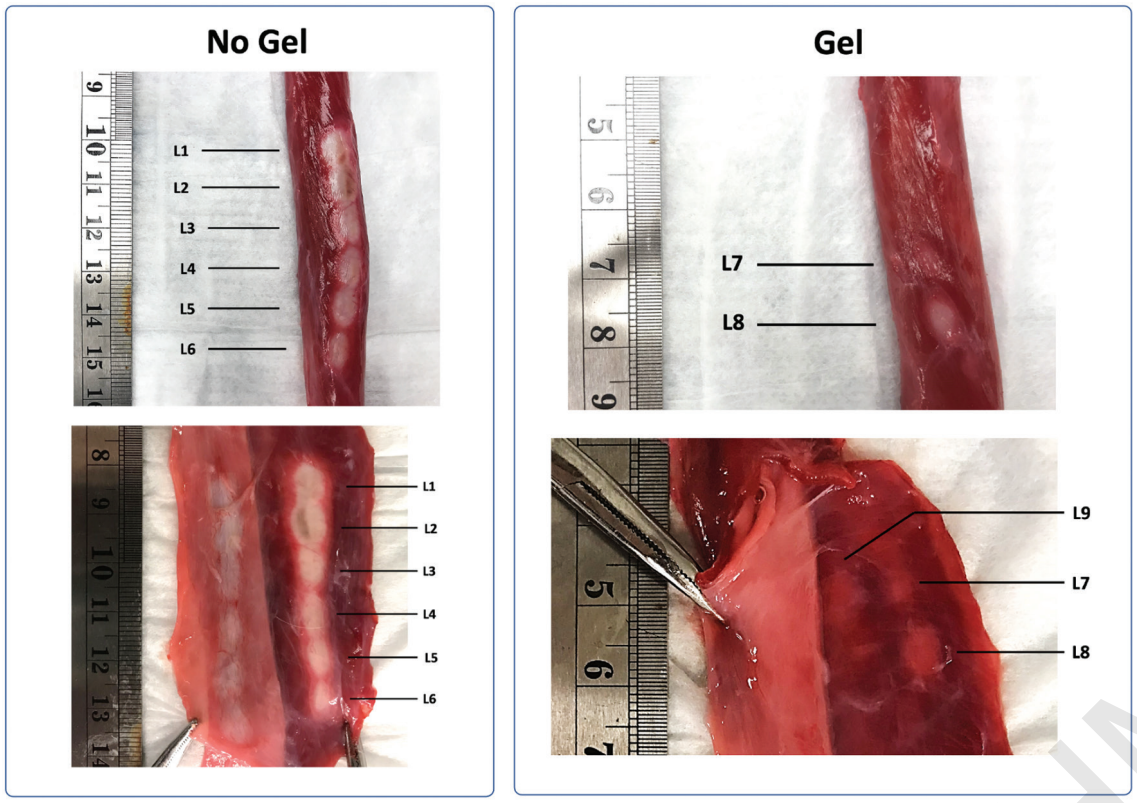

Figure 2. Intraluminal use of a high-thermal conductance gel (top, outer esophageal surface; bottom, internal view of the muscularis and mucosa). Intraluminal gel was associated with smaller esophageal lesions. No transmural lesion was identified with the gel.

relationship between the esophagus and the LA, or altering its thermal properties. By virtue of the loose connection between the esophagus and surrounding structures, active displacement of the esophagus can be achieved in most patients and seems to convey a protective effect, especially with esophageal deviation of more than 20 mm.[28] Data on the use of transesophageal echocardiographic probes, dedicated stylets, pre-shaped inflatable balloon retractors, and temperature-sensitive stylets (which automatically changes its shape at body temperature) have shown similar results. Some patient-related characteristics may restrict esophageal mobility, rendering suboptimal results, and esophageal displacement may hinder appropriate TP positioning and/or cause local trauma.

Multiple studies have investigated the protective role of esophageal cooling. Preliminary data on low-heat extraction strategies such as cooled-tip esophageal balloons and cold liquid intraluminal instillation showed reduction of esophageal lesion size.[29,30] More recently, esophageal expandable balloons circulated with a high flow of cold water, primarily used for target temperature management, have also shown promising results in a randomized clinical trial (IMPACT study) as a protective strategy during AF ablation, wherein patients under therapy held a lower incidence of mucosal lesion and gastroparesis.[13]

The short-term prophylactic use of proton pump inhibitors (PPIs), initiated either before or immediately after AF ablation, has become an accepted strategy against esophageal injury and fistula formation. The safe and highly tolerable profile of PPIs, their established role in reducing the intraluminal esophageal acidity in patients with acid reflux, and preliminary evidence of increased acidity levels among patients who underwent AF ablation, all collectively have supported its increasing use in most centers. Nevertheless, it is worth noting that the value of the systematic use of PPIs in preventing esophageal ulcer formation and fistulization remains controversial and lacks evidence from large, randomized trials.

Altering the esophageal content to modulate thermal conductance across the esophageal wall may play a protective role. Preliminary preclinical data using intraluminal, high-thermal conductance gel was associated with a significant reduction of esophageal lesion size when compared to absence of gel (15.3 ± 10.4 [gel] vs 29.3 ± 10.7 mm^2 [no gel - air]; $P<.003$). In addition, while all lesions formed without gel were transmural, no transmural lesion was found with the gel (Figure 2).[11] These findings suggest that a higher intraluminal thermal conductance allows for a faster heat distribution along the esophageal wall, reducing focal energy accumulation along the ablation site. Also, filling the esophagus with gel removes air pockets, which may contribute to minimizing local heat concentration (insulation effect).

Summary

ETI is a complex, multifactorial problem, and thus, no single esophageal protective measure has proven to be sufficiently effective to truly eliminate the risk. Rigorous IET monitoring using more sensitive TPs, low-power and short-duration ablation, as well as periprocedural adjunctive strategies such as the use of anti-reflux therapy and esophageal cooling or deviation, all seem to collectively reduce the risk of ETI. Single-shot balloon technologies have shown encouraging results to isolate the PV. Growing data on PFA have shown the procedure to be effective in the long run with a low risk of esophageal injury, making it an attractive option for fast and safe CA. Regardless of the protective strategy applied, post-procedural vigilance and early screening in patients at risk are key in the management of ETI, as early intervention of AEF remains the most important outcome modifier. ■

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