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**EDITORIAL**

# Putting fear into perspective: estimating the true incidence of oesophageal fistula formation post-atrial fibrillation ablation

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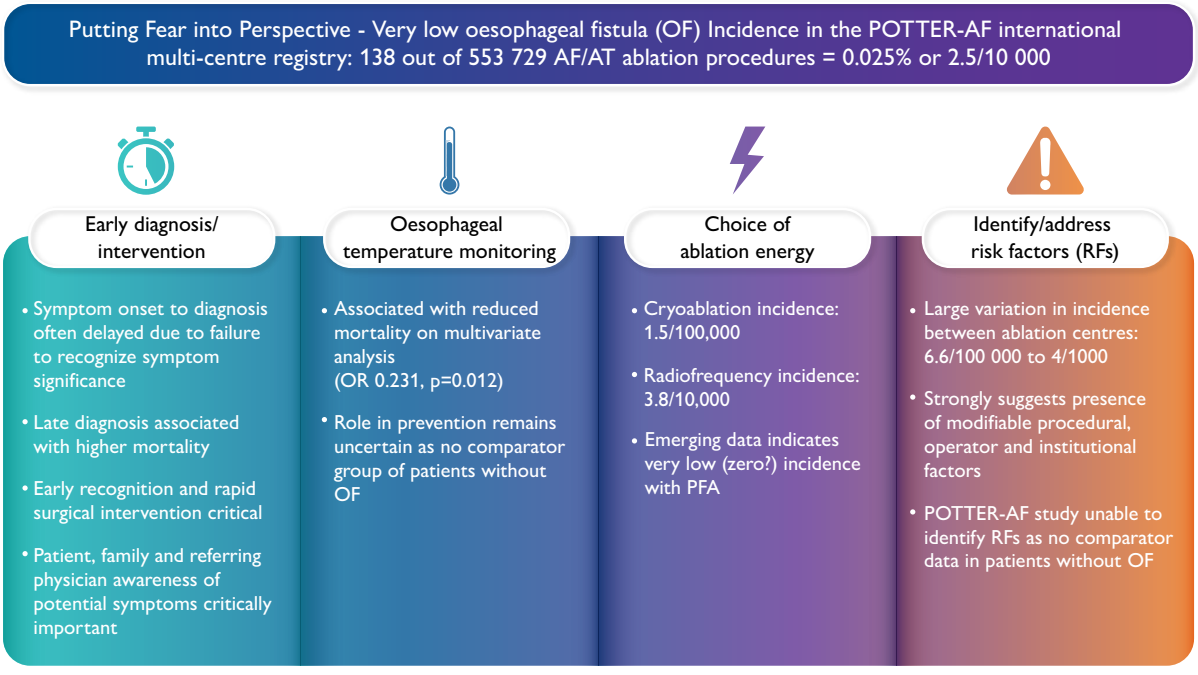
**This editorial refers to 'A worldwide survey on incidence, management, and prognosis of oesophageal fistula formation following atrial fibrillation catheter ablation: the POTTER-AF study', by R.R. Tilz *et al.*, https://doi.org/10.1093/eurheartj/ehad250.**

## Graphical Abstract




Putting fear into perspective: very low OF incidence in the POTTER-AF International Multi-centre Registry: 138 out of 553 729 AF/AT ablation procedures = 0.025% or 2.5/10 000.



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Atrio-oesophageal fistula (AOF) formation, with its exceedingly high reported morbidity and mortality, is a much-feared complication amongst atrial fibrillation (AF) ablation proceduralists.[1] The pathogenesis of AOF post-AF ablation remains the subject of further research. However, it is generally accepted that ablation energy delivered endocardially causes injury to the oesophagus as it traverses in close proximity to the posterior left atrium. Proposed mechanisms of injury include direct thermal injury, ischaemia due to anterior oesophageal artery injury, acid reflux exacerbated or caused by ablation, and oesophageal dysmotility related to nerve injury.[1] While this complication was first reported almost two decades ago, its rarity has meant that estimation of risk to date has largely been informed by relatively small case series.[2,3] Recently, a large retrospective national survey from 82 centres reported 33 AOFs from a total of 129 286 ablations (0.026%) between 2006 and 2019.[4]

In this issue of the *European Heart Journal*, the POTTER-AF study authors report the results of a retrospective, international multicentre registry study evaluating the incidence, management, and prognosis of patients with AOF formation post-catheter ablation for AF.[5] With data collected from 214 centres in 35 countries encompassing 553 729 catheter ablation procedures between 1996 and 2022, this is the largest study published on the subject to date. The key finding is that in this sizeable dataset of AF ablation procedures, only 138 patients were diagnosed with an AOF, equating to a 0.025% incidence post-ablation. Though subject to potential underreporting and underdiagnosis, it represents the best available estimate of the true incidence of this rare complication and mirrors the rates reported in smaller studies and in the national survey described above.[3,4] While confirmation of a low incidence is reassuring, the major limitation of this study is that in the absence of data from a comparator cohort of AF ablation patients who did not develop post-procedure AOF, it was unable to identify risk factors for AOF formation which could serve as targets to reduce risk. Nonetheless, within the constraints of a retrospective registry, this study demonstrated several important findings (*Graphical Abstract*).

In keeping with prior reports, the time from symptom onset to diagnosis in this study was long, with a median of 3 days and a range of up to 42 days.[4] There are likely to be multiple contributing factors to this delay. Firstly, the non-specific nature of the common initial symptoms of AOF such as retrosternal pain may result in symptoms being attributed to less serious conditions such as post-ablation pericarditis or trauma related to transoesophageal echocardiogram or oesophageal temperature probe insertion. Secondly, patients with non-cardiac symptoms such as fever, altered neurology, or respiratory symptoms may initially be managed at non-cardiac centres or by other medical specialties less familiar with this complication. Further, the significant potential lag time between the procedure and symptom onset (median of 18 days but up to 60 days in this study) may result in patients and physicians failing to identify the link between their symptoms and recent ablation.

From a pathophysiology perspective, it stands to reason that prompt diagnosis would impact outcomes. In patients with AOF, development of the fistula appears to proceed from the oesophagus toward the atrium. Isolated oesophageal perforation has been well reported while left atrial perforation in the absence of an AOF has not been described.[1] Case reports have also previously documented progression from oesophageal ulceration, to connection to the mediastinum and pericardial space, to perforation into the left atrium on serial computed tomography (CT) scans.[1,6] The 100% survival rate of the four patients in this study with oesophago-pericardial fistulae compared with the 65.8% overall mortality from AOF highlights the need to diagnose AOF as early as possible. Prompt diagnosis may also allow for surgical or endoscopic intervention before development of haemodynamic instability or neurological sequelae render them prohibitively risky or futile. Illustrating this point, in the POTTER-AF study, patients with earlier AOF diagnosis were more likely to receive intervention while patients with late diagnosis more often received conservative treatment which was associated with higher mortality. Accordingly, a focus on increasing awareness of the variable clinical presentations of AOF amongst both patients and physicians seems crucial to improving outcomes. In this context, many departments provide patients and their next of kin with a list of 'red flag' symptoms with written instructions to immediately contact the managing team should these occur.

However, even when an AOF is suspected, diagnosis may be challenging. CT scans may show only subtle mediastinal change or no abnormality at all early in the process, and serial imaging may be required. In some reports, air in the mediastinum or even in the left atrium has been overlooked when the imaging radiologist was unfamiliar with this potential complication.[3] Cardiothoracic surgeons will be reluctant to operate in the absence of a definitive diagnosis, potentially creating further delay.

Given the rarity of AOF, demonstrating benefit of any preventative intervention is challenging. Furthermore, it is not clear that surrogate markers such as endoscopic oesophageal ulceration are useful predictors of AOF development. Among a range of protective approaches that have been suggested, use of oesophageal temperature monitoring is the most widely adopted but remains controversial. Data using oesophageal ulceration as an endpoint have varied markedly, with some reporting reduced risk and others increased risk, with the suggestion that uninsulated electrodes may act as a heat sink.[1,3] The current study indicated a suggestive trend between oesophageal temperature probe use and reduced mortality on the univariate analysis (odds ratio 0.0449, *P*-value 0.068) which became statistically significant (odds ratio 0.231, *P*-value 0.012) on multivariate analysis. This was despite the fact that the mean maximal measured oesophageal temperature was 40.2 ± 2.2°C, a value higher than expected and suggesting that stringent protocols for limiting ablation in the setting of oesophageal heating were not strictly adhered to at all participating centres. While interpretation of this finding is significantly affected by the limited proportion of AOF patients who had oesophageal temperature probes (24.6%) as well as the lack of information regarding the type of probe and the ablation strategy in response to temperature rises, it adds credence to the argument for routine oesophageal temperature monitoring. Despite the current absence of a consensus document recommendation regarding temperature monitoring, this approach is nevertheless routine in many electrophysiology centres worldwide. Advocates point to the ability to modify power, duration, and location of ablation lesions and prevent 'heat stacking' that occurs with repeated adjacent lesions. Large registry studies, similar to the current study but with details on oesophageal probe type and utilization protocols as well as comparator data in patients without AOF, may provide more definitive evidence regarding efficacy, but will be difficult to achieve.

The current study also provides important information supporting the currently held perception that risk of AOF is lower with cryoablation than with radiofrequency (RF) energy. Investigators observed a 0.0015% incidence of AOF with cryoablation compared with 0.038% ($P < 0.0001$) using RF ablation. The strength of this observation is confounded by the fact that 45.5% of patients who underwent RF ablation received linear ablation in addition to pulmonary vein isolation (PVI) whereas the cryoablation group received PVI alone.

This large registry also supports prior smaller studies indicating that mortality following surgical (51.9%) or endoscopic treatment (56.5%) is

significantly lower compared with conservative management (89.5%).[1,3,4] It is probable that the conservative management group would have encompassed those patients deemed unfit for intervention, but the fact that early intervention is critical seems overwhelmingly clear.

Given the extremely high mortality whichever treatment strategy is employed, the focus must remain on minimizing the incidence of this devastating complication. The dramatic variability in incidence of AOF between centres (0.0066% to 0.4%) is an important finding of the current study that strongly points to the presence of modifiable procedural, operator, and institutional risk factors that could be targeted to improve outcomes. It is most likely that a further reduction in incidence of this complication will occur with the continuing evolution in ablation technology. For example, a recent study indicated a temporal association between a drop in the overall incidence of AOF and the availability of contact force-enabled ablation catheters.[4] The pulsed field ablation (PFA) 'revolution' that is currently sweeping through the world of international electrophysiology threatens to reduce this feared complication to a footnote in AF ablation history. Whether the promise of tissue selectivity and absence of oesophageal complications will be fully realized when tens of thousands of patients have undergone PFA ablation is unknown, but early signs are promising indeed.[7]

The authors should be congratulated on this important study establishing the incidence of AOF in a large, international cohort of patients following AF ablation. While it has demonstrated that the overall risk is low, further research to identify modifiable risk factors and safer novel technologies combined with efforts to increase awareness among patients and physicians will be pivotal to further reducing the prevalence and impact of this dreaded complication.

## Data availability

No new data were generated or analysed in support of this research.

## Conflict of interest

None declared.

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