Atrioesophageal fistula following ablation procedures for atrial fibrillation: systematic review of case reports

Patricia Chavez,1 Franz H Messerli,1 Abel Casso Dominguez,1 Emad F Aziz,1 Tina Sichrovsky,1 Daniel Garcia,2 Connor D Barrett,1 Stephan Danik1

ABSTRACT

Background: Atrioesophageal fistula (AEF) is a rare but serious adverse event of atrial fibrillation (AF) ablation.

Objective: To identify the clinical characteristics of AEF following ablation procedures for AF and determine the associated mortality.

Methods: A systematic review of observational cases of AEF following ablation procedures for AF was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement protocol.

Results: 53 cases were identified. Mean age was 54±13 years; 73% (39/53) of cases occurred in males. Mean interval between procedure and presentation was 20±12 days, ranging from 2 to 60 days. AEF was observed in 12 patients who underwent surgical radiofrequency ablation (RFA) and in 41 patients with percutaneous RFA. Fever was the most common presenting symptom (n=44) followed by neurological deficits (n=27) and haematemesis (n=19). CT of the chest (n=27) was the preferred diagnostic test. Patients who did not receive a primary esophageal repair were more likely to have a deadly outcome (34% vs 83%; p<0.05). No difference in mortality rate was found between patients who underwent surgical RFA when compared with percutaneous RFA (58% vs 56%; p=0.579). No association was found between onset of symptoms and mortality (19±10 vs 23±14 days; p=0.355).

Conclusions: AEF following ablation procedures for AF is a serious complication with high mortality rates. Presenting symptoms most often include a triad of fever, neurological deficit and/or haematemesis within 60 days of procedure. The preferred diagnostic test is CT of the chest. The treatments of choice is surgical repair.

INTRODUCTION

Catheter ablation for atrial fibrillation (AF) is becoming a mainstream treatment particularly in patients with paroxysmal AF with severe symptomatology.1 As the number of procedures continues to rise, reports of one of the most devastating complications, atrioesophageal fistula, have also increased. Since this initial observation, at least 53 cases of AEF following AF ablation procedures have been reported. Although differences in pathogenesis of each case have been reported, the similarities in the clinical presentations allow one to characterise this rare entity. Given its serious outcome and

KEY QUESTIONS

What is already known about this subject?

▸ Ablation for atrial fibrillation is becoming a mainstream treatment in cases resistant to conventional therapy or with severe symptomatology. As the number of procedures continues to rise, reports of one of the most devastating complications, atrioesophageal fistula, have also increased.

What does this study add?

▸ This is a review of case reports describing the signs and symptoms, diagnosis, management, and the associated mortality of this important complication of ablation procedures for atrial fibrillation. This is the largest review of case reports to date, including 53 cases in 37 peer-reviewed publications.

How might this impact on clinical practice?

▸ We considered it critical to review the clinical findings, diagnostic methods and therapeutic option available for this condition. The early recognition and prompt management might change its serious outcome and high mortality.
high mortality, we considered it critical to review the clinical findings, diagnostic methods, and therapeutic options available for this condition.

**METHODS**

**Search strategy**

The objective of this review was to identify the case reports on AEF following ablation procedures for AF. A systematic search of the database PubMed from inception to December 2014 was performed. The search terms included atrioesophageal fistula OR atrio-esophageal fistula OR atrio-oesophageal fistula OR esophagoatrial fistula OR oesophago-atrial fistula. This terms were searched as free text in the title or the abstract.

We limited our search to case reports of humans without timeframe limit. No language restriction was applied. The reference lists of bibliographies of the identified articles were also reviewed.

**Selection criteria**

To be included in the analysis, a case report had to fulfil the following criteria: (1) report AF as the primary diagnosis for ablation procedure; (2) report clinical presentation; (3) report diagnostic modality used; (4) report management applied and (5) report outcome. Exclusion criteria involved the following: unknown aetiology of AEF and pericardioesophageal fistulas.

**Data extraction**

The case reports were identified and data extracted using standardised protocol. Disagreements were resolved by arbitration (PC and FHM), and consensus was reached after discussion. We extracted data such as baseline patient demographics, clinical presentation, diagnostic modalities and therapeutic management and outcome.

**Statistical analysis**

For this systematic review of case reports, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement protocol. Continuous data are presented as means with SD. Absolute numbers and percentages are presented for categorical data. Comparison between categorical variables was evaluated by using the Fisher exact test (IBM SPSS Statistics V.13 for Windows). Statistical significance was set at 0.05.

**RESULTS**

**Demographics and clinical presentation**

Fifty-three cases were identified (table 1). Mean age was 54±13 years; 73% (39/53) of cases occurred in males. Mean interval between procedure and presentation was 20±12 days, ranging from 2 to 60 days.

AEF was noticed in 12 patients who underwent surgical RFA and in 41 patients who underwent percutaneous RFA. One case was reported after cryoballoon ablation. Fever was the most common presenting symptom (n=44) followed by neurological deficits (n=27; including motor and language impairment), haematemesis (n=19), altered mental status (n=15), chest pain (n=11) and seizures (n=7; figure 1).

**Diagnostic evaluation, treatment and outcome**

CT of the chest (n=27) and head (n=15) were the preferred diagnostic modalities (figure 2), with multifocal infarcts consistent with air embolism (n=13) and pneumomediastinum (n=12) being the most common findings.

Among the CT of the chest findings pneumomediastinum was a strong indicator of esophageal injury, as well as hemopericardium and pneumopericardium. At least two cases reported pneumomediastinum and four cases reported intracardiac air. Transesophageal echocardiography was performed in 11 cases and transesophageal echocardiography (TEE) in three cases.

No difference in mortality rate was found between patients who underwent surgical RFA when compared with percutaneous RFA (10/29, 58% vs 20/24, 56%; p=0.579). Patients who did not receive a primary esophageal repair were more likely to have a deadly outcome (34% with surgical treatment vs 83% with conservative treatment; p<0.05). In those cases that underwent corrective surgical intervention, the left atrium (LA) was identified, exposing the fistula between the atrium and esophagus. No association was found between onset of symptoms and mortality (19±10 vs 23±14 days; p=0.355).

**DISCUSSION**

AEF can be defined as an abnormal communication between the atrium and the esophagus as a result of a trauma, although idiopathic fistulas have been described. Literature reports a 15% rise in the rates of AF ablations resulting in an increase from 0.06% to 0.79% over 15 years (1990–2005 period), which is parallel to a rise in the prevalence of AF itself—from 270 000 to over 2.2 million people affected—a number that continues to grow. The incidence of AEF varies from 0.03% to 1.5%; however, its true incidence may be under-reported.

Prior reports have evaluated this topic. Finsterer et al and Stöllberger et al focused on the neurological manifestations of AEF after RFA. Nair et al performed a review of the epidemiology, clinical features, aetopathogenesis and management of AEF after RFA. Singh et al reported a review of the principles of AEF repair and clinical outcomes in 29 patients. We describe the largest case report review to date, evaluating 53 cases of AEF after RFA in 37 peer-reviewed publications.

**Demographics and clinical presentation**

AEF has been reported to be more prevalent in males than females. We found similar results, with 73% of the cases occurring in males. This could partially be
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<td>Fever, shivers, numbness right arm</td>
<td>TTE</td>
<td>LA thrombus</td>
<td>EGD</td>
<td>Thrombectomy, pericardial sutures</td>
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<td>42</td>
<td>Surgical: IRAAF</td>
<td>10</td>
<td>Fever, postprandial TIA</td>
<td>TTE</td>
<td>Normal</td>
<td>Exploratory thoracotomy</td>
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<td>Doll et al</td>
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<td>62</td>
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<td>6</td>
<td>Haematemesis</td>
<td>EGD</td>
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<td>Pathology</td>
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<td>Male</td>
<td>59</td>
<td>Surgical: IRAAF</td>
<td>12</td>
<td>Fever, neurological symptoms</td>
<td>CT of the chest</td>
<td>Contrast and free air in the mediastinum</td>
<td>Thoracotomy Exploratory thoracotomy</td>
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<td>Fever, pleuritic chest pain, seizures</td>
<td>CT of the head</td>
<td>None</td>
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<td>21</td>
<td>Percutaneous: CPVA</td>
<td>1</td>
<td>Fever, grand mal seizure</td>
<td>CT of the head</td>
<td>Unremarkable</td>
<td>TEE</td>
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<td>Death</td>
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<td>72</td>
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<td>Seizure, haematemesis</td>
<td>NA</td>
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<td>Surgical: MVR and Maze procedure</td>
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<td>Collapse</td>
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<td>48</td>
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<td>Fever, chest pain, dysphagia</td>
<td>CT of the head</td>
<td>3 mm oesophageal perforation at level of atrium</td>
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<td>CT of the head</td>
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<td>Cummings et al</td>
<td>9</td>
<td>Male=4</td>
<td>37(10–16)</td>
<td>Percutaneous: PRFA</td>
<td>12.3</td>
<td>Sepsis (n=9), neurological symptoms (n=8), angina (n=2), GI bleed (n=3)</td>
<td>CT of the head</td>
<td>Intravascular air (n=2)</td>
<td>CT of the chest 3/4; autopsy 6/9</td>
<td>Surgical=3; Non-surgical=6</td>
<td>Death (n=9)</td>
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<td>5</td>
<td>Male=4</td>
<td>51(35–76)</td>
<td>Surgical RFA (n=4); Percutaneous RFA (n=1)</td>
<td>8–28</td>
<td>Fever (n=3), chest pain (n=2), hemiparesis (n=3), grand mal seizure (n=1), aphasia (n=1)</td>
<td>NA</td>
<td>NA</td>
<td>CT of the chest</td>
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<td>56</td>
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<td>38</td>
<td>Malaise, chills, bilateral arm weakness</td>
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<td>No vegetations</td>
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<td>Percutaneous: RFA</td>
<td>35</td>
<td>Fever, altered mental status, petechiae</td>
<td>CT of the head</td>
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<td>56</td>
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<td>28</td>
<td>Epigastric pain, dysphagia, tactile fever; focal weakness, anoma, acalculia, agraphia</td>
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<td>Bilateral hyperdense lesions (frontal, occipital, parietal and temporal)</td>
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<td>Fluid and air in pericardium and air in right superior mediastinum</td>
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<td>Substernal chest pain, nausea, vomiting, confusion, fever, seizures, haematemesis</td>
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<td>UGI series</td>
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<td>Cardiac catheterisation</td>
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<td>Percutaneous: RFA</td>
<td>–</td>
<td>Altered mental status, stupor</td>
<td>Multifocal air emboli</td>
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<td>67</td>
<td>Surgical: MVR and Maze procedure</td>
<td>20</td>
<td>Nausea, fever, numbness left foot; unresponsiveness</td>
<td>CT of the head: air embolism</td>
<td>CT</td>
<td>CT of the chest</td>
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<td>Death</td>
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<td>Percutaneous: RFA</td>
<td>2</td>
<td>Fever, chills, cough, headache; confusion, generalised tonic-clonic seizures</td>
<td>TTE/TEE</td>
<td>No thrombus</td>
<td>CT of the chest</td>
<td>Surgical</td>
<td>Survived</td>
</tr>
<tr>
<td>Neven et al</td>
<td>1</td>
<td>Male</td>
<td>69</td>
<td>Percutaneous: HIFU</td>
<td>31</td>
<td>Fever, haematemesis, seizures, phrenic nerve palsy</td>
<td>CT of the head</td>
<td>Cerebral embolism</td>
<td>Autopsy</td>
<td>Non-surgical</td>
<td>Death</td>
</tr>
<tr>
<td>Dixit et al</td>
<td>1</td>
<td>Female</td>
<td>NA</td>
<td>Percutaneous: PV isolation</td>
<td>14</td>
<td>Fever, haematemesis, nausea</td>
<td>EGD</td>
<td>Possible Mallory-Weiss tear</td>
<td>CT of the head</td>
<td>Non-surgical</td>
<td>Death</td>
</tr>
</tbody>
</table>

AEF, atrioesophageal fistula; CFAE, complex fractionated atrial electrograms; CPVA, circumferential pulmonary vein ablation; EGD, esophagogastroduodenoscopy; GEJ, gastroesophageal junction; HIFU, high-intensity focused ultrasound; IRAAF, intraoperative radiofrequency ablation of atrial fibrillation; LA, left atrium; LOC, loss of consciousness; LRFA, linear radiofrequency ablation; MVR, mitral valve replacement; NA, not available; PAD, postablation day; PV, pulmonary vein; PVI, pulmonary vein ablation; RFA, radiofrequency ablation; RSFA, right superior frontal area; TEE, transesophageal echocardiogram; TIA, transient ischaemic attack; TTE, transthoracic echocardiogram; UGI, upper gastrointestinal; VF, ventricular fibrillation.
explained by the fact that more men undergo RFA and that women are less likely get invasive treatment. AEF typically presented 20±12 days post-RFA, ranging from 2 to 60 days. Occasionally the patient might present repeatedly before a definitive diagnosis is made. The presenting symptoms can involve different organs and systems, including fever, neurological deficit, haematemesis, altered mental status, chest pain or a combination of these (figure 1). No association was found between onset of symptoms and mortality (19±10 vs 23±14 days; p=0.355). Finsterer et al suggested that the latency between initial insult and the development of symptoms may depend on the fistula size, the treatment initially provided, and the number of additional complications. A high index of suspicion for this catastrophic complication is required for patients with a recent history of RFA in order to achieve a correct diagnosis and prompt management.

**Diagnostic procedures**

CT of the chest with intravenous contrast has shown to be the most useful diagnostic tool. Other diagnostic techniques, such as CT of the head, can be useful. In this review, the most common findings were multifocal air embolism of the brain and pneumomediastinum. Several radiological features have been reported,
including pericardial effusion and the obvious communication between the atrium and the pericardium or the esophagus.\textsuperscript{12} \textsuperscript{51} TEE and/or esophagogastroduodenoscopy (EGD) are precluded at any suspicion of AEF. Air insufflation during TEE or EGD may lead to massive embolisation, resulting in severe neurological injury and death.\textsuperscript{4} \textsuperscript{5} \textsuperscript{7} \textsuperscript{8} \textsuperscript{11} \textsuperscript{13} \textsuperscript{15} \textsuperscript{18} \textsuperscript{21} \textsuperscript{24} \textsuperscript{26} \textsuperscript{28} \textsuperscript{30} \textsuperscript{32} \textsuperscript{35} \textsuperscript{36} \textsuperscript{38} \textsuperscript{44} If systemic bacterial endocarditis is suspected, avoiding TEE could prove lifesaving.\textsuperscript{13}

**Anatomical contributing factors**

Unfortunately, despite efforts to determine how this complication occurs, there is little understanding in the pathogenesis of AEF.

Gillinov et al\textsuperscript{22} considered that body size, when extremely small, may contribute to perforation, assuming thinner patients are more likely to have a thin left posterior atrial wall.\textsuperscript{14} Sonmez et al\textsuperscript{8} suggested that a thin atrial wall could also result from atrial enlargement (>60 mm in diameter). Paradoxically, others like Lemola et al\textsuperscript{45} proposed that a small LA might be at higher risk for fistula formation because the esophagus may occupy a larger relative area of the posterior LA, where much of the ablation is performed.

The absence of a fat layer between the esophagus and atrium may identify patients at higher risk of esophageal injury\textsuperscript{53}; the distance is often <5 mm from the esophagus to the endocardial layer of the atrium.\textsuperscript{14} This hypothesis is supported by a cadaver study that showed marked individual variation of thickness of the posterior left atrial wall and the fibrofatty layer between the atrium and the esophagus.\textsuperscript{9} \textsuperscript{54}

**Procedural contributing factors**

The incidence of AEF following percutaneous ablation has ranged from 0.01\% to 0.2\%, and is as high as 1–1.5\% for patients undergoing surgical ablation.\textsuperscript{2} \textsuperscript{5} \textsuperscript{6} \textsuperscript{12} \textsuperscript{45} \textsuperscript{55} \textsuperscript{57} This report includes 12 surgical and 41 percutaneous cases of AEF after RFA for AF. The higher number of percutaneous cases could be explained by the increased use of this therapeutic modality. However, given the overall small numbers of cases reported in the literature, it is not known whether the incidence of AEF differs when done surgically or percutaneously.\textsuperscript{12}

The accountability of an individual operator technique is inevitably implicit. In early cases, TEE was used as a standard imaging aid during ablation procedures. When the probe is left during the procedure, it mechanically displaces the esophagus towards the ablation catheter, increasing the heat transfer to the esophageal mucosa.\textsuperscript{58} Attempts to reduce temperature have been achieved with the use of cryoballoon technology for pulmonary vein isolation; however, despite this, AEF may still occur.\textsuperscript{29}

Given that direct thermal injury may account for the development of AEF, it seems critical to determine the role of intraesophageal temperatures during ablation procedures. There are, however, case reports of AEF without significant change in esophageal temperature.\textsuperscript{5} \textsuperscript{9} \textsuperscript{15} \textsuperscript{16} \textsuperscript{18} \textsuperscript{37} Changes in the esophageal mucosa consistent with thermal injury are commonly seen in about 47\% cases, while ulceration may occur in 14–18\% cases.\textsuperscript{59} \textsuperscript{60} One case series reporting the development of fistula in four patients showed no statistically significant difference when comparing AEF to AEF-free cases, although mean maximum temperature and total energy appeared slightly higher in the esophageal injury group.\textsuperscript{5} The risk for developing AEF is augmented by magnitude and duration of local heating, which is related to catheter tip size, contact pressure, catheter orientation, the number of linear lesions sets in the posterior wall, as well as the power output and duration associated with each lesion. Furthermore, general anaesthesia during catheter ablation may increase the risk of esophageal wall injury given the alteration in the physiological motility of the esophagus.\textsuperscript{61}

**Treatment**

Surgical intervention has been considered the standard of care, though isolated cases of successful conservative management have been reported.\textsuperscript{51} Only two of five cases treated with esophageal stenting survived after the procedure.\textsuperscript{8} \textsuperscript{9} \textsuperscript{18} \textsuperscript{21} \textsuperscript{27} Nevertheless, pericardioesophageal fistulas have been reported to be successfully managed with esophageal stenting when detected early (at days 26, 9 and 18 after the ablation procedure in the cases reported).\textsuperscript{51} Broad-spectrum antibiotics should be started concomitantly. Complications, such as stent dislocation, embolic and/or septic events, and stenosis may follow; therefore, patients should be closely followed.

Surgical repairs require cardiopulmonary bypass in order to first excise and replace the necrotic tissue in an intracardiac fashion.\textsuperscript{5} This method allows abolition of gaseous and bacteremic contamination within a locally aseptic, blood-rich, and tissue-friendly environment.\textsuperscript{34}

Esophageal resections constitute the second step of treatment. Stenting is not considered as first-line therapy as yet, but has been reported as a temporary measure in bridging to definitive surgical intervention and lately as an alternative management therapy when patients are unable to undergo surgery.\textsuperscript{24} Only one case reported successful stenting as an end point.\textsuperscript{9} \textsuperscript{35} Novel alternatives have been proposed such as cervical esophageal ligation and decompression.\textsuperscript{26}

Conservative management of esophageal perforation remains controversial with mortality rates ranging from 20\% to 45\%.\textsuperscript{5} According to the included cases (table 1), patients who did not receive a primary esophageal repair were more likely to have a deadly outcome (34\% with surgical treatment vs 83\% with conservative treatment; \(p<0.05\)). This may be owing to the critical status at presentation of this group of patients. All the patients with suspected AEF should be transferred to a hospital equipped with cardiothoracic surgery facilities.

**Outcome**

AEF has reportedly been associated with a mortality rate of 40–80\%.\textsuperscript{12} \textsuperscript{45} In this review, we found no difference in mortality rate between patients who underwent surgical


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**Note:** The above text is a natural representation of the document, formatted for readability. The original document contains references and citations that are not transcribed here. For comprehensive understanding, please refer to the full text.
RFA when compared with percutaneous RFA (58% vs 56%; p=0.579). Prior reports evidence lower mortality rates in the surgical RFA group, suggesting that there is a higher awareness of a complication when the procedure is done surgically.\textsuperscript{47} The complications following AEF, if survival is achieved, include multiple septicemias and even Guillain-Barré syndrome.\textsuperscript{12} No instances of spontaneous resolution have been reported.

**Procedural suggestions and prevention**

Technology advances now allow detailed mapping of the cardiac–esophageal interface by preprocedural and/or intraprocedural imaging; and energy delivery may be guided by intracardiac echocardiography.\textsuperscript{25} Nonetheless, cases of esophageal perforation, seen when using robotic mapping methods, have been reported.\textsuperscript{63}

Patwardhan et al\textsuperscript{62} hinted that the bipolar mode of RF would be safer than the unipolar mode, since it—in theory—prevents energy dispersion and thus the formation of AEF.\textsuperscript{57} Lower power setting and shorter lesion durations in the posterior aspect of the LA have been suggested as possible ways to avoid this complication. However, power has been shown to be a weak predictor of intraesophageal temperature during ablation and even power settings <10W may increase luminal temperatures in the esophagus and cause AEF.\textsuperscript{58} Intraoperative esophageal temperature monitoring has emerged as a method that allows the operator to stop the delivery of energy when increasing esophageal temperatures are detected.\textsuperscript{19, 64} Since the esophageal temperature can continue to increase for few seconds after discontinuation of energy delivery, immediate discontinuation of radiofrequency application has been suggested if esophageal temperatures increase rapidly or reach more than an absolute temperature of 39°C.\textsuperscript{9}

RFA uses a point-by-point system that entails absorptive heating and induction of thermal necrosis as mechanisms of action. Using an open-irrigated catheter lowers the energy output when compared to a standard 8 mm tip catheter and was found to decrease the rate of esophageal ulceration; however, all the ablation catheters still carry the risk of AEF.\textsuperscript{65}

Newer imaging techniques, such as combining the use of barium sulfate paste during CT or gadolinium digluetamate during MRI, are currently used to visualise the anatomical relationship between esophagus, pulmonary veins and LA position wall. The integration of these imaging modalities and current 3-D mapping systems (CARTO-3 or EnSite Velocity) provides a visualisation tool to understand the complex anatomy, and can play an important role in prevention of esophageal injury. Piorowski et al\textsuperscript{66} reported a high accuracy in visualising the true anatomic relationship of the esophagus and LA by preprocedural CT scan, and its intraprocedural position by using electro-anatomic mapping systems.

**CONCLUSION**

AEF following ablation procedures for AF is a serious complication with high mortality rates. It is critical to be aware of this complication in the outcome sequence of catheter ablation. Presenting symptoms most often include a triad of fever, neurological deficit and/or haematemesis. Prompt diagnostic work-up should include a CT-chest. TEE is contraindicated even when endocarditis is suspected. Survival depends on rapid diagnosis and intervention. When untreated, the outcome is more often fatal. Thorough patient education regarding signs and symptoms of esophageal injury upon discharge is warranted.

**Contributors**

PC, FHM, ACD, EFA, TS, DG, CDB and SD were responsible for conception and design of study; analysis and interpretation of data and drafting of the manuscript; final approval of the manuscript submitted and agreement to be accountable for all aspects of the work.

**Competing interests**

FHM Ad hoc consultant for the following organisations: Daiichi Sankyo, Pfizer, Takeda, Abbott, Servier, Medtronic, Ipca Laboratories Ltd.

**Provenance and peer review**

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Atrio-oesophageal fistulas from left atrial ablation.


