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Strategies to Minimize the Risk of Esophageal Injury During Catheter Ablation for Atrial Fibrillation

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Abstract and Introduction

Abstract

Esophageal injury is a rare but serious complication of catheter ablation for atrial fibrillation using radiofrequency energy. Recent studies have begun to identify variables that may determine heat transfer to and thermal injury of the esophagus. There is significant variability in the relationship between the esophagus and left atrium among individuals. New imaging techniques can facilitate assessment of esophagus position relative to intended ablation targets. Strategies to minimize the risk of esophageal injury include avoidance of ablation near the esophagus, titration of RF energy delivery at the posterior left atrial endocardium, and the use of alternative ablation methods.

Introduction

Atrioesophageal fistula was first reported as a fatal complication of endocardial surgical radiofrequency (RF) ablation for atrial fibrillation (AF),[1] and has since been reported after percutaneous endocardial RF catheter ablation for AF (catheter ablation).[2,3] The incidence of atrioesophageal fistula after catheter ablation is estimated to be between 0.03%[4] and 0.5%[5]; however, underreporting is likely, and the true incidence is unknown. A recent report of 28 patients undergoing esophagogastroscopy 24 hours after catheter ablation revealed that 47% of patients had esophageal mucosal changes consistent with thermal injury and 18% demonstrated necrotic or ulcer-like changes.[6] In this study, left atrial RF lesions were delivered without regard to the location of the esophagus. Thus, there is clear potential to produce transmural esophageal injury during catheter ablation for AF when employing a lesion set targeting the posterior left atrial wall and pulmonary vein (PV) antra using contemporary large-tip or irrigated-tip catheter ablation systems when endocardial target sites are in close proximity to the esophagus.

Atrioesophageal fistula after catheter ablation is thought to occur due to conductive heat transfer to the esophagus[7,8] that causes transmural tissue necrosis,[9] mediastinitis, and a fistulous connection between the esophageal lumen and the left atrial blood pool. This can lead to sepsis and stroke.[10] Other mechanisms of esophageal injury resulting from injury to the esophageal blood supply, or to the nerves and nerve plexi on the surface of the esophagus, have not been excluded. Though incompletely described, factors that likely determine heat transfer to the esophagus during catheter ablation include the magnitude and duration of local tissue heating, which is related to the total ablation energy delivered to cardiac tissue at an ablation site near the esophagus.[11] Catheter tip size, contact pressure, and catheter orientation are important variables that determine what percentage of applied RF energy is actually delivered to cardiac tissue. Heat transfer to the esophagus is also dependent on atrial tissue thickness,[11] and the thickness and character of intervening connective tissue including adipose tissue between the heart and esophagus,[8,11,12] which together determine the minimum possible distance between an ablation site at the posterior left atrial endocardium and the esophagus and the rates of heat conduction through tissue to the esophagus. Cadeveric and computed tomography (CT) studies of humans suggest that the connective tissue layer between the posterior LA wall and esophagus varies significantly in thickness between individuals, and also at different rostral-caudal levels of the esophagus-atrial contact region in the same patient.[13-15] Further, the thickness of the PV wall and PV antrum has been described to be as little as 2-3 mm, much thinner than atrial myocardium at the posterior or anterior free walls.[16] Together, these observations suggest that heat transfer to the esophagus may be enhanced during RF ablation near the vein ostia if the esophagus is located adjacent to these regions, especially when coupling between ablation catheter and tissue is optimal for RF energy transfer, and when intervening tissue between heart and esophagus is minimal or absent.[8] Indeed, an initial report of atrioesophageal fistulae after catheter ablation described fistula formation in the region of the posterior left PV antrum near the left superior PV os.[3] Other factors could influence progression of esophageal injury to fistulae after RF ablation, such as inflammation or acid reflux; however, the respective roles of these or other variables are as yet unknown. Some centers routinely use proton pump inhibitors or other antacid or antireflux therapies such as sucralfate after catheter ablation; however, evidence is lacking regarding whether these therapies prevent progression of thermal esophageal injury to fistula formation.

Localizing the Esophagus

Variable Course of the Esophagus

Any strategy to limit or avoid RF energy delivery in close proximity to the esophagus requires that the clinician have accurate information about exactly where the esophagus is located relative to intended sites of ablation. Between patients, the course of the esophagus is variable. We have observed the esophagus to be located rightward of the spine, compressed between the spine and left atrium, behind the atrium in the groove bounded by the aorta and the spine, compressed between the aorta and the left atrium, and leftward of the aorta. Furthermore, the esophagus position relative to the left atrium can be adjacent to the right PV antra and ostia, the posterior left atrium between the right and left PVs, or the left PV antra and ostia.[13,15,17,18] The esophagus is often compressed between the left atrium and surrounding structures, causing the esophagus to take a flattened and ovoid shape with a broad contact patch abutting the atrium, and we have observed cases where this contact patch spans most of the posterior left atrial wall,[17] consistent with a previous CT study that reported an average contact patch width of 1.9 cm.[19] In the individual patient, the esophagus can be adjacent to or overlay the right or left PV antra, or can course diagonally to overlay both the left and right PV antra.[15] Figure 1 depicts some clinical examples of the variable relationship between the esophagus and left atrium. Thus, the esophagus could be at risk for thermal injury during RF ablation from virtually anywhere at the posterior left atrial endocardium or within the PV near the os, depending on the individual's anatomy.

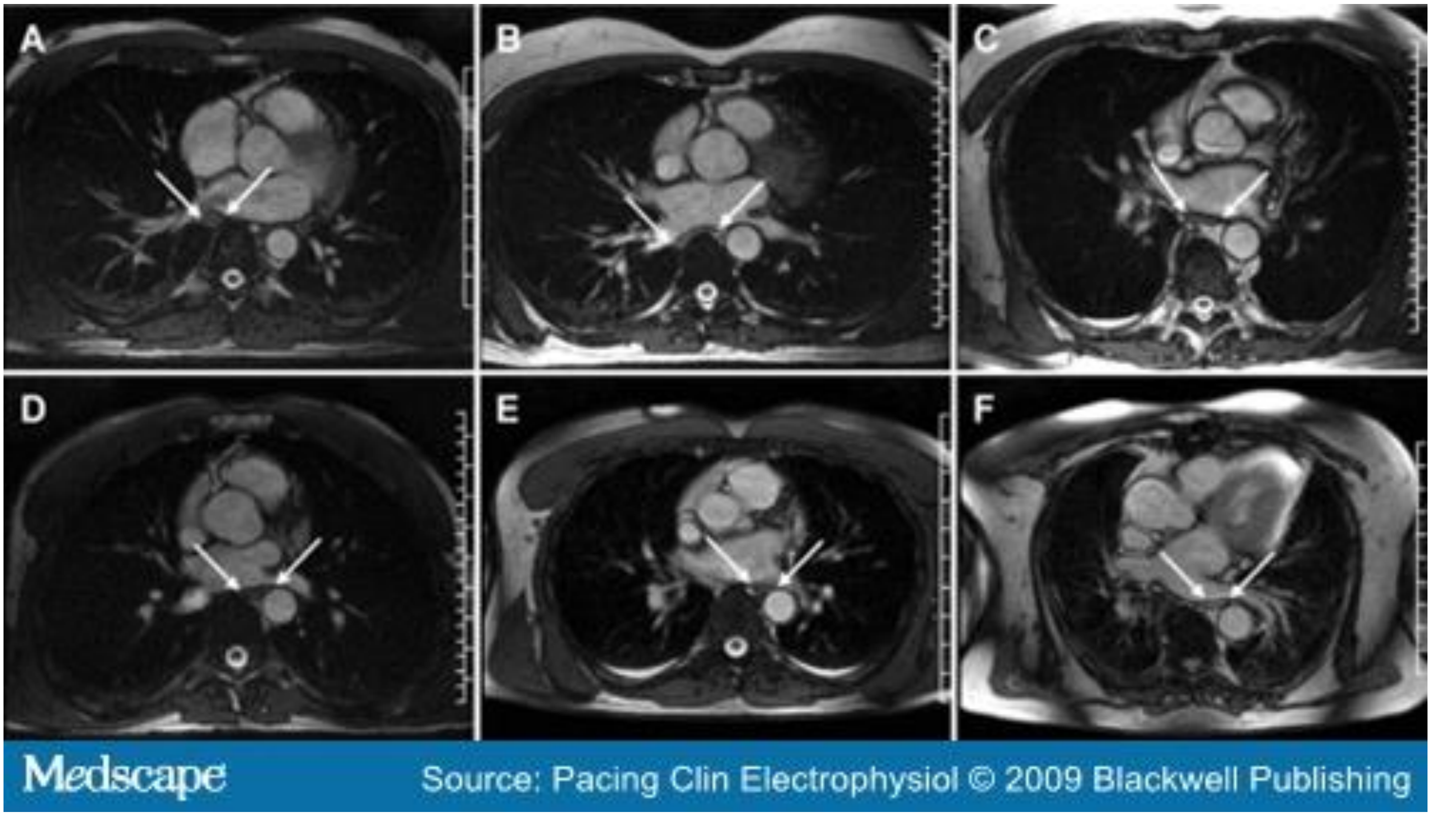

Figure 1.

Examples of the variable anatomic relationship between the esophagus and left atrium. Panels A through F are transverse bright blood MRI images from different patients. The esophagus appears immediately posterior to the left atrium in each panel. The arrows indicate the span of the atrium-esophagus contact area. Panel A, the esophagus is rightward of the spine adjacent to the right PV antrum; panel B, the esophagus is compressed between the spine and atrium spanning the region from the right PV antrum and os to the posterior wall near the left PV antrum; panel C, the esophagus spans the entire posterior wall of the atrium; panel D, the esophagus is adjacent to the left PV antrum and os; panel E, the esophagus is partially compressed by the descending aorta and is adjacent to the left PV os; panel F, the esophagus is compressed by the aorta and spans a broad region adjacent to the left PV, the PV os, and the PV antrum.

Movement of the Esophagus

In addition to having a variable course, it has been reported that the esophagus position relative to the left atrium can be dynamic. Peristalsis and deglutition in the awake but sedated patient,[20] or changes in patient position from the left to the right recumbent position,[21] have been reported to cause the esophagus to shift laterally up to several centimeters in relationship to the atrium. However, other evidence suggests the esophagus may have a consistent "resting" position. For example, stability in the location of the esophagus during a second ablation procedure, as compared to that during the first, has been reported.[22] Further, when esophageal position defined by preprocedure CT scan with a barium swallow was compared with the intraprocedure position defined using an electroanatomic mapping system, the esophagus position corresponded to that identified with the CT scan done on another day, and did not change during the procedure.[23] Likewise, another group reported stable intraprocedure esophagus position using real-time monitoring with an electroanatomic mapping system in patients undergoing catheter ablation while under general anesthesia.[24] It is unclear what role, if any, instillation of barium paste into the esophagus has in stimulating or accentuating esophageal movement, whether general anesthesia reduces the likelihood that the esophagus will move during catheter ablation, and what other factors may favor significant lateral excursion of the esophagus during catheter ablation. Our experience is that most patients demonstrate a stable and fixed esophagus position during the catheter ablation procedure when general anesthesia is employed, and that the esophagus position observed during the procedure corresponds closely with that defined by pre-procedure magnetic resonance imaging (MRI) or CT done days to weeks beforehand. The esophagus position revealed by follow-up imaging done months later is similarly stable in most patients. Nonetheless, the potential for significant lateral displacement of the esophagus remains, recommending the use of "real-time" imaging during catheter ablation to confirm the location of the esophagus during ablative energy delivery.

Methods to Localize the Esophagus Before RF Energy Delivery

Specific imaging methods to define the esophagus-atrium relationship can be grouped into real-time methods that yield images during RF-energy delivery, and non-real-time methods that yield static images generated sometime before RF energy delivery. The later category includes the following: (1) preprocedure CT[25] or MRI[26]; (2) importation of registered CT-generated shells of left atrium *and* esophagus (Figure 2); (3) tagging the esophagus location at the start of the procedure on an electroanatomic map generated with Carto™ (Biosense Webster, Diamond Bar, CA, USA) or NavX™ (St. Jude Medical, Sylmar, CA, USA) using fluoroscopic visualization of the esophageal lumen containing barium or some other luminal marker as a guide (e.g., NG tube, esophageal temperature probe, or catheter)[17,24]; or (4) using an electroanatomic mapping system to generate a static representation of the esophagus. The last method could involve using a luminal catheter recognized by the NavX™[24] or Carto™ systems, or using intracardiac ultrasound to render a static 3-D representation of the esophagus together with a rendering of the left atrium[27,28] (Carto SoundStar™; see Figure 2). The Carto SoundStar™ systems renders 3-D structures like the esophagus and left atrium by merging contours of these structures, as annotated on each of multiple separate 2-D intracardiac echocardiography (ICE) imaging planes to produce the 3-D image. Real-time imaging features of the Carto SoundStar™ system are discussed below.

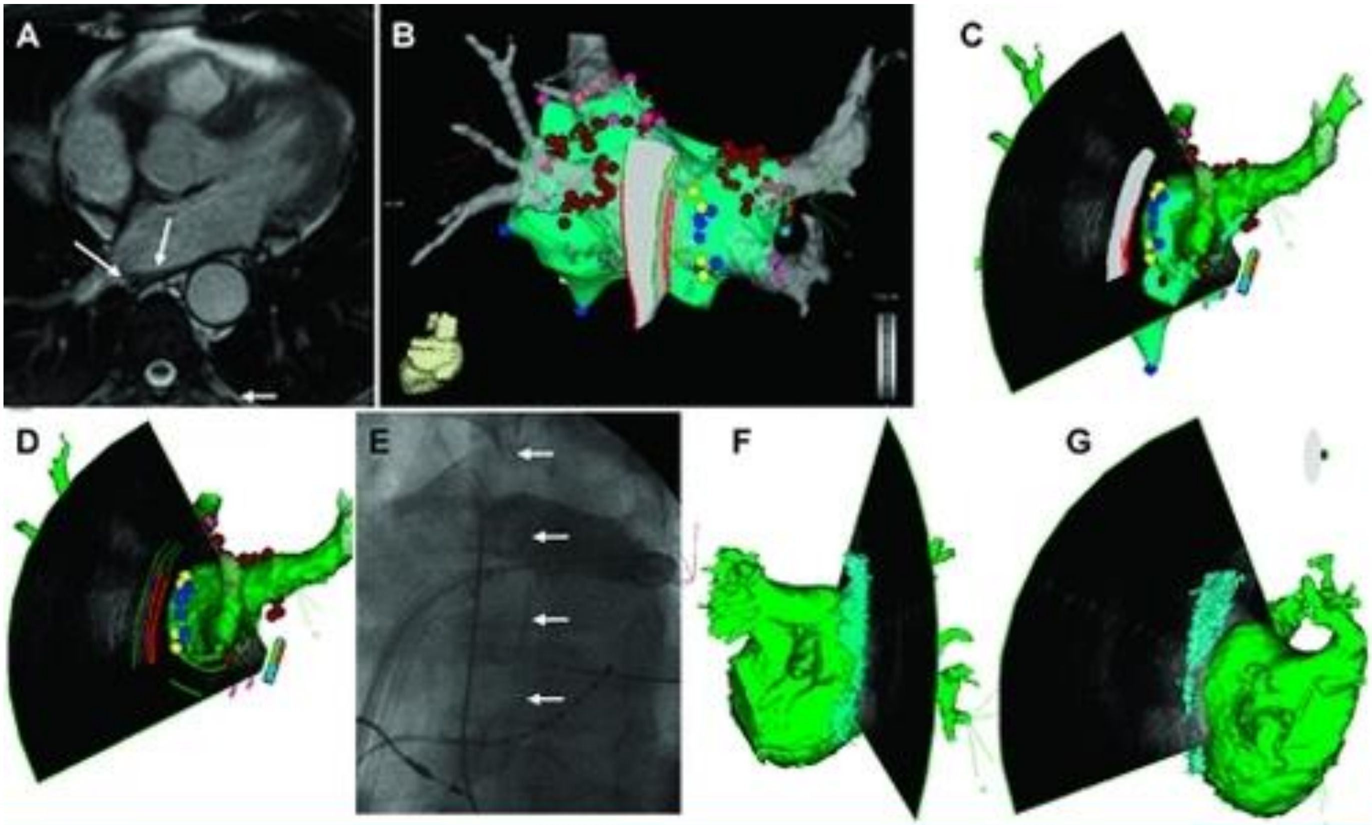

Figure 2.

Different imaging modalities reveal the anatomic relationship between the esophagus and left atrium. Panels A-D are from one patient with the esophagus adjacent to the right PV antrum and os, and show (A) a transverse MRI image, (B) a rendering of the left atrium and esophagus generated with intracardiac ultrasound (Carto-Sound™) together with a segmented MRI scan of the left atrium registered to the ICE-rendered structures, (C) a still frame of a real-time 2-D ICE image superimposed on the rendered structures and registered MRI shell, (D) the same as C with removal of the ICE-rendered esophagus to allow confirmation in real time of the esophagus position and registration of the MRI shell. Note that the 2-D ICE image is correctly displayed relative to the registered and rendered images due to location sensors in the ICE probe. Yellow tags represent biplane fluoroscopic determination of the location of the esophageal luminal probe, blue tags represent cryothermy ablation sites, and red tags represent RF ablation sites. Panels E through G are from another patient with the esophagus adjacent to the left PV antrum and os as depicted in panel E. In panel E, white arrows indicate the course of the luminal esophageal probe in the left anterior oblique view (43°), and the left superior PV is opacified with hand injection of Isovue via a pigtail catheter in the vein. Two transseptal sheaths, a permanent pacing lead, and the coronary sinus catheter are also visible. Panel F shows a posterior view with leftward angulation of the segmented left atrial shell and esophagus from a prior CT scan, registered to the ICE rendering of the left atrium (hidden in this example). The esophagus shell is incomplete due to lack of esophageal contrast during CT imaging. Panel G is the same except for rightward angulation. Real-time confirmation of the registration and of the position of the esophagus is depicted with the overlying 2-D ICE image.

Of these non-real-time imaging methods, "bright blood" axial MRI images or CT can be useful to depict the breadth and location of the esophagus, including information about the extent of the esophagus-atrium contact patch. For example, some patients have a very broad esophagus-atrial contract patch, which, if identified, would recommend caution in relying solely on a discreet luminal esophageal marker for designation of regions of the posterior left atrium (LA) wall that are adjacent to the esophagus (Figure 1 and Figure 3). Whereas near real-time intraprocedural tagging or rendering of the esophagus on an electroanatomic map can confirm findings from CT or MRI and provide complimentary information about potential proximity of intended ablation target sites to esophageal tissue, these methods do not provide reliable information about the extent of the esophagus-atrial contact region or thicknesses of intervening tissue between catheter tip and esophagus at the moments of ablation. Furthermore, none of these methods can detect motion of the esophagus that might occur after image acquisition.

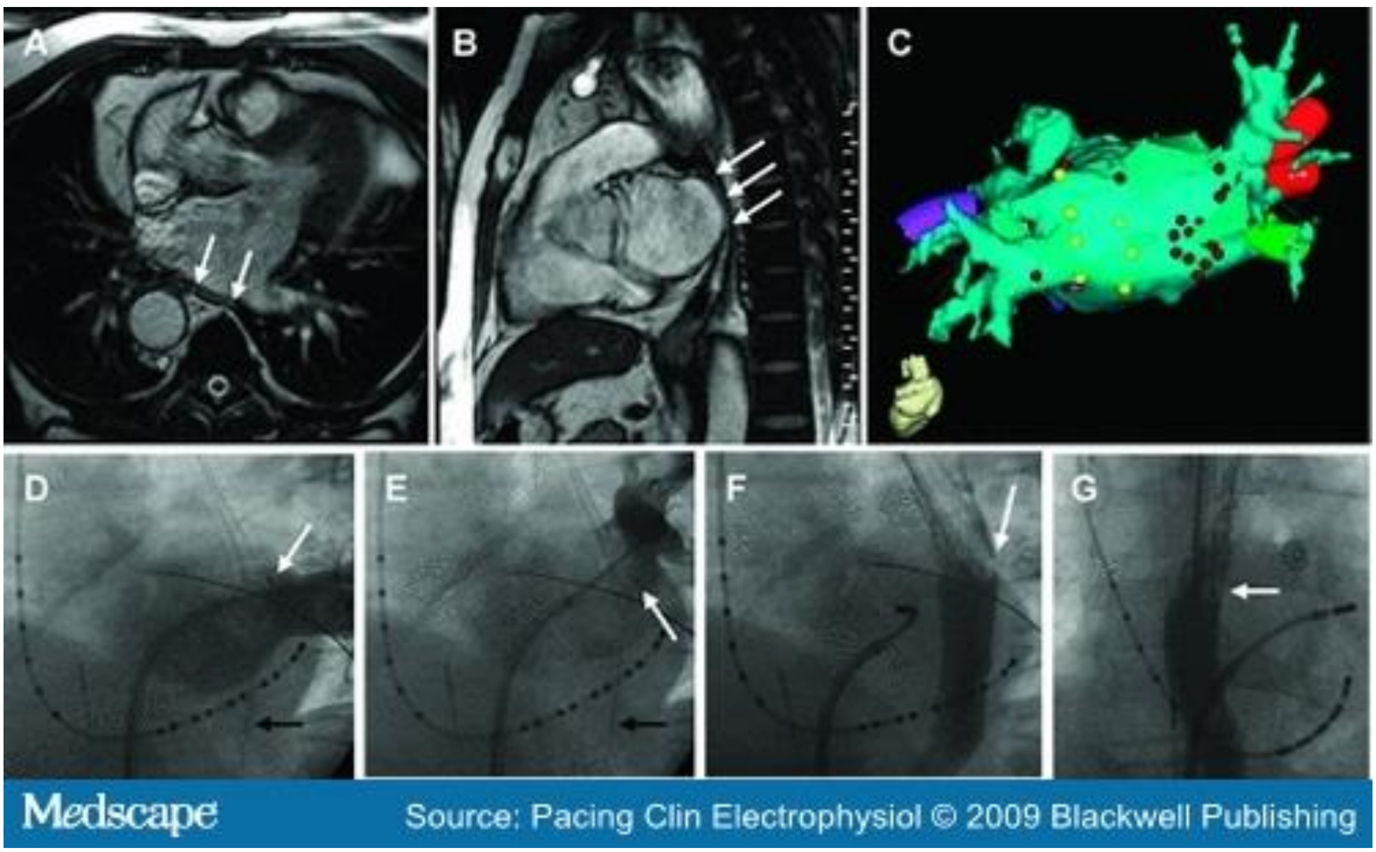

Figure 3.

Complimentary imaging of the esophagus in a single patient. Panels A and B show transverse and sagital "bright blood" MRI images. The esophagus is compressed and spans a broad region adjacent to the left PV antrum. Panel C shows an electroanatomic (E-A) map with a superimposed segmentation of the left atrium from MRI, registered to the map. The left and rightward margins of the esophagus are tagged (yellow). Panels D and E show venograms of the left inferior and left superior PVs in the left anterior oblique projection. The tip of a luminal esophageal probe is indicated with the white arrow, and a nasogastic tube advanced to the stomach is indicated with the black arrow. Panels F (left anterior oblique) and G (right anterior oblique) show the orientation of the temperature probe tip within the broad esophageal lumen opacified with Gastrografin introduced via a nasogastric tube withdrawn to the mid esophagus. The probe tip is seen to be displaced to the leftward margin, and is anteriorly located immediately adjacent to the left PV antrum. Without opacification of the esophageal lumen, the rightward extent of the esophagus, spanning more than 1 cm from the probe tip position, would not be appreciated.

Methods to Localize the Esophagus During RF Energy Delivery

Real-time visualization of the esophageal position can be achieved with repetitive fluoroscopic visualization of the esophageal lumen containing barium or another luminal marker during the procedure,[17,29,30] with real-time display of a multi-polar catheter in the esophagus lumen recognized by the NavX system,[24] or with real-time intracardiac ultrasound from the right[26,31] or LA.[32] Ultrasound is the only real-time imaging modality that allows visualization of the extent or thickness of the esophagus wall, especially when imaging is done from the left atrium.[33] Barium paste can allow visualization of the true width of the lumen, but information about esophageal wall thickness is difficult to infer as only the lumen is visualized. Likewise, a luminal marker like a temperature probe cannot provide information about esophageal wall thickness. In addition, a luminal probe or catheter can provide misleading information about the medial to lateral extent of the esophagus-atrium contact patch because it may be positioned eccentrically to one side of a broad and flattened lumen whereby ablation-directed 1-2 cm more medially or laterally from the probe based on fluoroscopy may in fact be immediately adjacent to the opposite margin of the esophagus[17] (see Figure 3). Real-time imaging can also confirm information about the esophagus provided by preprocedure imaging and by the near real-time imaging techniques discussed above (see Figure 2 and Figure 3). Thus, intracardiac ultrasound can accurately reveal the location and extent of the esophagus and is uniquely well suited to assess true proximity of actual ablation sites to esophageal tissue.[26] Without use of real-time intracardiac ultrasound with good visualization of the esophagus, it may be best to assume that the "danger zone" for RF-induced esophageal injury extends 1-2 cm to either side of a discreet marker like a luminal temperature probe.

The most significant limitation of intracardiac ultrasound relates to the technical difficulty of maintaining orientation of the 2-D imaging plane to visualize the catheter tip and/or esophagus during RF pulses owing to the limited view of a 2-D ICE imaging plane in combination with movement of the imaging plane relative to the heart during the cardiac cycle. In addition, "shadowing" is often seen to extend from the catheter tip, making it difficult to assess the exact tip location, especially when the catheter shaft is imaged and oriented parallel to the radiating ultrasound beam. Intracardiac ultrasound imaging from the left atrium may be useful to overcome some of these limitations and can facilitate imaging of both the esophagus and ablation catheter tip during lesion delivery.[33]

Aside from rendering a static 3-D representation of the esophagus, the Carto SoundStar™ system has important real-time imaging features to help address some of these limitations of 2-D ICE imaging during left atrial catheter ablation. First, the system annotates in real time the exact location of the ablation catheter tip on the 2-D ICE image to facilitate orientation of the 2-D imaging plane to allow accurate visualization of the catheter tip. Second, the 2-D imaging plane is displayed as a "fan-like" image, superimposed on the 3-D rendering of the esophagus and left atrium in real time to facilitate optimal orientation of the ICE imaging plane relative to structures of interest such as the PV antra or esophagus (Figure 2).

Real-time 3D ultrasound is a new technology that has potential to enhance catheter ablation for AF by reducing the difficulty of maintaining structures of interest such as the ablation catheter tip and Ligament of Marshall within the ultrasound imaging field during catheter ablation. Whereas this technique has been employed to guide catheter ablation for AF,[34] the potential utility of real-time 3-D ultrasound imaging to define the course of the esophagus during catheter ablation has not been reported.

Specific Methods to Minimize Esophageal Injury During Ablation

Fundamentally, there are three techniques that can be employed to minimize the likelihood of esophageal injury during RF ablation at the posterior left atrium: (1) avoidance of any RF ablation whatsoever when adjacent to the esophagus, (2) titration of RF energy delivery or other techniques to limit or reduce heat transfer to and thermal injury of the esophagus when ablation is needed at the posterior left atrium near the esophagus, and (3) use of methods other than RF energy that may have a lesser tendency to produce esophageal injury leading to fistula formation when targeting tissue near the esophagus. Each will be considered in turn.

Avoidance -- Moving the Ablation Lines

Kottkamp et al. reported a strategy of altering the lesion set for circumferential isolation of the PV and PV antral regions in order to avoid the esophagus.[35] In this report, ablation lines were moved away from the PV antral region in some and closer to the PV os in others to avoid delivery of RF pulses very near the esophagus. This can be an effective approach in some instances depending on the specific location and breadth of the esophagus-atrium contact region. Two other groups have reported a lesion set surrounding all PVs to minimize the need for ablation at the posterior left atrial wall, thus minimizing RF energy delivery at sites potentially adjacent to the esophagus.[36,37] A potential pitfall of these approaches is that expansion of the circumferential ablation lines away from the PV antrum increases the technical difficulty to achieve acute and/or persistent electrical isolation of the PV and PV antrum due to the need to ablate regions with thicker myocardium[16] and to create uninterrupted ablation lines that span a greater total distance. Our experience is consistent with increased difficulty in achieving PV isolation when the ablation line is moved farther away from the PV ostium.

Avoidance -- Moving the Esophagus

Another approach to avoid delivery of RF pulses in close proximity to the esophagus is to move the esophagus out of the way with a luminal transesophageal echo probe.[38] When successfully implemented, ablation sites, otherwise presenting risk, might be safely targeted with RF energy. However, there is always a potential risk associated with placement of a large luminal device into the esophagus during RF energy delivery at the posterior left atrium, whereby there could be unintentional displacement of the esophagus or passive application of pressure toward the left atrium ablation sites that in turn reduces the distance between the ablation catheter tip and esophagus and enhances heat transfer during ablation.[8] The ability of an esophageal luminal device to displace the esophagus toward the atrium and consequently enhance heat transfer to and injury of the esophagus has been reported in animal models when an expandable esophageal balloon device was present *in situ* during endocardial RF energy delivery.[39,40] Another potential limitation of this approach is that deflection of a luminal device may simply deform portions of the esophagus wall without necessarily moving the portion of the esophagus immediately adjacent to the left atrial ablation sites.

RF Energy Titration -- Use of Luminal Esophageal Temperature Monitoring

RF energy titration is likely the most common approach to minimize risk of esophageal injury during catheter ablation for AF. However, the challenge of this approach is in knowing how much delivered RF energy is "safe." Ideally, some real-time method to assess heat transfer to or lesion formation within the esophagus could guide RF energy titration during ablation; however, no method has yet been convincingly demonstrated to achieve this. Observational studies employing real-time luminal esophageal temperature measurements during left atrial catheter ablation reveal that esophageal heating can indeed be observed during some RF energy applications.[17,29,30] Preliminary evidence[41] suggests that rapid esophageal heating (e.g., rates >0.05-0.1°C per second) may herald instances of efficient heat transfer to the esophagus due to some combination of optimal catheter contact for energy transfer, minimal or absent intervening connective tissue,[12] good contact of the luminal temperature probe with the anterior luminal surface of the esophagus, or other factors. Thus, rapid elevation of luminal temperature is likely specific for mural esophageal heating. Early use of luminal temperature monitoring also suggests an additional factor relevant to energy titration and assessment of esophageal heating, namely that the esophagus cools slowly[41] and repeated RF energy applications can result in "temperature stacking," whereby a greater degree of mural esophageal heating is achieved with subsequent RF pulses (Figure 4). Further studies are required to characterize the relationship between temperatures reported with a luminal probe and mural temperature of the esophagus.

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(Enlarge Image)

Figure 4.

Time course of esophageal heating measured with a luminal probe during RF ablation at the posterior left superior PV antrum in proximity to the probe. The upper panel depicts an RF energy application of 20 W mean power for 23 seconds, mean temperature 48°C, maximum 52°C using an 8-mm-tip catheter. The middle panel depicts esophageal heating with brief latency to onset, rapid temperature rise (see text), overshoot, and delayed cooling. In this example, more than 140 seconds was required for temperature to return to baseline. The bottom panel shows "temperature stacking" when a second RF pulse was initiated (third arrow) about 45 seconds after the first RF pulse was terminated (second arrow) in another patient.

Limitations of Luminal Esophageal Temperature Monitoring

The sensitivity of luminal temperature monitoring to recognize all instances of esophageal heating and to accurately report the degree of significant heating is questionable. Initial clinical studies suggested that there is a poor correlation between total energy delivered during an RF pulse and elevation of luminal esophageal temperature,[30,41] implying that factors other than total energy delivered determine esophageal heating or that a luminal probe does not report true mural esophageal heating with fidelity. It is likely that both explanations are true.

Tissue thicknesses and composition between atrial endocardium and esophagus are variable between patients[13-15] and can significantly alter heat transfer to the esophagus,[12,42] as discussed above. Further, a preliminary animal study suggests that actual tissue heating and esophageal injury may be critically dependent on catheter tip-tissue contact force.[39] In aggregate, these variables cannot be reliably measured during the catheter ablation procedure, and would result in very different effects on the esophagus of otherwise equivalent RF energy pulses delivered to the endocardial surface. In addition, the fidelity of luminal temperature monitoring to estimate mural esophageal temperature can be poor because there is the potential for large offsets between actual mural esophagus temperature and that reported by a probe located in the esophageal lumen as described in a preliminary report in animals,[43] and using other model systems.[11,41,42] The potential for significant underestimation of RF-induced esophageal heating using luminal esophageal temperature monitoring may be related to the potential for variable orientation of a temperature probe within the esophageal lumen[17] (Figure 3), and has been borne out by two reports of atrioesophageal fistula formation after catheter ablation for AF despite continuous intraprocedural esophageal temperature monitoring without evidence of significant esophageal heating.[4,44] Accordingly, lack of evident esophageal heating via a luminal temperature probe might not exclude RF-induced esophageal injury and may have poor sensitivity to detect thermal injury. When a luminal temperature probe is employed to identify esophageal heating, it should be emphasized that it is important to adjust the rostral-caudal position of the probe repeatedly during RF energy delivery to minimize the distance between probe tip and ablation target site to minimize so much as possible temperature offsets between maximum mural esophageal temperature and that reported by a luminal probe.

Alternate Methods to Monitor for Thermal Injury of the Esophagus During Catheter Ablation

Methods other than luminal temperature monitoring have been proposed to monitor for thermal injury of the esophagus during catheter ablation. Intracardiac ultrasound imaging can often visualize the ablation catheter tip and esophagus simultaneously in real time when endocardial regions adjacent to the esophagus are targeted.[26,31,32] Furthermore, ICE has been reported to reveal thickening of the atrial myocardium during RF lesion formation with increased risk of thermal injury to the adjacent esophagus inferred. However, utility of ICE to directly monitor for esophageal injury may be limited, at least when imaging is done from the right atrium, because no clear changes in the esophagus during RF ablation have been identified with ICE imaging.[31] Accordingly, the primary utility of ICE imaging appears to be to identify ablation target sites that are in fact immediately adjacent to esophagus tissue rather than to provide real-time monitoring for thermal injury of the esophagus.

Approaches for RF Energy Titration -- How Much Power Should Be Applied During RF Ablation at the Posterior LA?

A general strategy for titrating RF energy during catheter ablation might well include multimodal imaging to define the location of the esophagus, use of a luminal temperature probe, avoidance or significant limitation of RF energy delivery whenever ablation targets are potentially near the esophagus regardless of luminal temperature probe data, and termination of RF energy delivery whenever a temperature probe reports rapid elevation of luminal esophageal temperature. Data from a luminal probe can provide added information about esophageal heating when these data are properly acquired and interpreted, and have been reported to help guide RF energy titration to minimize thermal injury to the esophagus during catheter ablation.[45,46] Placement of a luminal temperature probe also allows for fluoroscopic localization of the esophagus (again, with limitations; see Figure 3).

There are sparse and largely indirect data available to support specific recommendations regarding how much RF energy is safe when ablation is done near the esophagus. Rapid esophageal heating can occur with even relatively brief and low-energy RF pulses delivered at the posterior left atrial wall, whereby catheter ablation at the right or left PV antra near the PV os with 20 W average for less than 20 seconds resulted in rapid heating at a luminal temperature probe[17] (Figure 4). Further, we have observed transmural esophageal heating rates of greater than 0.2°C per second during select RF energy application in patients undergoing ablation with slightly higher power settings of 30-35 W. Preliminary data using both a 2-D finite element model and an *in vitro* model of heat transfer to the esophagus during RF catheter ablation suggested that, in the absence of an adipose tissue layer between the atrium and esophagus, transmural heating of the esophagus to greater than 50°C could occur in as little as 50 seconds.[12] By definition, a luminal temperature probe will report the minimum transmural temperature; actual magnitudes and rates of temperature rises in the esophagus wall are, if anything, higher than that reported by a luminal temperature probe. Delayed cooling of the esophagus and temperature stacking (Figure 3) has also been observed using luminal temperature monitoring during RF ablation at the posterior left atrial wall (Figure 4). Pending more definitive data, it would seem reasonable to limit RF energy to under 20 W for less than 15-20 seconds when delivering RF energy near the esophagus, and to allow at least 180 seconds for esophageal cooling between limited additional RF energy applications within a single region adjacent to the esophagus. These recommendations are speculative and derive from the practical need to titrate in some way RF energy delivery to the left atrial posterior wall during catheter ablation for AF. New approaches to titrate RF energy during ablation have been proposed, including use of high-energy pulses for very short periods.[47] Evidence-based guidelines for RF energy titration have yet to be established.

Another novel method to limit heat transfer to the esophagus having bearing on RF energy titration is to place a cooling device such as a cold saline-irrigated balloon into the esophageal lumen to counteract conductive heat transfer to the esophagus during RF ablation.[40,48,49] Because esophageal heating during RF ablation is likely due to conductive heat transfer,[7] cooling from the luminal surface of the esophagus would be expected to limit transmural thermal injury.[49] Theoretically, this technique might allow for safe delivery of higher levels of RF energy and minimize the need to titrate energy delivery. However, as discussed above, animal studies have also demonstrated that inflation of a balloon in the esophagus can enhance heat transfer to the esophagus and increase thermal injury, presumably by displacing the esophagus toward the endocardial ablation site.[39] Accordingly, additional investigation will be required before the safety and utility of approaches employing active esophageal cooling and optimal RF energy titration, while using such systems, are established.

In summary, heat transfer to the esophagus is likely dependent on variables including catheter tissue contact pressure, catheter orientation, atrial wall thickness, thickness of intervening connective tissue, exact location and extent of the esophagus-atrial contact patch, and esophageal wall thickness. These variables are difficult to define in the clinical setting. Nonetheless, general characteristics of RF-induced esophageal heating such as latency to heating, delayed cooling, temperature-stacking, inter-individual variability in the efficiency of heat transfer to the esophagus, variable fidelity of luminal temperature monitoring to reflect mural esophageal heating, and the ability of brief low-energy RF pulses to heat the esophagus under select conditions should be considered when making clinical decisions regarding RF energy titration during ablation at the posterior left atrial endocardium.

Alternate Ablation Modalities

The ability of an operator to define all variables that determine RF energy transfer into heart tissue or the esophagus, or to monitor RF-induced esophageal heating, is limited. Thus, RF energy titration to avoid esophageal injury is empiric and would be expected to carry some risk. Cryothermy is an alternate tissue ablation method that has been used extensively for arrhythmia surgery, and more recently for endocardial catheter ablation of supraventricular arrhythmias with a 4-mm-tipped catheter.[50] Larger-tip cryothermy catheters with similar design (CryoCath, Inc. Montreal, Quebec) are available and have been approved for epicardial ablation. These catheters have also been used off label for endocardial ablation for atrial fibrillation.[17,51] Investigational use of another large-tip cryothermy catheter for endocardial ablation for AF has also been reported.[52] These studies show that cryothermy can be used to achieve PV isolation and/or to target left atrial tachycardia foci. The question is whether or not cryothermy has the same potential to produce esophageal injury with fistula formation as does RF ablation. Preliminary results from a small clinical series suggested that RF ablation and cryothermal ablation both act on the esophagus through conductive heat transfer because the magnitude and rate of temperature change with each ablation modality was observed to be similar.[7] Ripley et al. reported that direct cryothermy ablation to the outside surface of the bovine esophagus, *in vivo*, resulted in transmural lesions; however, unlike RF ablation that produced transmural necrosis and ulcer formation in the same model, cryothermy ablation preserved cellular architecture and no chronic ulcerations or fistula formation was evident.[53] Another *in vitro* study suggested that cryothermy ablation preserved the structural integrity of porcine esophageal tissue whereas RF ablation did not,[54] consistent with preservation of tissue architecture and absence of coagulation necrosis and destruction of interstitial structural proteins. Preliminary evidence in an animal model of focal endocardial cryothermy ablation suggested that transmural injury to the esophagus could occur after cryothermy ablation but the injury did not progress to deep ulcers or fistula formation.[55] Trials of cryothermy balloon therapy for PV isolation in humans are ongoing. This technology results in cryothermal tissue injury over broad regions of the posterior left atrial wall and PV antrum, and significant overlap with the esophagus is likely to have occurred in many patients. A recent preliminary report of 346 patients undergoing cryoballoon ablation for AF did not identify any patient with clinical evidence of esophageal injury or atrioesophageal fistula despite rigorous patient follow-up.[56] A separate report of four patients undergoing endoscopy after cryoballon catheter ablation revealed that one of the patients had superficial ulceration at the retrocardiac esophageal lumen that healed completely within a month.[57] Yet another preliminary report suggested that focal endocardial cryothermy at regions immediately adjacent to the esophagus was apparently safe in a small number of patients.[7] Taken together, these data suggest that cryothermy can cause transmural injury to the esophagus but may be less likely to result in deep ulceration and fistula formation. Though definitive data are lacking, this preliminary and indirect evidence suggests that cryothermy may be the preferred ablation modality when targeting left atrial posterior wall endocardial sites adjacent to the esophagus, either alone or in combination with RF ablation. In addition to the apparent reduced risk of transmural esophageal necrosis with fistula formation, cryothermy ablation appears also to have a lesser tendency to produce PV stenosis.[51,52,58] Given that it is preferable not to deliver ablation lesions immediately adjacent to the esophagus even with cryothermy, an option to redirect cryothermy lesions to the vein ostium or just within the vein and away from the esophagus in select patients may further enhance safety of cryothermy vis-à-vis the esophagus; this is not an option with RF energy-based ablation due to the risk of PV stenosis. An important limitation of these data regarding use of cryothermy for left atrial ablation in humans is that the occurrence of A-E fistula, even with RF energy, is quite low, and would not be expected to be higher with cryothermy. Thus, many ablation procedures employing cryothermy at the posterior wall would be required to realize statistical power to detect clinically significant cryothermy-induced esophageal injury. Alternate endpoints after cryothermal left atrial ablation such as upper endoscopy 1-3 days after the procedure could provide valuable information about the safety of cryothermy (or any other method to reduce risk) because early mucosal changes recognized with endoscopy are thought to be requisite harbingers of A-E fistula formation; however, such studies have not yet been reported.

Catheter Ablation for AF Using a Combination of RF and Cryothermy Ablation -- a Practical Approach

As previously discussed, an operator has limited ability to define all variables that determine RF-induced heat transfer to the esophagus, and there are no proven methods to monitor for heat transfer to and thermal injury of the esophagus during ablation. Accordingly, specific assessment of the potential for or occurrence of esophageal injury during RF ablation in an individual cannot reasonably be made in clinical practice, and it may be safest to assume that heat transfer to the esophagus will be efficient and the risk of esophageal injury high whenever delivering RF energy near the esophagus. Given these uncertainties the author uses the following approach to minimize risk of esophageal injury during catheter ablation:

We assume that the potential for efficient heat transfer to and thermal injury of the esophagus is high whenever any of the following are noted: (1) the MRI (or CT) shows the esophagus to overlay the right or left PV antrum and/or ostium, (2) rapid mural esophageal heating is suggested by recording an early and rapid rise in luminal esophageal temperature during an RF pulse, or (3) real time monitoring with ICE or fluoroscopic visualization of the luminal probe suggests that the intended site of ablation is within 1-2 cm of the esophagus. When ablation targets are so deemed risky, our approach is to employ the above strategies alone or in combination.

Preprocedure imaging with CT or MRI is done in all patients to provide baseline imaging of the PV anatomy and morphology. These studies often allow for an initial assessment of the location and breadth of the esophagus-atrium contact region. In particular, the finding of a broad esophagus covering much of the posterior left atrial wall recommends caution when using a discrete luminal marker like a temperature probe as the sole modality to define the location of the esophagus during ablation. During the procedure the esophagus location relative to the atrium is displayed using fluoroscopy of a luminal marker, a segmented shell of the esophagus from CT when available as a registered structure (Figure 2, panels F and G), and ICE to confirm location of the esophagus in real time. Recent implementation of Carto-Sound™ is helpful to achieve informative real-time imaging during ablation. As already considered above, a temperature probe or catheter might well be positioned eccentrically within the esophagus lumen, suggesting that any endocardial ablation sites within 1-2 cm medially or laterally to the fluoroscopically defined luminal probe could in fact be immediately adjacent to esophageal tissue (Figure 3) unless real-time ICE imaging clearly indicates that a particular site visualized to be near the luminal marker with fluoroscopy is not. ICE imaging from the right atrium has some limitations in making this determination due to the narrow 2-D imaging plane and the likelihood that the catheter tip and adjacent esophagus tissue, each viewed obliquely from the right atrium, might not fall within a single imaging plane even when the catheter tip is adjacent to some part of the esophagus.

When a potential ablation target is deemed risky, we typically attempt limited ablation near the esophagus with one or two RF pulses limited to less than 20-25 W, and lesion duration limited to less than 20 seconds, independent of readings from the luminal temperature probe tip that is actively positioned immediately adjacent to the ablation site. If a rapid temperature rise is recorded by the luminal probe, suggesting an instance of efficient heat transfer to the esophagus, RF energy delivery is immediately discontinued and subsequent RF energy delivery at this site avoided. Lack of a rapid temperature rise is not used as justification for more extensive RF energy delivery at ablation sites deemed near to the esophagus by other criteria. If additional ablation is required to achieve PV isolation or to ablate tissue at the posterior PV antrum thought to be arrhythmogenic, the author replaces either the lasso catheter or RF ablation catheter with a 6-mm-tip cryothermy ablation catheter (CryoCath, Inc). In the former case, the retained mapping catheter is used to tag cryothermy ablation sites on the electroanatomic map as they are delivered (Figure 5, panels A-C), and in the latter case a fluoroscopic image of each cryothermal site relative to the circular mapping catheter is saved (Figure 5, panel D), and the sites later marked under fluoroscopic guidance after the cryoablation catheter are again replaced by the electroanatomic mapping catheter (Figure 2, panel B). Other investigators (Ken Ellenbogen, M.D., pers. comm.) place a 10.5 French sheath in the beginning of the case if preoperative anatomy suggests the esophagus is located close to the pulmonary veins, or uses a stiff guidewire to exchange the 8 or 8.5 French transseptal sheath with the larger sheath to allow introduction of a large-caliber 8-mm-tip cryothermy catheter. This catheter is capable of greater refrigerant flow and would be expected to produce larger cryothermy lesions per unit time of application. The cryothermy catheter location can alternatively be monitored directly when the NavX™ (St. Jude Medical, Fullerton, CA, USA) system is used. Target cryothermy ablation parameters employed by the author include tip temperature ≈-75°C for 250 seconds with one or two cycles of cryothermy at each ablation site. This approach results in a limited segment at the posterior wall being targeted with cryothermy and all remaining ablation accomplished with RF energy, and, in our experience, has resulted in longstanding PV isolation. Significant cooling of the esophagus, as previously reported,[17] is often observed during cryothermy ablation consistent with the targeted site being a risky one for RF ablation had extensive RF energy been employed, due to thermal coupling with the esophagus. Figure 5 shows two representative patients in whom the esophagus was located near intended ablation targets and in whom a hybrid approach was used employing RF ablation for all regions except those adjacent to the esophagus that were targeted with cryothermal energy. When important sites of ablation are identified to be near the esophagus by any imaging methods, or by observing rapid elevation of luminal esophageal temperature during initial RF energy delivery, and isolation of the PV and PV antrum cannot be achieved with limited RF energy delivery (e.g., 1-2 low power and brief RF energy pulses), it may be reasonable to consider an alternate ablation strategy such as cryothermy. Prospective outcomes studies will be required in larger numbers of patients to define the relative risks of specific ablation strategies to result in clinically significant esophageal injury.

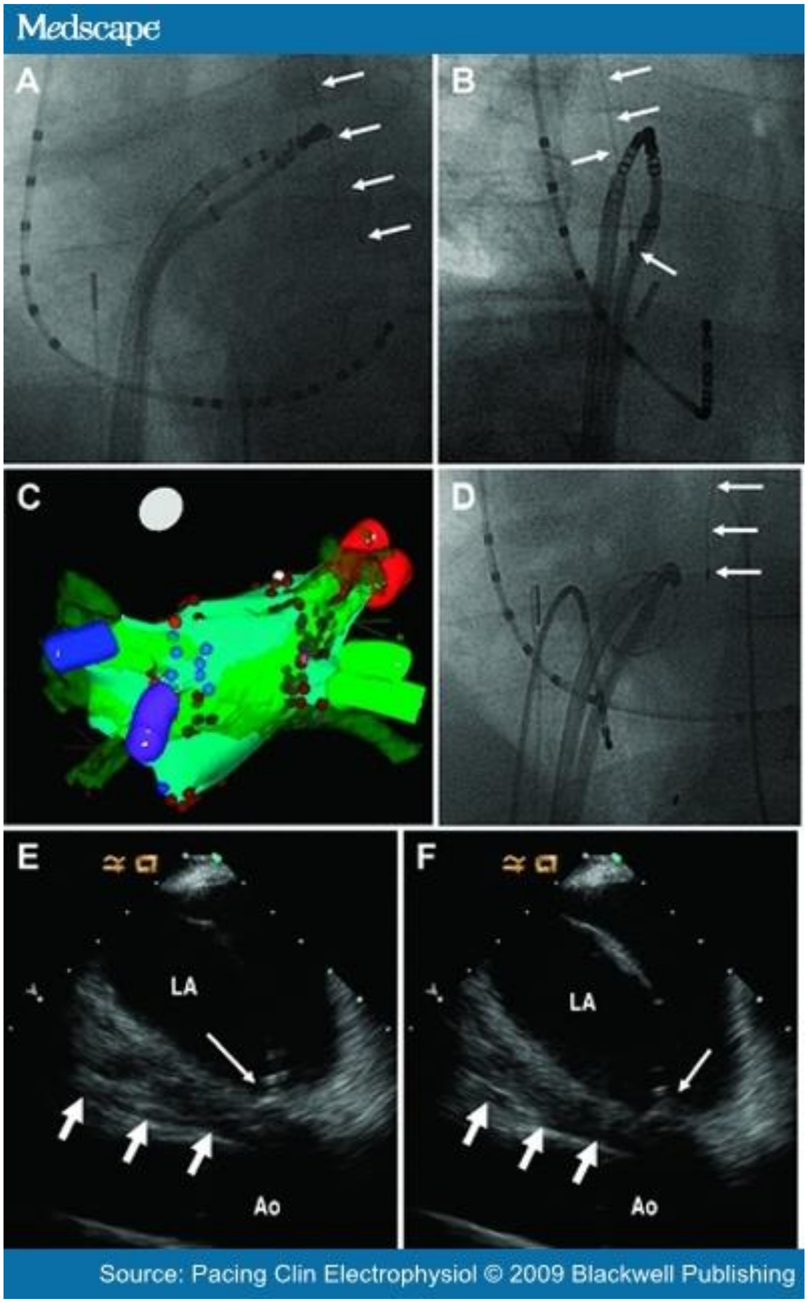

Figure 5.

Examples of hybrid therapy employing cryothermy for ablation when adjacent to the esophagus. Panels A through C are from the patient depicted in Figure 1, panel D. In the LAO and RAO views, respectively, the luminal probe is marked with white arrows, and the location of the cryothermy catheter is confirmed by briefly positioning the Carto catheter (Thermocool™) at the cryothermy site. Cryothermy sites are tagged in blue as seen in panel C on the E-A map with a superimposed segmented and registered shell of the left atrium from a previous MRI image. The MRI image does not include the entire left atrium in this example. Panel D shows cryothermy ablation at the right inferior PV guided by a circular mapping catheter positioned at the vein os in the patient from Figure 2, panels A-D. Sites of cryothermy were tagged after lesion delivery as seen in Figure 2, panels B-D based on biplane fluoroscopy with the circular mapping catheter used as reference. White arrows point to the luminal temperature probe. Catheters are also seen in the coronary sinus, and RV (panel D only). The ICE catheter is in the RA. Panels E and F are from the patient depicted in Figure 2, panels E-G. These 2-D ICE images were obtained in real time during cryothermy at the left superior PV antrum in proximity to the esophagus, and represent two frames of an acquired image loop less than one second apart. The left atrium (LA), aorta (Ao), and posterior margin of the esophagus (thick arrows) compressed between the LA and Ao, are marked. The cryothermy catheter tip is seen (thin arrows) contacting the posterior atrial wall. The high frequency of the refrigerant pump used by this cryothermy system (CryoCath, Inc.) causes a blurring artifact of the catheter. An echogenic spot at the catheter tip in panel E depicts the forming "ice ball," and adherence of the catheter to the endocardium is depicted in panel F by the "tenting" of the tissue at the catheter-tissue interface due to motion of the heart relative to the catheter during the cardiac cycle.

Complimentary imaging techniques are useful to identify when ablation target sites for treatment of atrial fibrillation are near the esophagus. Methods to monitor heat transfer to or thermal injury of the esophagus are limited. Alternative ablation strategies should be considered when endocardial ablation is indicated at sites near the esophagus. Whatever lesion set is chosen for therapeutic ablation, it seems most reasonable to limit, so much as possible, endocardial RF ablation adjacent to the esophagus. Hybrid therapy employing a combination of cryothermy for ablation near the esophagus and RF ablation at other endocardial sites is an option that has been used by several centers to achieve pulmonary vein isolation in patients with drug refractory AF. Although available large-tip cryothermy catheters are not labeled for endocardial ablation, and specific outcomes data are lacking, preliminary evidence suggests that cryothermy ablation may be a reasonable alternative to RF when endocardial ablation is required near the esophagus.

Medscape

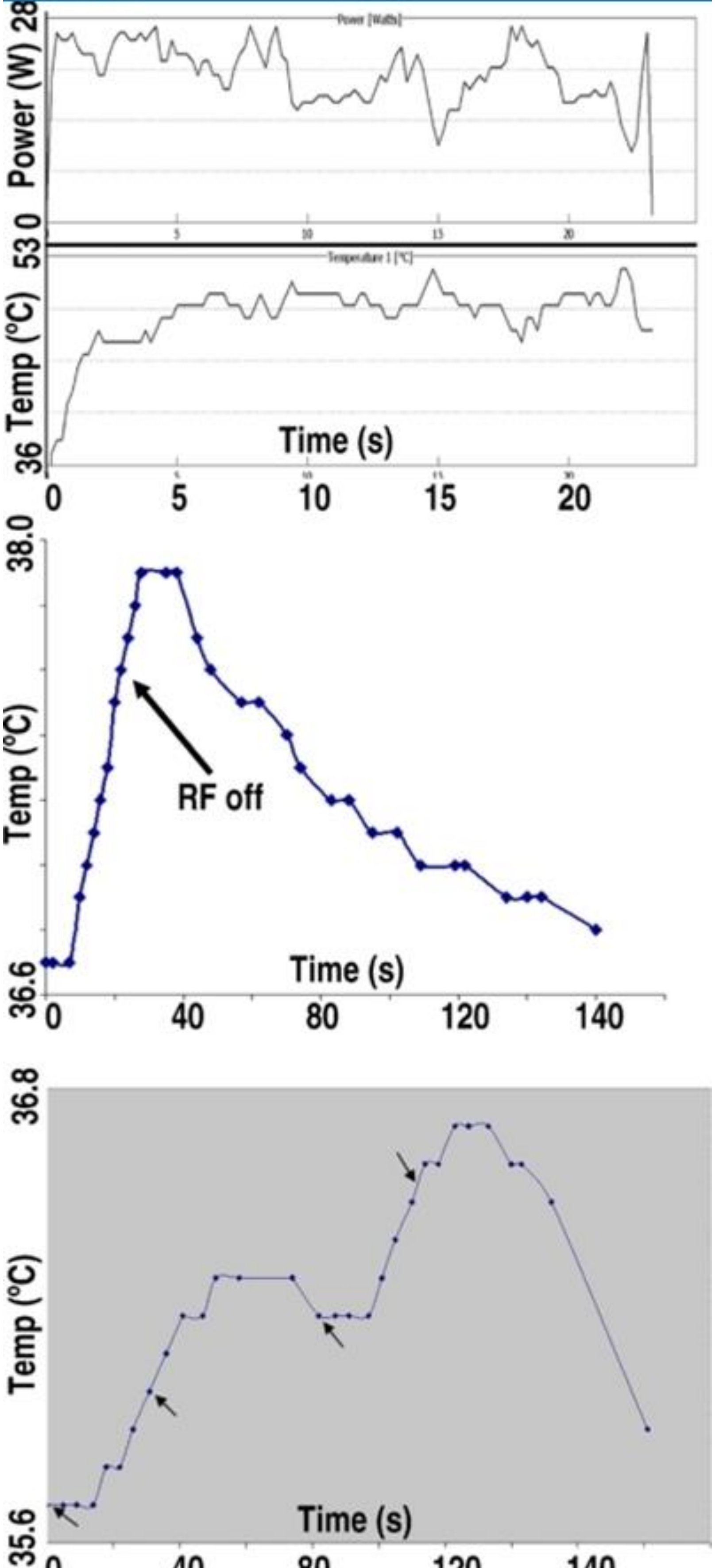

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Figure 4.

Time course of esophageal heating measured with a luminal probe during RF ablation at the posterior left superior PV antrum in proximity to the probe. The upper panel depicts an RF energy application of 20 W mean power for 23 seconds, mean temperature 48°C, maximum 52°C using an 8-mm-tip catheter. The middle panel depicts esophageal heating with brief latency to onset, rapid temperature rise (see text), overshoot, and delayed cooling. In this example, more than 140 seconds was required for temperature to return to baseline. The bottom panel shows "temperature stacking" when a second RF pulse was initiated (third arrow) about 45 seconds after the first RF pulse was terminated (second arrow) in another patient.