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Complications in the Catheter Ablation of Atrial Fibrillation

— Incidence and Management —

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Radiofrequency catheter ablation is widely performed as an effective treatment for recurrent, drug-resistant atrial fibrillation (AF). Recently, various types of ablation strategies, such as extensive encircling pulmonary vein (PV) isolation, linear ablation and complex fractionated electrogram-guided ablation, have been used to achieve a high efficacy for all types of AF. However, several complications (thromboembolic events, PV stenosis and atrio-esophageal fistula etc) with an incidence of 3.9–6%, have been reported. It is important to understand the incidence, prevention and management of complications in order to develop safe ablation strategies. (*Circ J* 2009; **73:** 221 – 226)

Key Words: Atrial fibrillation; Catheter ablation; Complications

Since the discovery of the main role of pulmonary vein (PV) foci in the initiation of atrial fibrillation (AF),[1] radiofrequency (RF) catheter ablation, basically targeting the PVs, has been developed as an effective treatment for recurrent, drug-resistant AF.[2–4] Moreover, various types of ablation strategies, such as extensive circumferential PV isolation including the atrial tissue in the adjacent left atrium (LA),[5–12] linear ablation[13–16] and complex fractionated electrogram-guided ablation,[17–21] have been used to achieve a high efficacy for all types of AF. However, these extensive and complex ablation strategies are associated with a relatively higher incidence of complications,[22,23] compared with ablation of other arrhythmias. Moreover, devastating complications, such as atrio-esophageal fistulas, have been reported,[24,25] caused by extracardiac penetration of the ablative energy, which is 1 of the unsolved safety issues concerning AF ablation.

Incidence of Complications

Complications of AF ablation include vascular access accidents, cardiac perforation/tamponade, thromboembolic events, PV stenosis, extracardiac injury such as to the esophagus, nerve damage, and atypical atrial flutter. In a worldwide survey of 8,745 patients who underwent AF ablation reported by Cappato et al,[22] major complications occurred in 524 patients (6%), including 4 periprocedural deaths (0.05%) from massive cerebral thromboembolism in 2, extrapericardial PV perforation in 1, and an unknown cause in 1 patient. The incidence of cardiac tamponade was 1.2%, and significant PV stenosis >50%, stroke and atypical atrial flutter of new onset occurred in 1.31%, 0.28% and 3.7% of the patients, respectively. A large, prospective, multicenter Italian investigation of ablation-related complications recently reported that in 1,011 AF patients complications occurred in 40 (3.9%): 4 (0.4%) had a stroke, 6 (0.6%) had cardiac tamponade, and 4 (0.4%) had significant PV stenosis >50%.[23] Among our 1,600 patients who underwent extensive encircling isolation of both of the ipsilateral PVs guided by fluoroscopy between 2003 and 2008, overall complications occurred in 23 patients (1.4%): 4 (0.25%) had stroke, 10 (0.6%) had cardiac tamponade, 3 (0.19%) had damage to the peri-esophageal vagal plexus and 6 (0.38%) had transient phrenic nerve (PN) injury; however, there were no cases of significant PV stenosis >50% or atrio-esophageal fistula.

Predictors of complications in AF ablation have been reported by some investigators, such as coronary disease,[23] advanced age,[26,27] and female gender.[27] Spragg et al found that the complication rates were higher during the first 100 cases (9%) than during the subsequent 541 cases (4.3%), indicating the salutary effect of institutional or individual operator experience.[27]

Thromboembolism

The incidence of thromboembolism caused by AF ablation is 0.28–2.8%.[9,13,22,23,28–32] A worldwide survey reported periprocedural deaths because of massive cerebral thromboembolism in 2 patients.[22] Thrombus formation may be caused by activation of the coagulation cascade related to the placement of intravascular catheters and the duration of the ablation procedure.[33] Ren et al reported that a 10% incidence of LA thrombus formation was detected on the sheath or mapping catheter during the AF ablation (with the activated clotting time maintained at >250 s) using intracardiac echocardiography (ICE) imaging monitoring, and that LA thrombus formation was associated with a high prevalence of spontaneous echo contrast.[34] Several studies using ICE have shown that aggressive anticoagulation with an activated coagulation time maintained at >300 s and high-flow perfusion (180 ml/h) of the transseptal sheath significantly

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Table 1 Clinical Characteristics of 14 Patients With Atrioesophageal Fistula: Data From 5 Published Reports

Patient no.	*Age/ Gender*	*Maximum RF power (W)*	*Symptoms*	*Onset (days)*	*Outcome*	*Study reference no.*
1	*36/M*	*100*	*Fever, chest pain, seizure*	*3*	*Survival*	*24*
2	*59/M*	*70*	*Chest pain, fever, seizure*	*21*	*Death*	*24*
3	*72/M*	*60*	*Anorexia, dysphagia, fever, loss of consciousness, seizure*	*10*	*Death*	*25*
4–12	*4/M, 5/F*		*General malaise, fever, chest pain, seizure, gastrointestinal bleeding*	*10–16*	*All Death*	*42*
13	*59/M*		*General malaise, fever, seizure*	*35*	*Death*	*44*
14	*37/M*	*30*	*Fever, seizure, loss of consciousness*	*25*	*Death*	*43*

RF, radiofrequency.

reduced LA thrombus formation and embolic events.[34–38] Therefore, to prevent thromboembolism, careful screening for intracardiac thrombi before the ablation, administration of sufficient heparin, and careful flushing of the long sheaths or withdrawal of the sheaths to the right atrium during the procedure should be performed. This complication also occurs within 2 weeks after AF ablation,[39] suggesting the importance of an aggressive post-procedural anticoagulation regimen. Recently, Wazni et al reported the safety and efficacy of continuous oral anticoagulation throughout the AF ablation, and they concluded that this strategy may be used as an alternative to bridging strategies using enoxaparin or heparin in the peri-procedual period.[40]

Esophagus-Related Complications

Atrio-Esophageal Fistula

Esophageal damage, perforation, and atrio-esophageal fistulas were first described after posterior LA RF ablation procedures were performed during open-heart surgery.[41] The first descriptions of atrial-esophageal fistula formation in 3 cases after percutaneous RF ablation around the PV circumference from an experienced center were published in 2004 (**Table 1**).[24,25] Subsequently, a further 11 patients with atrio-esophageal fistula complications from 3 centers have been reported (**Table 1**).[42–44] The incidence of this complication is rare; 0.05% as reported by Pappone et al,[24] but it is devastating because 13 of the reported 14 patients died.[24,25,42–44]

The clinical features of those patients were similar (**Table 1**).[24,25,42–44] In all patients, nonspecific signs and symptoms, such as dysphagia, anorexia, chest pain or hematemesis, began 3–35 days after the catheter ablation procedure. Subsequently, endocarditis/pericarditis and finally embolism, including that associated with a myocardial infarction and cerebral infarction, occurred. Thoracic computed tomography (CT) enhanced with the use of oral and intravenous contrast medium was the most useful examination method, and very specific findings of an air pocket or fistula tract were observed in the mediastinum; 7 of the 14 patients received an accurate diagnosis by CT before the operation or death.[24,25,42–44] Transthoracic echocardiography was not very useful, because most of them only had nonspecific findings; however, some of them occasionally had very specific findings of a vegetation-like appearance in the LA posterior wall or gas bubbles in the LA appendage. Transesophageal echocardiography and gastroesophageal endoscopy are contraindicated because of the atrial-esophageal fistula.

Only 1 of the 14 patients with an atrio-esophageal fistula survived after emergency cardiac and esophageal surgery.[24,25,42–44] Therefore, rapid diagnosis and surgical intervention are essential for saving the patient's life. If the atrio-esophageal perforation can be detected before it begins forming a fistula, treatment with temporary esophageal stenting may be useful.[45]

To avoid an atrio-esophageal fistula, understanding the relationship between the esophagus and LA is paramount. Lenola et al[46] reported the topographic anatomy of the esophagus and posterior LA by using a 16-row multidetector CT scanner in patients with AF undergoing a percutaneous catheter ablation procedure. They identified that the esophagus and posterior LA were in close contact over a large area with an intervening fat layer of 0.9±0.2 mm, suggesting the potential risk of heat injury to the esophagus. In an anatomical study with examination by morphological dissection and histological sections, Sanchez-Quintana et al revealed the non-uniform thickness of the posterior LA wall and variable fibrofatty layer between the wall and the esophagus, which contains the esophageal arteries and vagus nerve plexus on the anterior surface of the esophagus.[47] These findings indicate that the esophagus is susceptible to heat damage by RF energy applications at the posterior LA.

Some recommendations have been proposed in order to prevent an atrio-esophageal fistula after RF catheter ablation of AF. Understanding the anatomical relationship between the esophagus and LA can be performed by CT angiography after a barium swallow,[48,49] magnetic resonance contrast angiography using swallowed barium sulfate paste and gadolinium diglutamate,[48] or electroanatomical mapping using CARTO™[48] or NavX™.[50] Reducing the RF power when ablating the LA posterior wall, monitoring the esophageal temperature, moving the LA posterior line to the roof, and esophageal cooling with a cooled water-irrigated intraesophageal balloon[51] might reduce that risk. We have reported an original esophageal temperature monitoring method with a deflectable temperature probe during catheter ablation of AF.[52] The deflectable temperature probe is advanced into the esophagus via an endogastric tube, and maneuvered during the ablation procedure in order to be placed as close as possible to the ablation electrode under fluoroscopic guidance (**Fig 1**). The RF energy delivery is applied with 35 W for 40 s at the LA posterior wall; however, when the esophageal temperature reached 42°C, the RF application ceased. After the esophageal temperature decreased to <38°C, RF delivery was restarted at the same site. With this method, none of 1,241 consecutive patients had an atrio-esophageal fistula following catheter ablation.

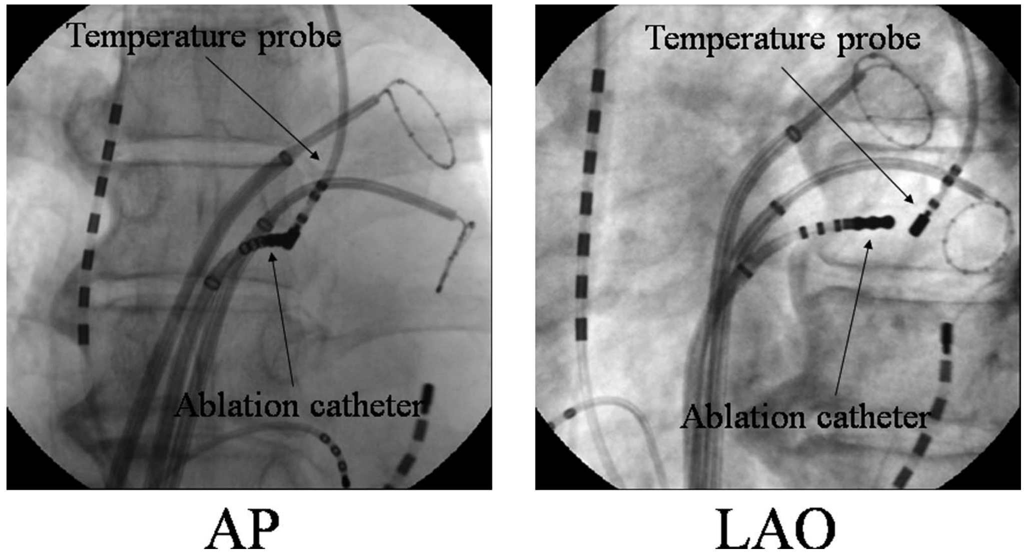

Fig 1. Two circular mapping catheters are placed in the superior and inferior pulmonary veins, respectively. A 14-pole, 2-site mapping catheter is inserted into the coronary sinus. When ablating the left atrial posterior wall, a deflectable esophageal temperature probe via an endogastric tube is maneuvered to a location as close as possible to the ablation catheter tip, which is confirmed in both the anterior-posterior (AP) and left anterior oblique (LAO) views. If the esophageal thermometer indicates a temperature of 42°C, the radiofrequency energy delivery is stopped. (Quoted from Kuwahara *J Cardiovasc Electrophysiol* 2009; **20:** 1–6 with permission.)

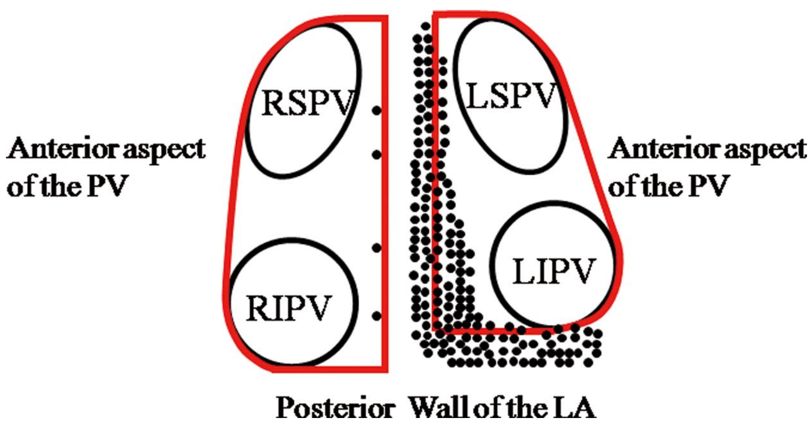

Fig 2. In the esophageal temperature (ET) monitoring group, there were 513 ablation sites where the ET reached 42°C in 100 patients. Each black dot represents 3 ablation sites where ET elevation occurred. Most of the sites are located along the right side of the left pulmonary veins (PVs), especially around the left inferior PV (LIPV), and only 12 sites are near the right PVs. LA, left atrium; LSPV, left superior PV; RIPV, right inferior PV; RSPV, right superior PV. (Quoted from Kuwahara *J Cardiovasc Electrophysiol* 2009; **20:** 1–6 with permission.)

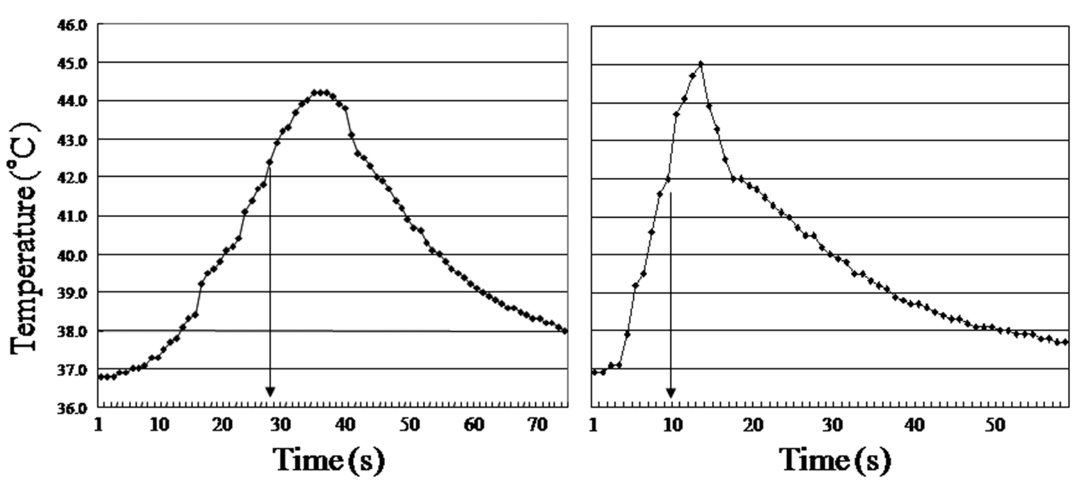

Fig 3. Esophageal temperature (ET) gradually increased to 42°C, 28 s after starting the radiofrequency delivery, with a subsequent overshoot of 2.3°C, and gradually decreased to <38°C (**Left**). In 10% of the patients, a rapid increase in the ET over 42°C occurred within the first 10 s (**Right**). Most of those sites are located near the left inferior pulmonary vein. (Quoted from Kuwahara *J Cardiovasc Electrophysiol* 2009; **20:** 1–6 with permission.)

Peri-Esophageal Nerve Injury

Another esophagus-related complication caused by extracardiac thermal damage is gastric hypomotility and pyloric spasms because of injury to the periesophageal vagal plexus, which is located on the anterior portion of the esophagus. This has been reported from 2 centers, including ours, and the incidence of this complication is 1.1%.[53] The clinical presentation in all patients is very similar, and is characterized by abdominal bloating and discomfort occurring within a few hours to 2 days after RF catheter ablation of AF. Upper gastrointestinal investigations reveal pyloric spasms, gastric hypomotility, and a markedly prolonged gastric half-emptying time. Improvement occurs usually within a few weeks, but an earlier onset of symptoms seems to correlate with significant residual gastric motor dysfunction. To avoid this complication, the same method as described for avoiding an atrio-esophageal fistula should be considered. In our report,[52] we had 3 cases of periesophageal nerve injury in the first consecutive 152 patients who underwent AF ablation without esophageal temperature monitoring, but none of patients had this complication in the subsequent 207 undergoing AF ablation with continuous esophageal temperature monitoring by deflectable temperature probe. In that study, most of the sites where the esophageal temperature increased to 42°C were located at the posterior LA near the left PVs (**Fig 2**) and 10% of the patients had a rapid elevation in the esophageal temperature >42°C within the first 10 s after start of the RF delivery (**Fig 3**). After that report, none of the 1,241 patients undergoing AF ablation with esophageal temperature monitoring in our center had that complication. These findings suggest the importance of careful esophageal temperature monitoring during AF ablation in order to avoid esophagus-related complications.

PV Stenosis

PV stenosis is a well-known complication of AF ablation, with the incidence having been reported to range from 3% to 42%, depending on the ablative technique used and the method of assessment.[54–60] This had decreased to <1% in a recent study,[23] because of changing the ablation site from inside the PVs to outside the orifice of the PVs, reducing the target temperature and amount of RF energy delivery during the ablation, using a 3-dimensional mapping system or intracardiac echocardiography to guide the catheter placement, and the "learning curve" of increased operator experience. The clinical symptoms of PV stenosis vary from asymptomatic to highly symptomatic with persistent cough, exertional dyspnea, chest pain, hemoptysis and recurrent pulmonary infections.[59–64] Symptom severity was related not only to the degree of stenosis, but also to the number of PVs with stenosis.[59,60] Because of the nonspecific symptoms, patients may undergo misleading diagnostic and therapeutic procedures, and definitive treatment may be delayed. Moreover, mild PV narrowing 3 months after the ablation does not preclude the future development of severe PV stenosis.[60] Therefore, repeat follow-up imaging studies, such as MRI or CT, to detect any PV stenosis should be performed after catheter ablation of AF.

In patients with symptomatic and severe PV stenosis, interventional procedures, such as balloon angioplasty and stent implantation, have been performed and resulted in significant dilation of the affected PVs and symptomatic improvement, but the incidence of restenosis is high and ranges from 33% to 67%,[59,60,63–65] requiring a repeat procedure.

PN Injury

The right PN runs along the lateral and posterolateral walls of the right atrium. An anatomical study investigating 19 human cadavers revealed the close proximity of the right PN to both the superior vena cava (minimum 0.3±0.5 mm) and the right superior PV (minimum 2.1±0.4 mm).[66] The anterior wall of the right superior PV was <2 mm from the right PN in 32% of the specimens. The left PN passed over the obtuse cardiac margin and the left obtuse marginal vein and artery in 79% of the specimens. In the remaining specimens, its course was anterosuperior, passing over the main stem of the left coronary artery or the anterior descending artery and great cardiac vein.[66]

A multicenter study reported that PN injury rarely occurred (18/3,755 patients, 0.48%) after AF catheter ablation.[67] Ablation of the right superior PV (n=12), superior vena cava (n=3), and LA appendage (n=2) were associated with PN injury. Immediate symptoms were dyspnea, cough, hiccups, and/or sudden diaphragmatic elevation in 9, and in the remaining subjects the diagnosis was made after ablation because of dyspnea (n=7) or during routine radiographic evaluations (n=2). Four patients were asymptomatic. Complete (66%) or partial (17%) recovery occurred in the majority. Bai et al reported 17 patients with PN injury: 13 after AF catheter ablation, 3 after sinus node modification and 1 after epicardial ventricular tachycardia ablation, with a prevalence of approximately 0.1%.[68] Ablation was performed with different energy sources, including RF (n=13), cryothermal (n=1), ultrasound (n=2) and laser (n=1) energy. The patients' symptoms varied broadly from being asymptomatic to dyspnea, and even to respiratory insufficiency that required temporary mechanical ventilation support. In 2 patients, the symptoms resolved immediately after the procedure and in another 15 patients they resolved within a mean time of 8.3±6.6 months.

High-output pacing is recommended for identifying the location of the PN before ablation at or near the right superior PV, superior vena cava or proximal LA appendage roof.[67,68] In the case of diaphragmatic contraction, ablation should be avoided.

Conclusion

With the recent development of strategies for catheter ablation of AF, therapeutic efficacy has been increasing, even for long-lasting AF. However, several complications have occurred in a small percentage of the patients undergoing AF ablation. Therefore, possible preventive measures and further refinement of the technique and equipment should be undertaken to increase the safety of the AF ablation procedure.

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