Pericardial-esophageal fistula complicating cryoballoon ablation for refractory atrial fibrillation

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Introduction

Atrial fibrillation affects an estimated 2.7–6.1 million people in the United States and accounts for more than 750,000 hospitalizations per year.1 Pulmonary vein isolation (PVI) has been well established as the most effective ablation treatment available for patients with symptomatic and medication-refractory atrial fibrillation.2 Previously, radio-frequency (RF) ablation was the mainstay for PVI. However, this was not without complications, which have been well documented,3,4 the most feared complication being atrioesophageal fistula formation.5,8,9 Nonetheless, there have been 5 reported cases of atrioesophageal fistula formation following CB ablation, which is the case we present here.

Case report

The patient is a 70-year-old woman with a history of nonischemic cardiomyopathy, suspected to be tachycardia mediated, who presented to our tertiary care center for evaluation of medically refractory atrial fibrillation. With regard to prior treatment, she previously had undergone an RF ablation procedure and had been on sotalol, amiodarone, and eventually dofetilide, all of which failed to maintain sinus rhythm. Given that her reduced left ventricular function was likely owing to tachycardia related to the atrial arrhythmia, which was medically refractory, the decision to undergo cryoballoon ablation was made.

The patient was brought to the electrophysiology laboratory and the procedure was performed under general anesthesia; sedation was maintained with the use of propofol and remifentanil. Radial arterial monitoring, an esophageal temperature probe, and intracardiac echocardiography were all employed during the procedure. Heparin was used for anticoagulation to maintain activated clotting time >350 seconds. Right and left femoral vein access was employed for the procedure; an SL1 sheath and guidewire were used for the transseptal puncture under fluoroscopic and ultrasound guidance. Four pulmonary veins with separate ostia were identified with ultrasound. Using a 28-mm Arctic Front cryoballoon (Medtronic, Inc, Minneapolis, MN) supported by a cryo lasso catheter (Achieve, Medtronic, Inc), cryoablation was performed at the ostium of all 4 pulmonary veins.

Each ablation lasted up to 3 minutes, achieving balloon temperatures between -30°C and -45°C. A total of 9 cryoablation lesions were placed. The left inferior pulmonary vein (LIPV) underwent 2 separate ablations; the first ablation was 180 seconds at -34°C. Of note, during the second ablation, which occurred 56 seconds after the first, the esophageal temperature was noted to be 24.8°F and the ablation was immediately terminated (171 seconds of application). Phrenic nerve pacing was performed during...
Ablation of the right pulmonary veins with a quadripolar catheter placed in the superior vena cava. A St. Jude catheter HD (St. Jude Medical, St. Paul, MN) was used for voltage gradient mapping. The patient was successfully externally cardioverted to sinus rhythm. After exit and entry block in each pulmonary vein was established, protamine was given to reverse the anticoagulation effect of heparin and sheaths were removed without complication. She was subsequently admitted for observation and dofetilide was initiated. The patient was discharged 2 days later after an uneventful hospital course in sinus rhythm. She received omeprazole 20 mg and sucralfate 1 G, both twice daily, while hospitalized and was discharged with 14 days of sucralfate and omeprazole for postprocedure care.

About 10 days later, the patient presented locally with complaints of crushing chest pain, worse with lying down and respiration but without hemoptysis or fever. Initial electrocardiogram and cardiac enzymes did not suggest myocardial ischemia. Computed tomography (CT) of the chest was obtained, which showed evidence concerning for pneumopericardium and pericardial effusion (Figure 1); this prompted transfer to our facility for a higher level of care. In transit, the patient developed hypotension, which was stabilized with intravenous fluids and vasopressors; owing to the concern for an infected pericardium, broad-spectrum antibiotics were also initiated. Cardiothoracic surgery was promptly consulted and the patient was taken to surgery the following day. During surgery, she was found to have a gross amount of fibrinous exudate surrounding and on the surface of the heart. This was cleansed with copious irrigation, at which time there was blood-tinged fluid noted within the pericardium. To enable full inspection of the area, the patient was placed on cardiopulmonary bypass. However, after aortic cannulation, there was no blood flow through the aortic cannula and a bluish hue was noted on the surface of the ascending aorta extending from the cannulation site proximally. Epiaortic ultrasound confirmed a hematoma in the adventitia in addition to a dissection flap at the area of the cannulation. The patient’s right axillary artery was then

**KEY TEACHING POINTS**

- Although cryoballoon ablation has been shown to have a safer complication profile compared with radiofrequency ablation, it is still an invasive procedure and carries real risk with regard to damage to surrounding structures.
- This is the first reported case of pericardial-esophageal fistula formation with sparing of the atrium, the mechanism of which is up for debate. Early recognition and treatment can potentially prevent a more complex complication with higher mortality.
- Although complications are unfortunate, they do occur and it is important to make adjustments to protocols or institutional structure when able and appropriate. Unfortunately, in this case, the esophageal probe had not been registering correctly during the case; we have made adjustments at our institution and now employ a different and more stable monitoring system.

![Figure 1](image.png)  
**Figure 1** Chest computed tomography images showing free air within the posterior pericardium.
cannulated for bypass. Once the patient was supported on bypass, the heart was lifted up and there was a gross obvious tear noted in the posterior pericardium, which was adjacent to a 2.5-cm tear in the esophagus (Figure 2). The esophageal tear was repaired with sutures because the edges appeared healthy; a pericardial flap was taken and secured over the esophageal repair. Attention was then turned to the aorta dissection, which was then repaired without leaving any prosthetic material in the body, as the field had been contaminated owing to the fistula. She was then admitted to the cardiovascular intensive care unit for continued care; a percutaneous endoscopic gastrostomy tube was placed for feedings, the patient was weaned off all vasopressor support, and she was extubated within the first few postoperative days. Cultures obtained during the surgery were positive for multiple organisms including *Lactobacillus* species, *Streptococcus* species, *Saccharomyces* species, *Candida* species, and *Mycobacterium avium*. She was treated with broad-spectrum antimicrobial therapy with vancomycin, piperacillin-tazobactam, and fluconazole. An esophagram for confirmation of healing was completed 1 week after the procedure and, unfortunately, showed evidence of a small, contained esophageal leak (Figure 3). She underwent esophagogastroduodenoscopy the following day; a small (2–3 mm) leak was noted midway between the proximal and distal end of the suture line, which was repaired. Repeat esophagram prior to discharge showed a stable, contained esophageal leak. Flexible esophagoscopy at follow-up 1 week after discharge showed the esophageal lesion was healing without evidence of mucosal defects. The patient completed a total of 4 weeks of antimicrobial coverage with the previously mentioned regimen. Treatment specifically for *Mycobacterium avium* was attempted; however, the patient has not been able to tolerate the medications owing to side effects but has done well and remains free of any evidence of persistent infection.

**Discussion**

PVI continues to be the cornerstone of ablation therapy for medically refractory atrial fibrillation. Initially, RF ablation was the only modality available, which carried well-
documented risks, of which the most feared is atrioesophageal fistula formation, given its significant mortality. The development of cryoballoon ablation had a significant impact, with its rapid learning curve, less dependence on operator dexterity, and apparently an improved safety profile with regard to the risks to adjacent structures. The mechanism of injury during cryoablation occurs in 3 phases: freezing/thawing phase, hemorrhagic and inflammatory phase, and, finally, the replacement fibrosis phase. During the first phase, ice crystals develop within both the intracellular and extracellular spaces. These extracellular ice crystals create a hypertonic environment, creating ion and water shifts resulting in cell shrinkage and, ultimately, biochemical destruction of the cells. After freezing of the tissues is complete, the tissues gradually return to normal body temperature, which is accompanied by a hyperemic vascular response. In addition, the intracellular and extracellular ice crystals combine and extend the cellular damage. The second phase, characterized by hemorrhaging and inflammation, occurs as the microvasculature circulation is returned to the frozen tissue. The associated edema causes excess fluid to cross through the damaged microvascular endothelial cells, causing ischemic necrosis. The final phase occurs within weeks of the therapy; apoptosis of cells and replacement with fibrosis tissue near the edges of the lesion creates a mature injury site and scar.

Although cryotherapy ablation has promising advantages compared with RF, no invasive procedure is fully free of all risks and CB ablation has been shown to carry a real, although possibly diminished, risk of damage to the esophagus. Some studies have suggested that the risk of ETLs increases based on the proximity of the esophagus to the posterior wall of the left atrium. Owing to the posterior course of the inferior pulmonary veins, these appear to carry the highest risk of injury to the esophagus, especially the LIPV. One study showed that a type B anatomic location of the esophagus (surrounded by the descending aorta, spine, and LIPV ostium on CT) carried a significantly higher risk of development of ETLs. They also demonstrated that when the esophagus was located closer to the LIPV with a cutoff of less than 2 mm, there was an increase of ETLs, although this result was not statistically significant. Other studies have shown similar vulnerability of the esophagus with respect to the LIPV, with 1 study noting that 5 out of 6 observed ETLs occurred with ablation of the LIPV. Even though imaging prior to a procedure may help to reduce the risk of damage to adjacent structures, it is unlikely to eliminate this risk altogether.

In addition to anatomic location of the esophagus, other strategies have been suggested to reduce the risk of esophageal injury. One group recommends that shorter ablation times be utilized, especially in areas of higher risk, and suggests that ablation be discontinued when posterior vein potentials are eliminated. Unlike with RF ablation, luminal esophageal temperature (LET) monitoring has also been shown to correlate with ETLs. One study demonstrated that an LET of <12°C had a sensitivity of 100%, specificity of 92%, negative predictive value of 100%, and positive predictive value of 71% for predicting development of ETLs after CB ablation. Of note, this same study showed that there was no correlation between the minimum CB temperatures (return gas temperatures) and the minimum LET, suggesting that using the CB temperature as a marker for potential esophageal injury is not reliable. Another group demonstrated that a cutoff of 10°C had a sensitivity of 100% and specificity of 93% for predicting ETLs. There are various types of esophageal temperature monitoring probes that can be used, and it has more recently been shown that both deflectable and nondeflectable probes are useful for predicting the development of ETLs but different cutoff temperatures should be utilized depending on the specific probe.

As a result of this complication, we have changed our procedural setup a great deal. In this patient, we had completed the first cryo application to the LIPV (180 seconds at -34°C) before it was noted that the single-electrode esophageal temperature probe was not properly recording. Our anesthesiology team had the only view of the probe readings, and anesthesia personnel tend to rotate throughout the procedure and have variable experience in the electrophysiology laboratory. During the second application of energy to the LIPV (56 seconds between applications), we asked the anesthesiologist for a temperature reading and stopped the freeze immediately upon hearing that the probe was reading 24.8°F (171 seconds into the application at -36°C). We have since changed to the Circa probe (Circa Scientific, Englewood, CO), which has multiple electrodes and automatically alarms when temperatures reach a preprogrammed limit. We no longer allow esophageal temperatures less than 30°C. Monitoring for pulmonary vein potential disappearance was not possible on this vein, as the Achieve mapping catheter had no discernible pulmonary vein activity. If pulmonary vein potentials are visible during ablation and are eliminated prior to 60 seconds of energy application, we will often ablate for 120 seconds postsilation and then perform the second cryo application for 120 seconds to minimize risk.

As has been demonstrated by the previously reported cases of atrioesophageal fistula, this is a catastrophic complication. Our case, however, is the first known reported case of pericardial-esophageal fistula formation with CB ablation. Although our patient developed an infected pericardium and pericarditis with an overall moderately complicated hospital course, she has made a very successful recovery. This suggests that although esophageal fistula formation is rare with CB ablation, this is still a very real possibility and early recognition and intervention can significantly improve the outcome.

Why this complication spared the atrium and injured only the pericardium and esophagus is open for conjecture. One thought is that this patient had a good deal of low-voltage left atrial scar when we performed a post-PVI voltage map using a St. Jude HD mapping catheter and the NAVIX system (Supplemental Figure 1, available online). It is possible that
scar is less vascular and would have less microvasculature to compromise and, therefore, is less vulnerable to injury than the more healthy pericardium and esophagus. Considering the mechanism of injury that occurs with cryotherapy, specifically the involvement of the microvasculature during the second phase, this could be an explanation for why the left atrium was spared. Alternatively, the LIPV tends to be more difficult to completely occlude and one could speculate that incomplete occlusion resulted in higher local tissue temperatures in the antral area, which helped spare the atrium itself. Lastly, the timing of the patient’s presentation may have played a factor in why the left atrium was spared. Currently, the exact mechanism of fistula formation is unknown. Studies have shown that as many as 19% of patients undergoing CB ablation have ELTs postprocedure, which have also been shown endoscopically to heal within a few weeks. The reason that some of these ELTs may progress to fistulas is uncertain. However, one could postulate that should a fistula form, the pericardium would be the first structure to be involved, likely leading to mediastinitis. If this were to go undiagnosed, it could subsequently evolve into an atrioesophageal fistula, given the close anatomic proximity of the posterior left atrial wall. Our patient presented with symptoms earlier than the other case reports of atrioesophageal fistula formation (10 days postprocedure for our patient compared with 2–4 weeks in other case reports). Therefore, the early presentation in addition to the prompt diagnosis and treatment of this complication may have prevented the progression of the fistula and avoided atrial involvement.

Postprocedure proton pump inhibitors (PPI) have also been suggested to theoretically reduce the incidence of ELTs secondary to a second hit theory. However, our patient had been discharged with sucralfate and a PPI for postprocedure care; another case report of atrioesophageal fistula formation despite postprocedural treatment with PPI has been described as well.

Conclusion

Although cryoballoon ablation has a lower rate of fistula formation compared with RF ablation, this devastating complication still occurs. Our case, which is the first known reported case of pericardial-esophageal fistula, suggests that because this is a very serious complication that requires emergent surgical intervention, early recognition and intervention is critical.

Acknowledgement

Open access publication of this article is supported by an unrestricted grant from Janssen Pharmaceuticals, a Johnson and Johnson Company. Janssen Pharmaceuticals was not involved in the selection, writing, or peer review of this article.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.hrcr.2016.12.002.

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