EDITORIAL COMMENT

Esophagopericardial Fistula
The Wolf in Sheep’s Clothing*

Thomas Deneke, MD, Kai Sonne, MD, Elena Ene, MD, Artur Berkovitz, MD, Karin Nentwich, MD

Collateral thermal injury of the esophagus is among the major drawbacks of current ablation technologies for atrial fibrillation (AF) therapy. Endoscopy reveals incidences of esophageal damage in approximately 10% to 20% of cases with current ablation modalities, and some of these injuries progress to perforation and fistulation into the pericardial space and/or the left atrium (1). The most severe esophageal perforating complication is esophagoatrial fistula (AEF) (stressing the course of esophagus-to-atrium progression), with a fatality rate of 60% to 80%. In AEF, early surgical intervention appears to be the only beneficial treatment option (2-5). Incidences of AEF have been stable over the past years, and although published survey-reported incidences have been approximately 0.02%, clinically detected incidences appear to be relevantly higher in more rigid follow-up studies (2-5), as well as potentially in real life. AEF may be the only AF ablation complication not related to operator or center experience, and therefore a high degree of suspicion is warranted in any AF ablation program. Procedural denominators have not been identified, but it has become clear that esophageal protection devices such as temperature monitors have not been able to eliminate AEF (2-5).

Delay of presentation is a limitation related to the patient’s awareness, and symptoms may initially be nonspecific. As a consequence of the appearance of symptoms up to 2 months after ablation, patients may present to remote facilities and be unaware of the correlation of the event with their previous AF ablation or unaware of the severity of their condition.

Whereas the usual chain of events culminating in AEF is initiated by thermal transmural esophageal wall injury at the time of ablation, some cases of “ischemic esophageal ulcerations” have been reported. This condition is defined by normal esophageal endoscopic findings after the ablation with the occurrence of esophageal ulcerating injury days later. The mechanism of progression appears to be related to reflux of gastric acid, potentially facilitated by damage to periesophageal nerves and esophageal motility (including sphincter plegia), ischemia, and delay of the healing process secondary to transmural damage of the vasculature and potentially also from decreased pain sensation and inflammation (1-5).

Some cases of esophageal perforation without communication to the left atrium have been reported, including cases of esophagopericardial fistula (EPF). Because these reports are even rarer than AEF, knowledge of presentation, prognosis, and management of EPF is even less precise.

The current case report by Kheslat et al (6) in this issue of JACC: Case Reports describes the course of a patient with documented EPF. In this report, the patient presented 18 days after an uneventful AF ablation with nonspecific symptoms, and the diagnostic work-up identified signs of nontamponade pericardial effusion or pneumopericardium. At 7 days after emergency surgical exploration and left atrial posterior wall patching, in addition to sewing of the esophageal perforation, the patient recurrent fistula developed, and the patient underwent reoperation, including empyema drainage and esophageal stenting. Another 8 days later, esophageal leakage was handled conservatively, and another 31 days later, after removal of the esophageal stent, a newly occurring fistula was clipped. Again, 32 days later,
management of patients with severe esophageal complications related to AF ablation. Multiple complex cardiac and esophageal surgical procedures were needed to resolve EPF effectively, and inflammation appears to be a consequence that is critical to manage and potentially life-threatening.

Available published reports usually summarize EPF with AEF cases, but it is important to differentiate these conditions because their outcome and mechanism vary dramatically. In reported case series of AEF, approximately 10% account for EPF cases, and mortality is relatively lower. In published reports, patients in 33 of 39 reported and summarized cases survived (85%), usually without major sequelae, and management ranged from broad-spectrum antibiotics alone to adding esophageal stenting in combination with pericardial drainage or complex surgical procedures (3-10).

The presentation of EPF may differ from that of AEF because no neurologic symptoms occur, and therefore thoracic pain or discomfort and fever are the 2 most important but nonspecific diagnostic indicators of perforating esophageal complications and mediastinitis. In this setting, emergency chest computed tomography using oral and intravenous contrast media is the only diagnostic measure that sufficiently allows for detection of EPF or esophageal perforating complications on the 1 hand and is able to rule out AEF on the other hand.

Early detection of EPF is crucial to initiate adequate treatment. Whereas in AEF, surgical repair is associated with lowest mortality (~30%), appropriate treatment of EPF remains unclear and may differ from clinical status and indicators of inflammation or sepsis (3,4). As identified in the current case report by Kheslat et al (6), surgical explorations, including cardiac reconstructive surgery, esophageal stenting, and esophageal surgery, are potential procedures used for effective sealing of the fistula entrance, in addition to controlling pericardial infection by continuous drainage and broad-spectrum antibiotic treatment to prevent or treat systemic inflammation. In most reported cases of EPF, nonsurgical treatment options were preferred and have yielded quite remarkable results.

The main denominators of outcome are early detection and effective initial treatment. In cases with delay of invasive treatment of more than 3 days, the prognosis is worse compared with cases with rapid diagnosis and initiation of treatment (2-5).

DIFFERENCES BETWEEN ESOPHAGOPERICARDIAL FISTULA AND ESOPHAGOATRIAL FISTULA

Esophageal complications are a consequence of tissue damage during the ablation procedure and may either relate to transmural tissue burns (or freezes) indicated as esophageal thermal injury or ischemia of the esophageal wall (due to damage of periesophageal vasculature). The effective endpoint of both mechanisms are esophageal ulcers that disintegrate the clear border of the esophageal lumen with air, congested nutritive material and also potentially lytic enzymes and gastric acid. It is unclear if EPF is an early form of esophageal perforating complications that may progress to AEF or why in some of these cases fistulation stops before entering the left atrium. In an interesting report by James (10) on cases of pneumopericardium stemming from esophageal perforating injuries (mostly from foreign body ingestions) no case of perforation into the left atrium was observed implying that the mechanism of AEF may also involve a “locus minoris resistentiae” of the left atrial wall (probably induced by the AF ablation (9). Therefore, the most obvious difference to AEF is
the lack of neurological complications in EPF, a known factor of poor prognosis in AEF cases (2-5).

The time delay between the ablation procedure and the onset of symptoms related to the occurrence of EPF or AEF is usually between 2 days and 2 months (most cases of AEF appear at approximately 3 weeks, and most EPF cases appear to occur between 2 and 4 weeks after ablation). The occurrence of EPF has been reported in patients with esophageal thermal and ischemic ulcers, and mechanisms for prevention remain unclear.

In conclusion, EPF is an esophageal perforating complication of AF ablation that is approximately 10 times rarer than AEF. If identified early and if invasive treatment is initiated immediately, EPF has a relevantly better prognosis than AEF. Nonetheless, some patients present with recurrent esophageal fistulation, and esophageal stenting alone may not sufficiently lead to healing. EPF can be seen as the wolf in sheep’s clothing because symptoms may be nonspecific, but adequate and early diagnostics are crucial for immediate treatment. It is always helpful to suspect the “wolf” in patients with suspicious symptoms hinting at perforating esophageal complications.

The management of patients with EPF may differ from that of patients with AEF, and the information provided the case report by Kheslat et al (6) is very helpful. Managing this esophageal injury is highly complex and may involve surgical or interventional attempts to seal the esophageal lumen and suppress inflammation and progression. Therefore, it is reasonable to consider transferring these patients to experienced centers with availability for interdiscipli-nary management on the basis of current scientific standards.

As in the case report by Kheslat et al (6), effective therapy of EPF involves a multidisciplinary approach to these patients, just as management of AEF requires high expertise and experience. In Germany, the German Working Group on Arrhythmias has been able to establish an online forum for obtaining fast and expert advice in cases of esophageal AF ablation-induced complications that offers help for diagnosis and treatment. The motto of this group is “diagnose and treat EPF and AEF the faster the better,” and therefore patients and also remote health care providers where these patients may present must be alert and educated to reduce delays from the onset of symptoms to appropriate expert treatment.

FUNDING SUPPORT AND AUTHOR DISCLOSURES
The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Thomas Deneke, Clinic for Interventional Electrophysiology, Heart Center Bad Neustadt, Rhön-Klinikum Campus Bad Neustadt, Von-Guttenberg-Strasse 11, GER-97616 Bad Neustadt, Germany. E-mail: thomas.deneke@campus-nes.de.

REFERENCES
1. Halbfass P, Pavlov B, Müller P, et al. Progression from esophageal thermal asymptomatic lesion to perforation complicating atrial fibrillation ablation: a single-center registry. Circ Arrhythm Electrophysiol. 2017;10(8):e005233.
2. Deneke T, Nentwich K, Halbfass P, Sommer P. There is glory in prevention! Atrio-esophageal fistula and atrial fibrillation ablation. Europace. 2020;23(4):491-3.
3. Gandjbakhch E, Mandel F, Dagher Y, Hidden-Lucet F, Rollin A, Maury P. Incidence, epidemiology, diagnosis and prognosis of atrio-oesophageal fistula following percutaneous radiofrequency catheter ablation of atrial fibrillation: a French nationwide survey. Europace. 2021;23(4):557-64.
4. Barbhaiya C, Kumar S, Guo Y, et al. Global survey of esophageal injury in atrial fibrillation ablation. Characteristics and outcomes of esophageal perforation and fistula. J Am Coll Cardiol EP. 2016;2:143-50.
5. Medeiros De Vasconcelos JT, dos Santos Galvao Filho S, Atie J, et al. Atrial-oesophageal fistula following percutaneous radiofrequency catheter ablation of atrial fibrillation: the risk still persists. Europace. 2017;19:250-8.
6. Kheslat HH, Kelly S, Singh H, Crozier I. Esophago-pericardial fistula following radiofrequency ablation for atrial fibrillation: insights into its management. J Am Coll Cardiol Case Rep. 2021;3:1132-5.
7. Eitel C, Rolf S, Zachäus M, et al. Successful nonsurgical treatment of esophagopericardial fistulas after atrial fibrillation catheter ablation. A case series. Circ Arrhythm Electrophysiol. 2013;6:675-81.
8. Han HC, Ha FJ, Sanders P, et al. Atrioesophageal fistula. Clinical presentation, procedural characteristics, diagnostic investigations, and treatment outcomes. Circ Arrhythm Electrophysiol. 2017;10(11):e005579.
9. Back Sternick E, Correa FS, Drumond LF, et al. Esophago-pericardial fistula after catheter ablation of atrial fibrillation: a review. J Cardiovasc Electrophysiol. 2020;31:2600-6.
10. James WB. Pneumopericardium. Am Med. 1904;8:23-7.

KEY WORDS ablation, atrial fibrillation, complication