EDITORIAL COMMENTARY

Esophagoscopy following cryoballoon pulmonary vein ablation: Can the promise be met?

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Use of cryoenergy for catheter ablation of atrial fibrillation (AF) has increased tremendously since the introduction of the Arctic Front cryoballoon system into clinical practice outside the United States. In Europe alone, approximately 70 sites are now using this system. Approximately 5,000 cryoballoon ablations have been performed worldwide to date. For ablation centers already performing pulmonary vein (PV) ablation on a routine basis, cryoballoon ablation has a relatively steep learning curve, after which it is a reasonably short and straightforward procedure. The left-sided PVs are most suitable. Ablation of the right superior PV can be limited by phrenic nerve approximation even when the big balloon size is used. Fortunately, almost all phrenic nerve palsies reported in the literature to date recovered in subsequent months. Cryoballoon ablation of the right inferior PV often is challenging due to insufficient stability at the PV ostium and often requires technical tricks such as the "hockey stick," "pull down," or "big loop" technique as described by Chun et al.[1]

One promise of cryoballoon ablation is the significantly reduced or even abolished risk of PV stenosis and atrio-esophageal fistula formation, which is the most feared subacute or chronic complication of AF ablation.

Recent studies report positive data with regard to PV stenosis. The largest series of cryoballoon ablations was reported by Neumann et al.[2] In their study, none of the 346 patients exhibited PV stenosis or >30% narrowing on follow-up magnetic resonance imaging (MRI) or computed tomographic (CT) scan. The second largest series reported by Van Belle et al[3] also found no PV stenosis or >25% narrowing in 141 patients examined by CT scan before and 3 months after cryoballoon PV ablation. Smaller series without systematic MRI or CT scan monitoring also reported no documentation or suspicion of PV stenosis during long-term follow-up.[1,4]

What about the promise of avoiding esophageal injury when using cryoballoon ablation? Atrio-esophageal fistula, which today is the most feared complication of AF ablation, was first described following intraoperative radiofrequency (RF) ablation for AF[5] and later following percutaneous catheter ablation using either RF[6,7] or focused ultrasound energy.[8] In an anonymous survey, the incidence of atrio-esophageal fistula was approximately 1:3,400 (0.03%) cases.[9] It is a rather eerie complication because it is somewhat unpredictable and presents with initially nonspecific symptoms such as malaise, fever of unknown origin, and leukocytosis after only about 2 weeks.[7] Septic shock, cardiovascular collapse, and embolic strokes as a consequence of air embolism or endocarditis usually follow.

Whether use of preprocedural and intraprocedural esophageal imaging as well as postprocedural proton pump inhibitors can prevent atrio-esophageal fistula is unclear. Almost all patients reported to date died of this complication. Early surgical intervention seems to improve survival.[6] Therefore, physicians must be very aware of this complication in patients who present with these rather unspecific symptoms following left atrial catheter ablation for AF.[7]

No instances of atrio-esophageal fistula formation after cryoballoon ablation have yet been reported. However, bear in mind that the number of patients treated with cryoballoons worldwide is approximately 5,000, and one estimate of atrio-esophageal fistula incidence after RF ablation is only 1:3,400 cases.[9] Ripley et al[10] reported an animal study comparing the influence of direct RF versus direct cryoenergy application to the outside of the esophagus. In their study, 16 calves received a total of 41 RF as well as 44 cryoenergy applications after operative exposure of the cervical esophagus. Even though lesion dimensions were similar between the two energy sources over the course of 14 days, the incidence of transmural esophageal ulceration was much higher after RF ablation (22% sites) that after cryoablation (0% sites). Therefore, *in vivo* study in animals provides some evidence that cryoenergy protects the structural integrity of the esophagus better than RF energy does.

An obviously suitable way to monitor clinically for esophageal lesions after catheter ablation is direct visualization by endoscopy. In a study of 28 patients by Schmidt et al,[11] ulceration of the anterior esophageal wall was seen in 36% of patients treated with an 8-mm-tip catheter and in none of the patients treated with an open irrigated 3.5-mm catheter. Erythema was documented in 21% and 36% of the

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two patient groups. Another study of 177 patients using open irrigated catheters at low-power settings (25 or 15 W at the posterior wall) reported a 2% incidence of esophageal ulcers. Statistically significant risk factors were persistent AF, power setting of 25 W rather than 15 W, use of a nasogastric tube, and additional left atrial ablation lines.[12]

Ahmed et al[13] are credited with reporting the first detailed information on the esophageal effects of cryoablation. In this issue of *Heart Rhythm,* Ahmed et al report luminal esophageal temperature measurements in 67 patients undergoing cryoballoon ablation as well as in seven patients undergoing focal cryoablation for completion of RF lesion sets close to the esophagus and results of postprocedural endoscopy in 35 cryoballoon patients and all focally ablated patients. They found that almost all patients exhibited temperature drops >1°C, which could lead to esophageal temperatures as low as 0°C, as in the case of the right inferior PV in one patient. Even more important, endoscopy showed esophageal ulcerations in 17% of patients after cryoballoon ablation and in none after focal cryoablation. One ulceration required several weeks for resolution. Of note, the incidence of ulcerations after cryoballoon ablation is much higher than that reported for irrigated-tip ablation (0% in one study,[11] 2% in another study[12]). Thus, one must assume that cryoballoon is at least as harmful with regard to esophageal injury as is irrigated-tip ablation, and no green light can be given with respect to the risk of atrio-esophageal fistula. Therefore, it appears prudent to recommend proton pump inhibitor prophylaxis not only in patients undergoing RF but also in those undergoing cryoballoon ablation for treatment of AF, although no randomized studies support this practice.

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