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COMMENTARY

Is the Esophagus Spared During Pulsed Field Ablation?

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ABSTRACT

Pulsed field ablation (PFA) has emerged as a new energy source for atrial fibrillation (AF) ablation, distinguished by its tissue-selective mechanism through irreversible electroporation. PFA offered theoretical advantages over conventional radiofrequency and cryoablation techniques, particularly regarding collateral damage to phrenic nerve and esophagus. However, accumulating evidence challenges this paradigm, with growing data highlighting those thermal effects are possible and may be clinically relevant during PFA procedures. No significant esophageal complications have been reported to date, but continued vigilance is warranted given the rapidly increasing number of procedures, the trend toward multiple lesions on the posterior wall and in consideration of new PFA catheters arriving in clinical practice. This article examines current evidence on esophageal warming during PFA.

1 | Introduction

Pulsed field ablation (PFA) has emerged as a new energy source for atrial fibrillation(AF) ablation, distinguished by its tissue-selective mechanism through irreversible electroporation [1]. This novel technology delivers high-voltage very short electrical pulses that create pores in cardiomyocytes, leading to cellular death while theoretically sparing cardiac neurovascular architecture and adjacent structures. Initially defined as purely nonthermal energy, PFA offered theoretical advantages over conventional radiofrequency and cryoablation techniques, particularly regarding collateral damage to phrenic nerve and esophagus. However, accumulating evidence challenges this paradigm, with growing data highlighting those thermal effects are possible and may be clinically relevant during PFA procedures [2–3]. In particular, recent investigations reveal PFA generates thermal effects at electrode-tissue interface and after repeated applications [2–3]. This viewpoint examines current evidence on esophageal warming during PFA.

2 | Clinical Evidence

Multiple clinical studies have recorded minimal or no esophageal injury following PFA. Cochet et al. found no esophageal late gadolinium enhancement(LGE) lesions in 18 PFA patients, contrasting with 43% incidence of acute esophageal LGE after thermal ablation [4].

The TESO-PFA registry provided critical insights into esophageal temperature dynamics [5]. In 43 patients' median esophageal temperature increase was 0.8 ± 0.6°C; 23% experienced rises ≥ 1°C, with one reaching 40.3°C. Despite these measurable changes, all patients remained asymptomatic [5]. The MANIFEST-17K registry, enrolling 17,642 patients from multiple international centers, reported zero esophageal complications [1]. The Eso-PFA study examined patients undergoing extensive posterior wall ablation and found no endoscopic lesions during a median follow-up of 606 days [6]. A recent study reported esophageal temperature elevations ≥ 39°C with a mean maximal temperature of 40 ± 0.9°C. Particular, in that study the temperature rises

Abbreviations: AF, atrial fibrillation; LGE, late gadolinium enhancement; PFA, pulsed field ablation.

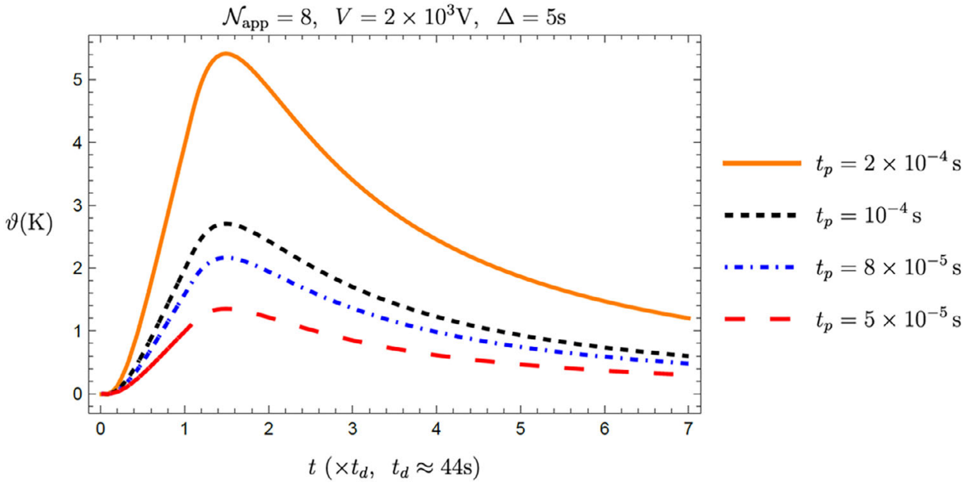

FIGURE 1 | Temperature increase above baseline at a distance of 4 mm from pericardium (possible location of esophageal lumen in critical cases) according to the mathematical model proposed in [10]. Distinctive feature of the model was the separation of the main timescales involved in the process (local heating and diffusion), showing that heat accumulates fast in the ablation site and then slowly diffuses to surrounding organs. $N = 8$ applications consisting in a series of 5 pulses each, with duration t_p, the time between consecutive pulses is 0.5 s. Peak amplitude: 2000 V. Pulse duration (t_p): four values between $5 \cdot \times 10^{-5}$ s and $2 \cdot \times 10^{-4}$ s. $\Delta = 5$ s time between successive applications. The dimensionless time t is rescaled by the diffusion time t_d = 44s, so the actual overall time shown in the figure is about 5 min. The parameters selection was based on the data retrieved from references [11–13]. Temperature turns out to be very sensitive on pulse duration. The predictions of the model refer to the worst case of an esophagus in contact with the atrium with no epicardial fat layer. [Color figure can be viewed at wileyonlinelibrary.com]

occurred exclusively when ablation was delivered within ≤ 5 mm of the esophageal probe [2].

While these clinical studies are reassuring, important questions remain whether current surveillance methods are sufficiently sensitive to detect subclinical injury or whether longer follow-up periods might reveal delayed complications.

3 | Preclinical Data

Preclinical studies have revealed more complex esophageal responses. Kocharian et al. conducted comparative studies in swine examining both high-power short-duration radiofrequency and PFA [7]. Both modalities produced significant esophageal temperature rises and histologically confirmed damage. However, these changes were undetectable at 30 days, suggesting transient and reversible injury. This temporal resolution raises important questions about assessment timing.

Nies et al. reported data regarding early histopathology and in vivo esophageal retraction during PFA [8]. Immediate post-ablation examination revealed acute esophageal tissue changes, providing direct evidence that the esophagus is not completely immune to PFA effects. Importantly, esophageal retraction techniques, physically displacing the esophagus during energy delivery, could potentially mitigate injury risk [8]. The mechanism appears multifactorial, involving both electroporation effects on esophageal smooth muscle or neural plexus and thermal contributions.

Zito et al. provided crucial insights into temperature dynamics using variable-loop circular catheters on bovine myocardium [9]. One waveform with low irrigation produced surface temperatures of 56.4°C with 19.4°C rises sufficient for thermal injury. However, waveform optimization with high-flow irrigation reduced temperatures to 40.8°C with only 3.8°C rises, demonstrating that an increased flow of saline can minimize thermal risk [9].

These findings raise critical questions. If reversible damage occurs in animals, could subclinical injury occur in humans undetected by standard endoscopy? Temporal resolution in animal models suggests single-timepoint assessments may miss transient injury. The dose-response relationship between PFA applications and esophageal injury remains poorly characterized.

3.1 | Posterior Wall Ablation

The left atrial posterior wall's proximity to the esophagus has long raised safety concerns. While clinical series report no endoscopic lesions after extensive posterior wall PFA, absence of observed injury does not guarantee absolute safety for esophagus and vagal nerve.

Recently, we developed mathematical models investigating thermal fields during successive PFA applications [10]. In particular, with our analysis we demonstrated that extreme pulse values may result in substantial heating of neighboring organs. The summary graphs of our study are shown in the Figure 1.

The convergence of evidence regarding significant thermal effects [3], mathematical confirmation of heat delivery [10] and comparative studies showing PFA produces esophageal heating similar to radiofrequency ablation [7] suggest that repeated applications on posterior wall may pose cumulative thermal risks. It should be considered that the esophageal wall disperses the accumulated

TABLE 1 | PFA parameters correlated to thermal effects.

Parameter	Range	Thermal impact	Mechanism of thermal effect
Pulse amplitude	1500–2500V	yes	Higher voltage increases heating at electrode-tissue interface
Pulse duration	50–200 µs	yes	A longer pulse duration increases energy in the tissues
Number of pulses per application	3–10 pulses	yes	More pulses increase cumulative heat generation per application
Number of applications	4–12+ applications	yes	More applications increase cumulative heat generation
Inter-application interval	5–20 s	yes	Shorter intervals correlate to insufficient cooling between applications
Catheter type	Different configurations	variable	Configuration affects field distribution and electrode heating
Irrigation flow-rate	0–30 mL/min	Protective	High flow reduces electrode heating
Contact force	variable	yes	Increased contact leads to better coupling and potentially increased local heating

heat very slowly compared to the cardiac tissue that benefits from the cooling guaranteed by the blood flow.

Nies et al.'s findings regarding early histopathologic changes and protective benefits of esophageal retraction [8] emphasize that anatomical proximity remains critical.

No clinical study has established safe upper limits for posterior wall PFA applications. The temperature rises documented in TESO-PFA [5], though generally modest, demonstrate that esophageal heating occurs and may become clinically significant with increased applications, prolonged delivery, or suboptimal irrigation.

4 | Discussion

PFA represents significant progress in AF ablation technology. Large international registries demonstrate remarkably low rates of clinically significant injury, with no reported a trio-esophageal fistula case. These results are genuinely reassuring and support PFA's expanding role in contemporary AF management.

However, the procedure should not be considered risk-free. Animal studies demonstrate reversible esophageal damage through both nonthermal and thermal mechanisms [7–9]. Recent investigations reveal PFA generates thermal effects at tissue interfaces, with temperatures potentially reaching injurious levels [3]. Direct histopathologic examination confirms the esophagus is not completely spared, with acute changes detectable immediately post-ablation [8]. If the mechanism is truly nonthermal and preserves extracellular structures, it may produce histological changes in the esophagus without the risk of atrio-esophageal fistula. However, the mechanism appears multifactorial, involving both electroporation effects on esophageal smooth muscle or neural plexus and thermal effects (Table 1).

The possibility exists that increased numbers of PFA applications, particularly targeting the left atrial posterior wall, may carry dose-dependent esophageal thermal injury risk that has not yet manifested in clinical practice. This may be attributable to the technology's relatively recent introduction and the limited long-term follow-up data currently available. As PFA adoption accelerates globally and procedural techniques evolve toward more extensive and aggressive ablation strategies, continued vigilance regarding esophageal safety remains essential.

Prudent practice should include minimizing posterior wall lesion density when appropriate, optimizing PFA parameters for lowest effective doses with maximal irrigation and maintaining systematic surveillance. Future research should establish dose-response relationships, define safe application limits, identify high-risk patient subgroups, and develop real-time monitoring strategies to prevent esophageal injury if needed.

5 | Conclusion

Contrary to previous reports, during AF ablation, PFA causes a warming in both cardiac tissue and the esophagus. No significant esophageal complications have been reported to date, but continued vigilance is warranted given the rapidly increasing number of procedures, the trend toward multiple lesions on the posterior wall and in consideration of new PFA catheters arriving in clinical practice.

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Conflicts of Interest

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Data Availability Statement

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