Periesophageal vagal nerve injury following catheter ablation of atrial fibrillation: A case report and review of the literature

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Introduction

Percutaneous catheter ablation is an established rhythm control strategy for the treatment of atrial fibrillation (AF).[1,2] Recent clinical trials show that catheter ablation of atrial fibrillation reduces the risk of recurrence of symptomatic AF, atrial flutter, or atrial tachycardia, and may also reduce subsequent hospitalizations and improve quality of life compared to antiarrhythmic drug therapy.[3,4] Catheter ablation has garnered a class I recommendation for patients with symptomatic paroxysmal AF who are refractory or intolerant to at least one class I or III antiarrhythmic medication, and has a class IIa recommendation as a reasonable initial rhythm control strategy in the 2014 guidelines published by the American College of Cardiology/American Heart Association/Heart Rhythm Society.[5]

Catheter ablation for AF is widely regarded as a safe procedure. A recently published retrospective analysis of AF catheter ablation (performed in 83,236 patients enrolled in a total of 192 published clinical trials) reported an overall periprocedural complication rate of 2.9%. The majority of the complications were vascular in nature with an incidence of 1.4%.[6] Gastrointestinal (GI) complications following catheter ablation for AF are exceedingly rare. The most serious GI complication after catheter ablation is formation of an atrioesophageal fistula, which has a very low incidence (0.03%-0.1% of cases). However, atrioesophageal fistulae can lead to potentially life-threatening sequelae including catastrophic bleeding, septicemia, cerebrovascular accidents, and air embolism, and carry a mortality rate exceeding 80%.[7,8]

KEYWORDS Acute gastric hypomotility; Radiofrequency ablation; Esophageal temperature monitoring

ABBREVIATIONS **AF** = atrial fibrillation; **3D** = 3-dimensional; **EPS** = electrophysiology study; **GI** = gastrointestinal; **ICE** = intracardiac echocardiogram; **LET** = luminal esophageal temperature; **PVI** = pulmonary vein isolation; **RF** = radiofrequency; **TEE** = transesophageal echocardiogram

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In recent years there have been several reports of other complications that affect the upper GI tract following catheter ablation for AF. One of these complications is periesophageal vagal nerve injury, which leads to acute onset of upper GI symptoms that typically develop within hours after ablation. Clinicians need to be aware of and recognize this complication, quickly distinguish it from other potentially life-threatening conditions such as esophageal perforation or bowel obstruction, and institute an appropriate treatment plan.

Case report

A 56-year-old man with hypertension, type 2 diabetes mellitus, hyperlipidemia, obstructive sleep apnea, chronic kidney disease, and diastolic heart failure was admitted for an elective catheter ablation for recurrent paroxysmal AF. A transesophageal echocardiogram (TEE) with echo-contrast performed 2 months prior demonstrated a thrombus within the left atrial appendage, and he was prescribed rivaroxaban at a renal-adjusted dose of 15 mg daily. The night prior to the procedure, rivaroxaban was discontinued and a weight-based continuous infusion of unfractionated heparin was started periprocedurally. Repeat TEE showed no residual thrombus in the left atrial appendage. A commercially available non-deflectable transesophageal temperature probe (Level 1 Acoustascope® with temperature sensor ES400-18; Smiths Medical ASD, Inc, Rockland, MA) was inserted to monitor luminal esophageal temperature (LET). A 10F SOUNDSTAR® (Biosense Webster, Diamond Bar, CA) intracardiac echocardiogram (ICE) catheter was placed in the right atrium for anatomic mapping of the left atrium, left atrial appendage, and pulmonary veins, and under ICE guidance a double transseptal puncture was performed using a Brockenbrough needle assembly. Three-dimensional (3D) mapping was performed using a 7F variable-curve Lasso catheter (Biosense Webster, Diamond Bar, CA) inserted through an SL1 sheath (St. Jude Medical, St. Paul, MN), and the CARTO® 3 mapping platform was used along with the CARTOSOUND® module, which enabled integration of the ICE images with the 3D mapping images (Figure). Pulmonary vein isolation (PVI) was performed using an 8F bidirectional 3.5-mm-tip THERMOCOOL® SF catheter (Biosense Webster, Diamond

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KEY TEACHING POINTS

- Periesophageal vagal nerve injury manifests as acute onset of nausea, vomiting, abdominal pain and distension within 3–12 hours after pulmonary vein isolation for ablation of atrial fibrillation (AF).
- This condition should be rapidly differentiated from other serious gastrointestinal complications after AF ablation, such as esophageal perforation or development of atrioesophageal fistula.
- Most cases will respond to conservative management, which includes complete bowel rest, mechanical decompression of the upper gastrointestinal tract, and oral or intravenous prokinetic agents.
- Various strategies can be employed to reduce the risk of periesophageal vagal nerve injury during AF ablation; these include avoiding ablation of the posterior left atrial wall, use of irrigated-tip catheters, reduction in power output and/or duration of delivery of radiofrequency energy, and use of esophageal temperature monitoring devices.

Bar, CA) inserted through an 8.5F large-curl long (71 cm usable length) Agilis™ NxT sheath (St Jude Medical, St Paul, MN), with bidirectional steering to facilitate maneuverability, improve access to difficult-to-reach sites, and assure optimal tissue contact in the absence of direct quantitative contact force measurement. Radiofrequency (RF) energy delivery to the posterior wall was initiated at 20 W and titrated (maximum of 35 W) until a 10 Ω drop in impedance and an 80% reduction in electrogram size was achieved. Energy delivery at other sites was limited to 35–50 W. Energy delivery to lesions near the esophagus was limited to $\leq$30 seconds and was stopped immediately if the LET increased by 1°C above baseline. No esophageal temperature recordings of more than 40°C were recorded during the entire procedure. An empiric bidirectional cavo-tricuspid isthmus ablation was also performed. The patient tolerated the procedures well, and he was admitted to the cardiac intensive care unit for postprocedure monitoring.

About 6 hours after the procedure, the patient developed intractable nausea and vomiting that was unresponsive to intravenous ondansentron and trimethobenzamide. In addition, he developed generalized abdominal pain and distension. On inquiry, he denied any GI symptoms prior to the ablation procedure. Physical examination revealed tenderness in the epigastric and periumbilical regions and hypoactive bowel sounds throughout the abdomen. An abdominal radiograph demonstrated prominent gas-filled "stacked"-appearing loops of small bowel consistent with early ileus. A computed tomographic scan of the chest did not demonstrate any air or swelling within the mediastinum. A nasogastric tube was inserted and connected to intermittent suction, which reduced his vomiting and abdominal pain, but the nausea and abdominal distension persisted. Gastroenterological consultation was requested, and he was started on intravenous erythromycin 3 mg/kg thrice daily, along with intravenous metoclopramide 5 mg every 6 hours as needed. Over the next 48 hours, his nausea and

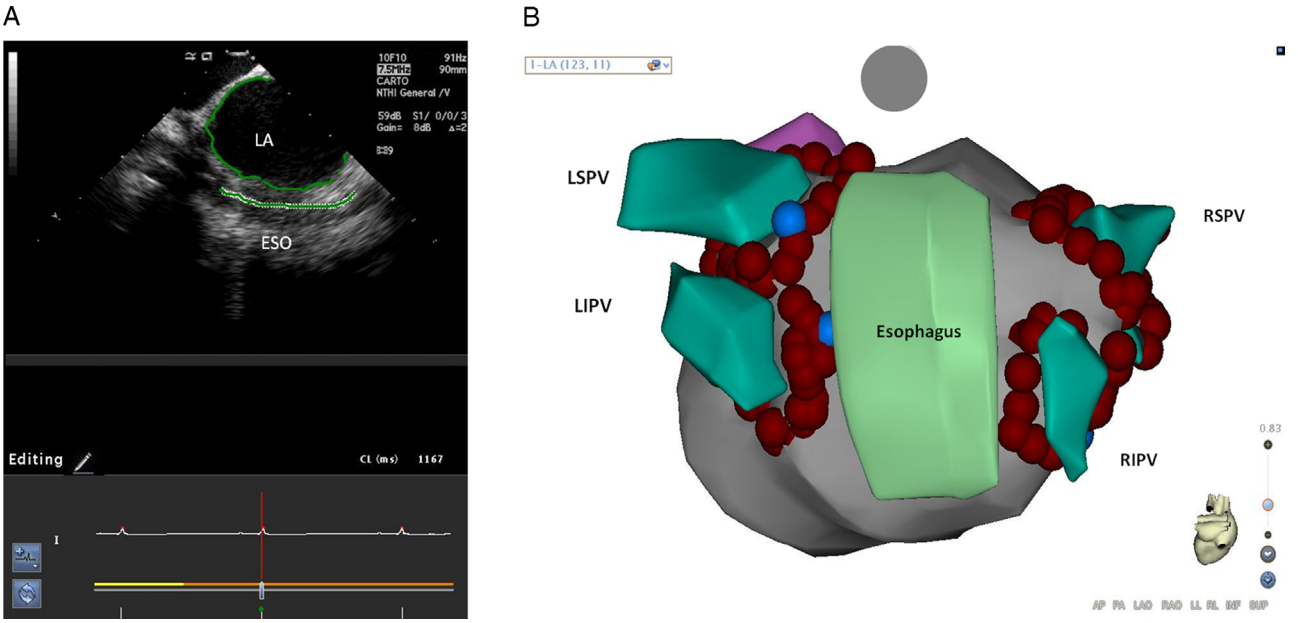

Figure Relationship of the lower esophagus, posterior left atrium, and pulmonary veins in our patient. **A:** Intracardiac echocardiogram image of the left atrium (LA) and the esophagus (ESO) as it courses close to the posterior atrial wall in our patient. **B:** Posterior view of the 3-dimensional map of the left atrium and the pulmonary veins, and the anatomic relationship between the esophagus and the ablation sites around the ostia of the pulmonary veins. Note the proximity of the esophagus to the ostia of the left upper and lower pulmonary veins. RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein.

abdominal distension slowly improved. A clear liquid diet was started on day 5, and the patient was advanced gradually to a regular diet by day 7. His GI symptoms had completely resolved at the time of discharge on postprocedural day 10. Erythromycin was continued orally at a dose of 400 mg thrice daily for a total of 4 weeks. Over the next 16 months of follow-up, the patient has not had any recurrence of GI symptoms and has also remained free of recurrent AF.

Discussion

The incidence of periesophageal vagal nerve injury is much lower than other complications after catheter ablation for AF, such as femoral pseudoaneurysm, arteriovenous fistulae, bleeding, pulmonary vein stenosis, pericardial effusion, cardiac tamponade, and cerebrovascular events. Periesophageal vagal nerve injury clinically presents with symptoms of acute gastric hypomotility and, in some cases, acute pyloric spasm as seen on abdominal imaging or by endoscopy. Most information about periesophageal vagal nerve injury after catheter AF ablation is obtained from case reports and case series, and the incidence of this complication may be as high as 0.3% following catheter AF ablation.[9–12]

The esophagus follows a variable course along the posterior aspect of the left atrium owing to displacement by the aortic arch, and the thickness of the esophageal wall adjacent to the left atrium varies from 1.5 to 4.5 mm. The posterior left atrial wall also varies in thickness, being thickest adjacent to the coronary sinus and thinnest superiorly. Behind the left atrial wall exists a layer of fibrous parietal pericardium and fibroadipose tissue of uneven thickness. Within the fat pad and in contact with the posterior left atrial wall through the parietal pericardium, branches of the left vagus nerve descend along the anterior aspect of the esophageal wall, before forming a plexus with branches from the right vagus nerve around the esophagus.[13] The space between the esophagus and the posterior wall of the left atrium is highly variable owing to differences in thickness of the connective tissue of the parietal pericardium and of the fibroadipose tissue between the esophagus and left atrium, and this may lead to variations in the vulnerability of the periesophageal nerve fibers to injury during application of RF energy. The periesophageal vagal nerve plexus controls gastric peristalsis, function of the pyloric sphincter, and gastric motility, and injury to this plexus can lead to acute gastric hypomotility and pyloric spasm.

Many theories exist about the pathophysiology of periesophageal vagal nerve injury during catheter ablation, but none have been substantiated in clinical studies. Potential mechanisms of injury include direct thermal injury to the esophageal wall due to conductive or convective transfer of RF energy through the thin-walled left atrium, ischemic injury to the esophageal wall, and inflammatory changes within the esophageal wall. Some experts opine that a combination of thermal and ischemic insults leads to progressive esophageal wall damage following catheter ablation. Another possible mechanism for progression of esophageal lesions after initial thermal injury from RF ablation is the reflux of acidic stomach contents bathing the lesion.[14,15] A small study showed that compared to baseline, both fasting and postprandial electrogastrogram abnormalities and bradygastria increased immediately after electrophysiology study (EPS) and ablation in patients with AF, but these changes were not observed in the patients undergoing EPS and ablation for non-AF conditions.[16]

Early studies in animals compared the effects of RF energy vs cryoablation on the incidence and time course of esophageal injury. Cryoablation and RF ablation created similar acute and chronic lesion dimensions in the esophagus, but cryoablation was associated with a significantly lower risk of partial- to full-wall esophageal ulceration seen by histology compared with RF ablation.[17] Ahmed and colleagues[18] noted a 17% incidence of esophageal ulceration following balloon cryoablation for PVI,[18] but studies comparing the effects of cryoablation vs RF ablation on the development of periesophageal vagal nerve injury are currently lacking.

Prevention

Although there is no established approach for avoiding injury to the periesophageal vagal nerve fibers, the risks can be minimized by using the same techniques for preventing other esophageal complications. Schmidt and colleagues[19] stopped energy delivery if there was sudden increase in microbubble density within the left atrium seen with ICE. One widely used strategy to limit the extent of esophageal injury is the use of esophageal temperature monitoring utilizing commercially available or improvised temperature probes. Delivery of RF energy should be discontinued when the esophageal temperature increases significantly, and most centers stop energy delivery if the esophageal temperature approaches 38.5°C–42°C.[20–22] It should be noted that LET may continue to rise further even after RF cessation. Another approach is to avoid delivering RF energy to the left atrial posterior wall, which is adjacent to the esophagus, with measures such as using a "box-isolation approach" PVI or reducing maximum energy output during ablation of the left atrial posterior wall. Musat

Table 1 Possible strategies to reduce the risk of periesophageal nerve injury during catheter ablation of atrial fibrillation

- Avoid ablation of the posterior left atrial wall, use of a "box-isolation" approach for atrial fibrillation ablation
- Use irrigated-tip catheters for radiofrequency (RF) ablations
- Reduction in RF power output (25–30 watts)
- Reduction in the duration of delivery of RF energy ($\leq$30 seconds)
- Use of esophageal temperature monitoring—stop ablation if luminal esophageal temperature approaches 42°C
- Consider preprocedural imaging studies to determine the distance between the posterior left atrial wall and the esophagus
- Consider screening of high-risk individuals for presence of reflux esophagitis

Table 2 Clinical management of periesophageal nerve injury following catheter ablation of atrial fibrillation

- Complete bowel rest (nothing by mouth) until symptoms subside
- Decompression of upper gastrointestinal tract using a nasogastric tube connected to intermittent or continuous suction
- Intravenous prokinetic agents (erythromycin 3 mg/kg 3 times daily as needed)
- Oral prokinetic agents if patients can tolerate oral intake (mosapride, metoclopramide)
- For persistent symptoms:
  - Oral erythromycin 400 mg thrice daily for up to 4 weeks
  - Injection of botulinum toxin A into the pyloric sphincter
  - Surgical diversion (esophageojejunal anastomosis)

and colleagues[23] found that the "safest" calculated real distance to the esophageal lumen to avoid LET increase during RF energy delivery at the posterior left atrium and pulmonary vein ostium was 24 mm, with a sensitivity of 90% and a negative predictive value of 98%. The esophagus may also be protected by mechanical displacement of the lower esophagus as it courses close to the posterior left atrial wall. Chugh and colleagues[24] used an endoscope to mechanically displace the esophagus by up to 2.4 cm during AF ablation, while Koruth and colleagues[25] used an endotracheal stylet within a chest tube, achieving an average displacement of 2.8 cm. Unfortunately, 60% of patients had evidence of trauma as a consequence of esophageal deviation in the latter study. Since thermal energy transmission to the esophageal wall is thought to be a major contributor, the esophagus may be protected using a cooling mechanism. Berjano and colleagues[26] reported the theoretical effectiveness of esophageal cooling with a cooled intraesophageal balloon, and a pilot study of 8 patients reported that using an irrigated intraesophageal balloon during ablation on the posterior wall (with concurrent LET monitoring) significantly reduced baseline and maximal esophageal temperature during ablation.[27] However, further studies are needed to determine the feasibility, safety, and efficacy of this strategy in reducing the risk of esophageal injury during ablation procedures.

Another strategy proposed in the literature is to screen for esophageal ulcerations in certain high-risk patients, and to treat them with antireflux medications if esophageal ulceration is discovered. Although prophylactic use of acid suppression therapy with proton-pump inhibitors or H2 antagonists either before or after AF ablation may be considered, the proper time for initiation and duration of therapy have not been clearly established.[28] The various strategies to reduce the risk of periesophageal nerve injury during catheter ablation of AF are summarized in Table 1.

Treatment

The clinical management of this complication is usually conservative. The patient should be placed on complete bowel rest for 2–14 days based on the persistence of clinical symptoms, and then small, low-fat, and low-fiber meals should be gradually introduced. Intravenous erythromycin, which increases gastrointestinal motility, probably by acting as a motilin agonist, may be effective in restarting gastric movement during acute episodes of gastric stasis when oral intake is not tolerated. Several studies have reported improvement in the severity and duration of symptoms from periesophageal vagal nerve injury with the use of intravenous erythromycin.[9,29] Oral mosapride or metoclopramide are also effective in alleviating the symptoms in some patients after they are able to eat and tolerate oral medications. Injection of botulinum toxin A into the pyloric sphincter has been reported to improve the delayed gastric emptying in patients with gastroparesis after AF ablation, but 1 controlled study reported that this improvement was similar to placebo.[30] In the occasional patient with persistence of symptoms with evidence of gastric hypomotility or pyloric spasms beyond 3–6 months, invasive treatment modalities such as injection of botulinum toxin A into the pyloric sphincter or surgical diversion such as an esophageojejunostomy may be needed.[9] The approach to management of patients with periesophageal nerve injury following catheter ablation of AF is summarized in Table 2.

Conclusions

Periesophageal vagal nerve injury is being increasingly identified in patients who have undergone catheter ablation for AF. The clinical presentation is characterized by acute onset of symptoms of gastric hypomotility (nausea, vomiting, abdominal pain and distension) that usually develop within 6–24 hours following the ablation, and may be accompanied by evidence of pyloric spasm as demonstrated by upper GI radiography or endoscopy. Proposed causative mechanisms include thermal injury to the esophageal wall, inflammation, and ischemic injury. Clinical experience is limited to small case series performed in high-volume centers and large multicenter studies investigating the effects of changing procedural settings (such as RF energy output, duration of RF delivery, number and location of ablation sites in particularly vulnerable areas such as the posterior left atrial wall), and preventive strategies (endoscopic displacement of the esophagus, esophageal cooling using irrigated balloons) are lacking. LET monitoring using an esophageal temperature probe may potentially help reduce the risk of periesophageal nerve injury, but currently there are no evidence-based guidelines on how to reduce this risk. Treatment is essentially supportive and consists of complete bowel rest, use of antiemetics and GI prokinetic agents, and acid suppression therapies in patients with known reflux esophagitis. The majority of patients will have complete resolution of symptoms within 1–3 weeks, while a small minority of patients may require additional, invasive treatments for persistent symptoms.

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