

The Phrenic Nerve And Atrial Fibrillation Ablation Procedures

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Abstract

Radiofrequency ablation is increasingly used as an option to optimally manage patients with symptomatic atrial fibrillation. Presently, ablationists strive to improve success rates, particularly with persistent atrial fibrillation, while simultaneously attempting to reduce complications. A well-recognized complication with atrial fibrillation ablation is injury to the phrenic nerve giving rise to diaphragmatic paresis and patient discomfort. Phrenic nerve damage may occur when performing common components of atrial fibrillation ablation including pulmonary and superior vena caval isolation. The challenge for ablationists is to successfully target the arrhythmogenic substrate while avoiding this complication. In order to do this, a thorough knowledge of phrenic nerve anatomy, points in the ablation procedure where nerve damage is more likely, and an understanding of the presently utilized techniques to avoid this complication is required. In addition, when this complication does arise, prompt recognition of its occurrence, knowledge of the natural history, and available methods for management are needed. In this review, we discuss the underlying anatomic principles, techniques of avoiding phrenic nerve damage, and presently available methods of diagnosing and managing this complication.

Introduction

Radiofrequency ablation is now well established as an option when treating patients with symptomatic atrial fibrillation (AF).^{1,2} Ablation of the AV node and placement of a permanent pacemaker as well as adjunctive atrial flutter ablation along with antiarrhythmic therapy has been used for drug refractory symptomatic patients for two decades. While these modalities were previously occasionally resorted to, more recently, there has been an explosion in the utilization of this treatment modality. The recognition that triggers for AF are associated with the thoracic veins and subsequent understanding of the need to circumferentially ablate atrial

tissue around these veins is directly responsible for the burgeoning use of these procedures.³⁻⁷

While the success rates for these procedures, particularly with paroxysmal AF, has been encouraging, several complications relatively specific to this type of ablation have been seen. Given the relatively benign nature of the treated arrhythmia (AF), it is critical to be sure that the treatment (AF ablation) is of minimal risk. Reported complications from AF ablation include stroke, pulmonary vein stenosis, cardiac perforation, esophageal damage, and phrenic nerve injury (PNI).⁸⁻¹²

Phrenic nerve injury had rarely been reported with ablation procedures for other arrhythmias (Figure

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1) including other atrial arrhythmias,¹³ however, this complication is well recognized, specifically with AF ablation. An integral part of most presently employed AF ablation procedures involves circumferential ablation to electrically disconnect the thoracic veins from the atria.^{14,15} While both right and left phrenic nerves may be injured,¹⁶⁻¹⁸ most commonly the right phrenic nerve is at risk when electrical isolation of the right upper pulmonary vein (RUPV) or the superior vena cava (SVC) is being performed.

When PNI occurs, patients are sometimes severely symptomatic with shortness of breath, particularly with exertion and when lying down.¹⁹⁻²¹ The diagnosis is usually straightforward with right hemidiaphragmatic elevation on routine chest radiography and further confirmation with paradoxical movement of the diaphragm when the patient is asked to sniff (Figures 2 and 3). Since the main goal of AF ablation is to improve patients' symptoms, the occurrence of PNI offsets this pri-

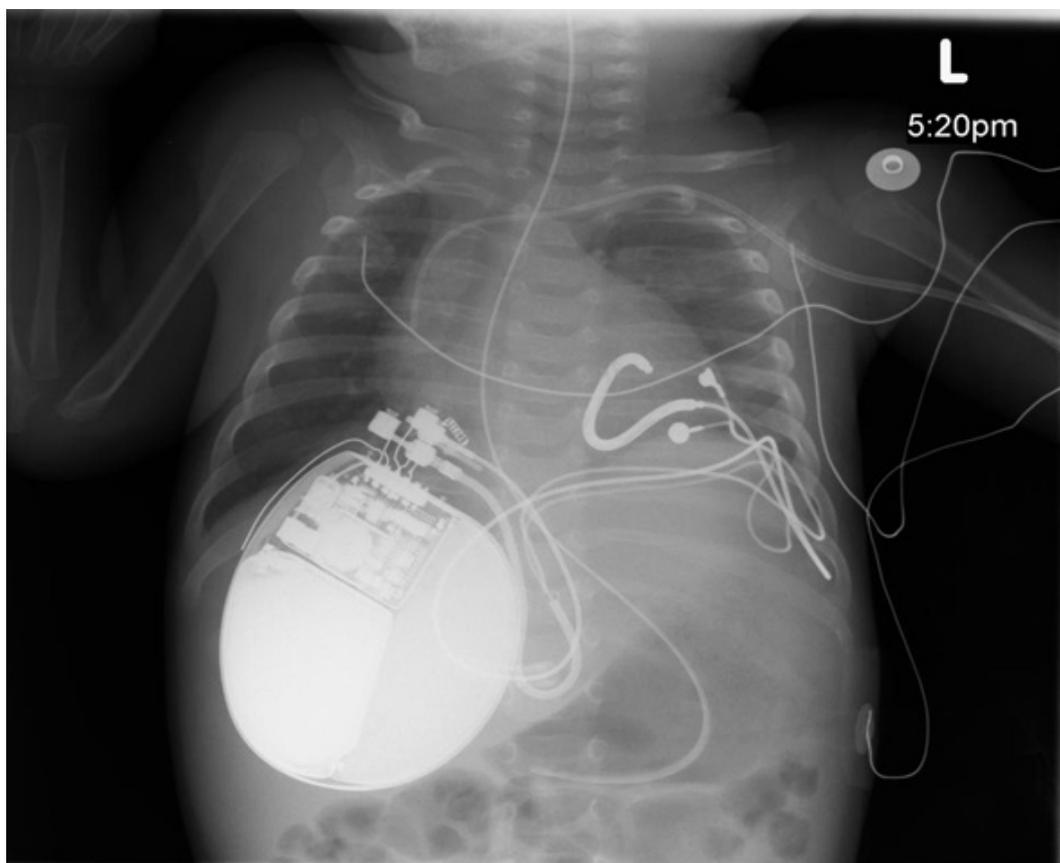
mary goal even when the ablation procedure is successful.

For ablationists to avoid this complication and yet successfully target the arrhythmogenic substrate for AF, significant background knowledge is required. First, a detailed understanding of the anatomical course and variation of the phrenic nerve is needed. In addition, appreciating the parts of the AF ablation procedure, which particularly pose a risk for PNI, and the available techniques to prevent this complication must be thoroughly understood.

Along with esophageal damage, PNI shares the difficulty with avoidance as a result of the highly variable and difficult to visualize the course of these anatomic structures.

In this review, we discuss the regional anatomy of the phrenic nerve, reports of specific parts of the AF ablation procedure where PNI has occurred,

Figure 1: Example of left phrenic injury with elevation of the left hemidiaphragm. Infant with ICD placed epicardially and generator over the right abdomen. The left phrenic nerve was injured during placement of the epicardial ICD lead.



and critically analyze the pros and cons of presently utilized techniques to avoid this troublesome complication.

Correlative Regional Anatomy of the Phrenic Nerves

Invasive electrophysiologists should be thoroughly cognizant with the anatomic course and relations of both the right and left phrenic nerve (Figure 4). Importantly, the variations that occur with the nerve course and with congenital and other structural heart disease must be appreciated. Specifically, the regional anatomy of the nerve in relation to the pulmonary veins, SVC, lateral right atrium, and the left atrial appendage must be well understood prior to the delivery of radiofrequency energy at these locations.

Anatomy of the Phrenic Nerve

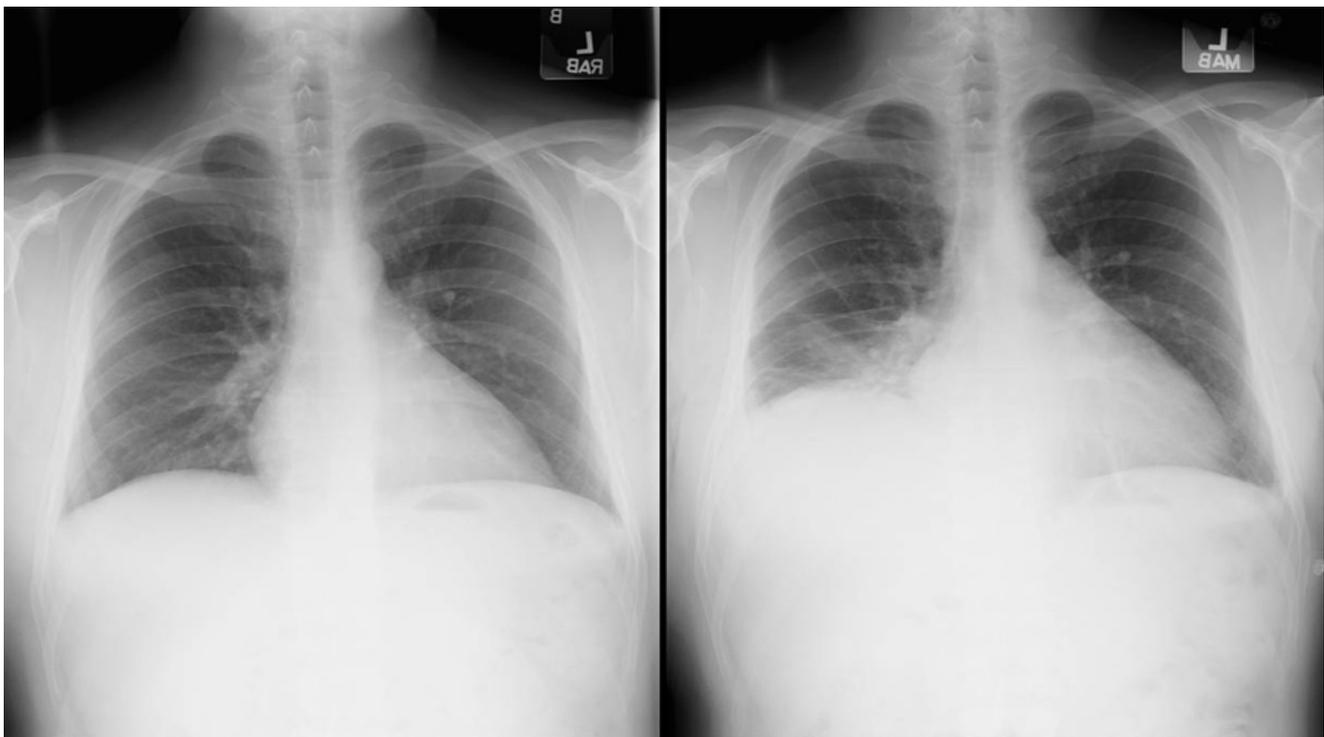
Right and Left Phrenic Nerve Course

The phrenic nerve is a mixed somatic nerve that

arises mainly from the anterior ramus of the fourth with contributions from the third and fifth cervical segments (although the 5th cervical nerve root is often seen to join the phrenic trunk on the anterior surface of the scalenus anterior, it may descend into the thorax before it joins the nerve). The phrenic trunk forms at the upper lateral border of the scalenus anterior muscle and descends along its anterior surface, behind the prevertebral fascia.²²⁻²⁴ In its descent, it passes behind the sternocleidomastoid, inferior belly of omohyoid, transverse cervical and suprascapular arteries, internal jugular vein, and thoracic duct on the left.

As the phrenic nerve enters the thorax, it crosses medially in front of the internal thoracic artery.^{25, 26} However, this relationship may not always be consistent as upon entering the thorax, the phrenic nerve has been recorded to cross the internal thoracic artery either superiorly, lie between the internal thoracic artery and the first rib, or cross it inferiorly where it is held against the artery by the adjacent lung and pleura as it passes into the mediastinum. In a study conducted by Owens et al,²³ the phrenic nerve conformed to the standard

Figure 2: Anteroposterior chest radiography of PNI. Left panel is preablation and shows normal diaphragmatic height. Right panel is following ablation with phrenic nerve injury and marked elevation of the right hemidiaphragm. Ablation involved energy delivery in the vicinity of the superior vena caval ostium.



description of its course in only 64% of specimens dissected. This relationship was found to be asymmetric in 46%.

Within the thorax, the phrenic nerve passes downward and in front of the hilum of the lung between the fibrous pericardium and mediastinal pleura and is accompanied by the pericardiophrenic vessels towards the thoracic diaphragm.

Anatomic Variation

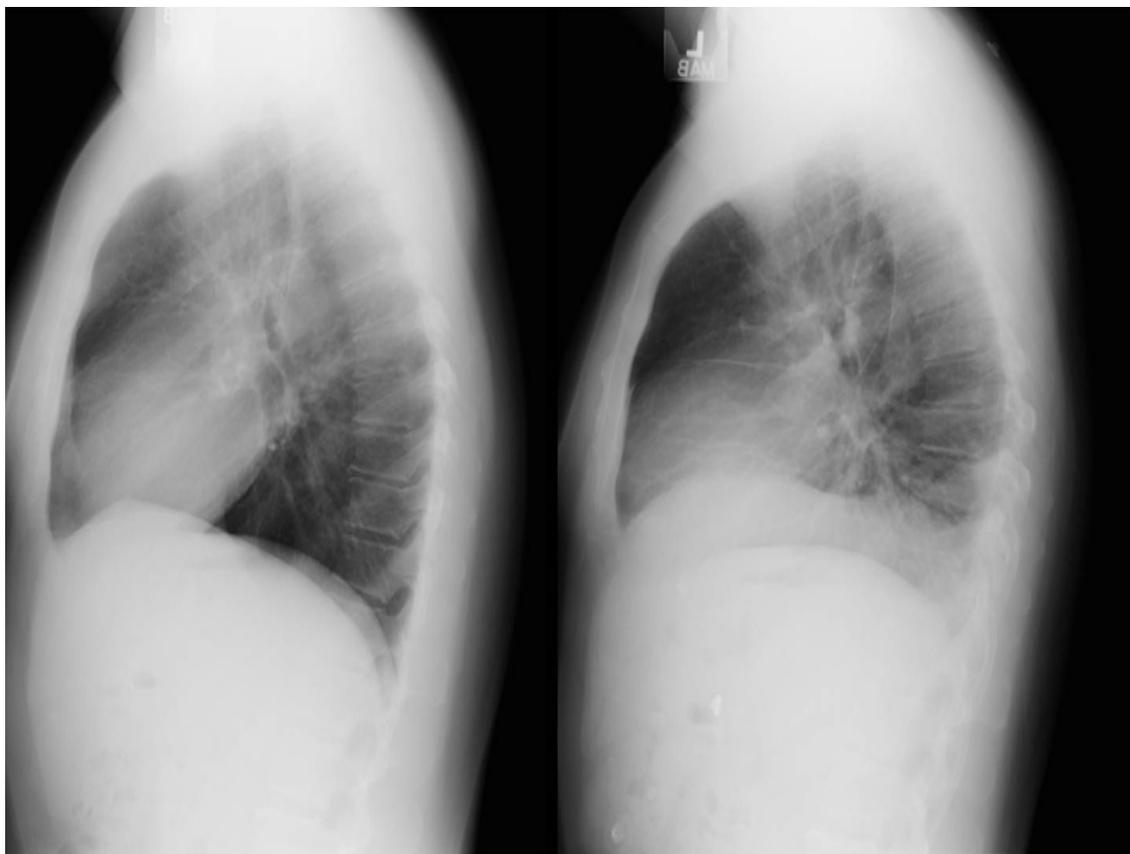
The accessory phrenic nerve is said to originate from displaced fibers of the 5th cervical ventral ramus (sometimes 4th or 6th cervical segments), which runs within a branch of the nerve to subclavius. In its course, it lies lateral to the phrenic nerve as it passes inferiorly posterior to the subclavian vein. In most cases, it joins the phrenic nerve near the first rib but may also join the nerve at the level of the pulmonary hilum or beyond.^{22, 27}

A recent incidental finding by Prakash et al²⁸ is that the phrenic nerve was seen to give off a communicating branch to C5 root of the brachial plexus and was located in front of the subclavian vein just as it entered the thorax.

The Right Phrenic Nerve and the Superior Vena Cava

The right phrenic nerve is covered by mediastinal pleura as it descends along the brachiocephalic vein and then along the right anterolateral border of the SVC (Figure 5). The nerve is separated from the SVC at its right atrial junction by pericardium. It continues inferiorly along the same line over the right atrial wall. Histological reports have shown a close relationship between the right phrenic nerve and the SVC, separated by variable amount of fatty tissue.²⁹ The right phrenic nerve appears to be closest to the SVC superiorly and as it curves posteriorly approaching the superior

Figure 3: Lateral chest radiography of phrenic nerve injury. Corresponding lateral radiographic images to those shown in Figure 2. Right panel is postablation and the marked elevation of the right diaphragm (no elevation of cardiac silhouette as would occur if this was the left hemidiaphragm) is noted



cavo-atrial junction.

The Right Phrenic Nerve and the Right Upper Pulmonary Vein

The right phrenic nerve shares an anatomically close relationship with the RUPV³⁰ with a minimal distance of about 2.1mm between them.²⁹ However, it must be noted that this relationship and the distance between the right phrenic nerve and the RUPV is highly variable (Figure 6). From a technical standpoint, therefore, this puts the phrenic nerve at high risk for injury during RUPV isolation.

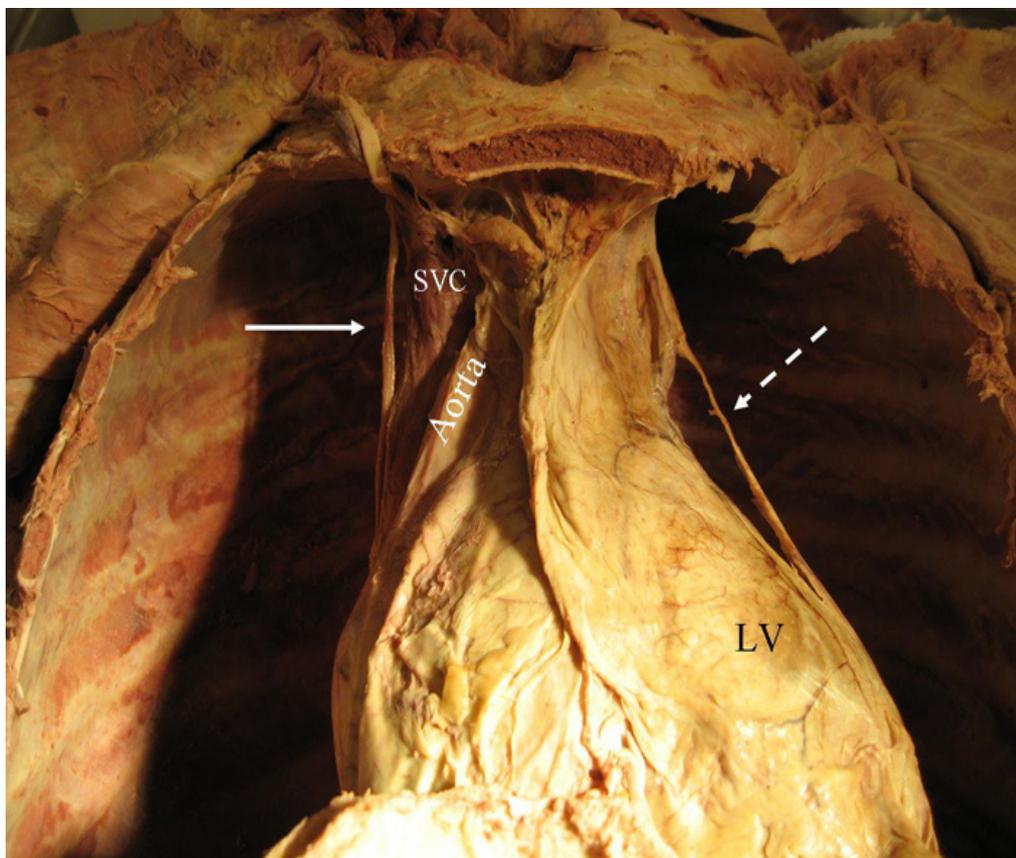
The right and left phrenic nerve receive its blood supply from the internal thoracic artery (ITA). A pericardiophrenic branch descends along each phrenic nerve within a fascial sheath to form a neurovascular bundle that adheres to the fibrous pericardium. Around 70% of blood supply is re-

ceived from the pericardiophrenic branch of the ITA with the remainder from pericardial and pleural branches arising from the upper segment of the ITA.³¹

The ITA and the phrenic nerve share an anatomically important relationship. The ITA has been recorded to cross the nerve obliquely from lateral to medial and sometimes anterior to posterior.³² A study by Puri et al recorded both phrenic nerves crossing the ITA anteriorly in 54%, posteriorly in 14%, the left phrenic nerve crossing anteriorly in 12%, and the right phrenic nerve crossing posteriorly in 12% with this position switched in 20% of cases.³³

Division of the phrenic nerve in the neck leads to paralysis of the corresponding half of the diaphragm. In its proximal course, the phrenic nerve may be impaired as a result of brachial plexus injuries. However, cardiac surgery remains one of the most common causes of damage to the phrenic

Figure 4: Anatomic dissection showing typical course of the phrenic nerve. Solid arrow points to the right phrenic nerve immediately adjacent to the SVC. As it courses posteriorly, the nerve becomes related to the RUPV (see text). Hatched arrow points to the left phrenic nerve. The dissection has lifted the nerve away from its typical adjacent location to the left atrial appendage. LV - left ventricle



nerves. Other causes of phrenic nerve damage include tumors of the lung, associated mediastinal structures, and infections.^{34,35}

Left Phrenic Nerve and Cardiac Relations

The left phrenic nerve continues over the aortic arch, pulmonary trunk, and left pericardial wall over the left atrial appendage as it continues along the underlying left ventricular surface. The left phrenic nerve may be separated from the pericardium by a variable layer of adipose tissue. In about 80% of individuals, the left phrenic nerve is closely related to the underlying left oblique marginal vein and the left marginal artery. It may also pass close to the left main stem, left anterior descending artery, or the great cardiac vein.²⁹

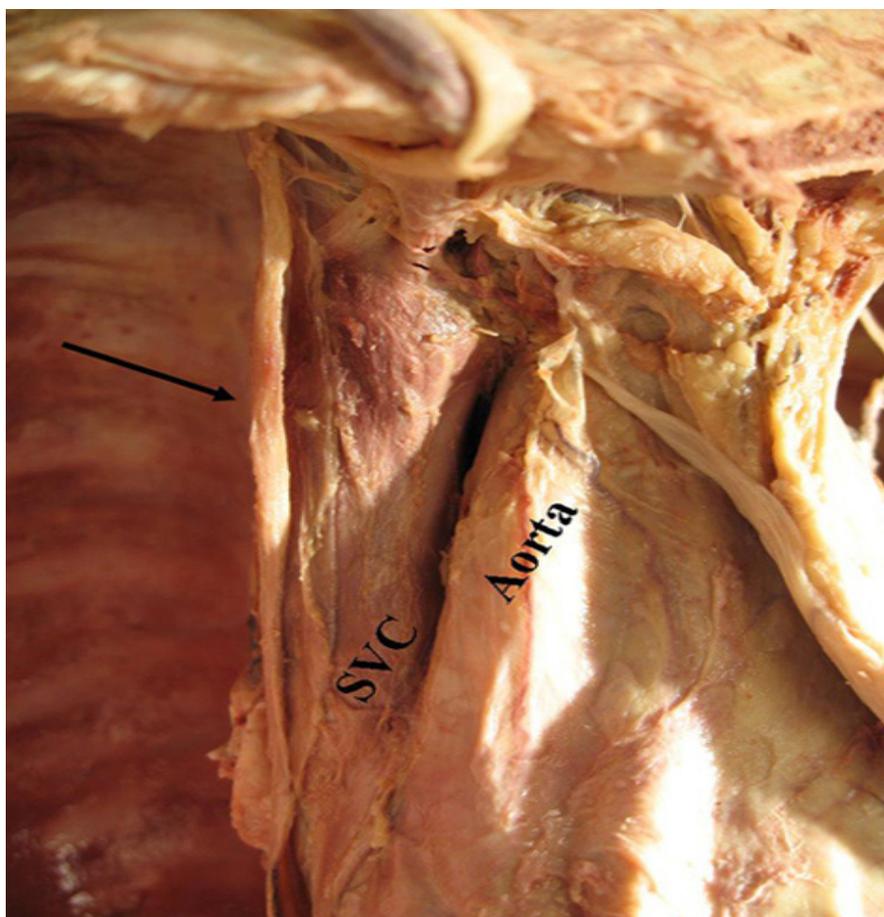
Phrenic Nerve Injury During Radiofrequency Ablation Procedures

Prior to the advent of thoracic vein-related abla-

tion for AF, rare reports of PNI with ablation for other arrhythmias existed. These typically involved ablation in the right atrium close to the superior vena caval junction as was performed to modify the sinus node (inappropriate sinus tachycardia), atrial tachycardias arising from the superior crista terminalis,^{13, 36-38} and ablation of right atrial flutters.^{23, 25, 26}

Once electrical isolation targeting the triggers in the thoracic veins became an integral part of AF ablation, PNI was increasingly recognized. Lee et al describe a 61-year-old woman with a 7-year history of paroxysmal AF.¹⁷ Radiofrequency ablation was performed. Isolation of the left superior, left inferior, and the right inferior pulmonary veins was completely achieved without difficulty. However, 25 radiofrequency pulses with a total duration of 1,297 seconds were required to isolate the right superior pulmonary vein. The procedure was well tolerated except for complaints of chest pain radiating to her back. One day after the ablation, the patient complained of shortness of breath

Figure 5: Anatomic dissection showing the adjacent and very close relationship of the right phrenic nerve (arrow) with the SVC close to the ostium. Attempts at circumferential isolation of the SVC often is limited because of this relationship.



and orthopnea, and chest radiography revealed right diaphragmatic elevation. Three days later, the patient's symptoms improved somewhat, and by day four, chest x-ray revealed a significant resolution of right hemidiaphragmatic elevation. Four weeks later, she was asymptomatic and the right diaphragmatic elevation disappeared completely.

Le et al demonstrate a similar case with a 61-year-old male with a 6-year history of paroxysmal AF.³⁹ He underwent 41 radiofrequency pulses for duration of 2080 seconds. He was symptomatic on post-procedure day one, and a chest x-ray revealed right hemidiaphragmatic elevation. Post-procedure day six, his symptoms had improved but the elevation persisted. Five months later, he was asymptomatic, but chest x-ray, fluoroscopy, and pulmonary function test revealed persistent right hemidiaphragm paralysis and restrictive pulmonary physiology.

Between 1997 and 2004, Sacher et al studied 3755 consecutive patients who underwent AF ablation at five centers [18]. Eighteen (0.48%) patients demonstrated PNI. Right PNI occurred during right superior pulmonary vein ablation or SVC disconnection, and left PNI occurred during left atrial appendage ablation. After a mean follow-up (36 +/- 33 months), 12 patients had complete recovery, 3 had partial recovery, and 3 had no recovery of diaphragmatic function.

Swallow et al present a 50-year-old man with recurrent AF that had undergone radiofrequency ablation to the ostia of the pulmonary veins.³⁸ The procedure was prolonged because of a large right superior pulmonary vein. The following day he was breathless, and a chest radiograph showed an elevated right hemidiaphragm. Six weeks after ablation, magnetic phrenic nerve stimulation showed right hemidiaphragm weakness. However, 9 months following ablation, a diaphragm function test showed full recovery.^{40,41}

Data from 17 patients with PNI caused by varying ablation techniques performed between December 1999 and December 2005 at 3 centers were reviewed by Bai and colleagues.¹⁶ Thirteen of these patients underwent an ablation for AF. Radiofrequency ablation was done in 9/13, cryoablation in 1/13, ultrasound ablation in 2/13, and laser abla-

tion in 1/13. Bai et al concluded that PNI caused by catheter ablation regardless of the energy source appears to functionally recover over time.

Right Upper Pulmonary Vein Isolation

Because of the relationship described above between the phrenic nerve and the right upper vein, this is a common location wherein PNI has been reported. Because the phrenic nerve has a closer relationship to the mid and distal portions of this vein, ablation that is performed entirely in the left atrium circumferentially isolating the vein ≥ 5 mm from the ostium of the pulmonary vein is recommended. Because of anatomic variation in the phrenic nerve, no ablation site or technique is foolproof and thus requires the adjunctive use of techniques to identify phrenic nerve location described below.

Superior Vena Cava

The most common site where phrenic nerve-related issues arise when ablating is the SVC. This vein is a well-established site for triggers of AF initiators.⁴²⁻⁴⁵ Unlike the situation with the right upper vein, the phrenic nerve crosses the ostium of the SVC, thus, a generalizable approach of ablation proximal or distal to the ostium cannot be recommended. Perhaps more so than ablation at any other site, precise knowledge on the course of this nerve is essential to avoid injury when attempting to electrically isolate this vein.

Other Locations for Potential Phrenic Nerve Injury with AF Ablation

Occasionally, ablation is required in or around the left atrial appendage to treat AF. Triggers of AF, if found to arise within this structure, may require isolation of a portion of the appendage to avoid energy delivery with the attendant risk of cardiac perforation deeper in the appendage. Because of the proximity of the left phrenic nerve with the lateral wall of the left atrial appendage, injury to this nerve may occur.

Following successful pulmonary vein isolation, occasionally, triggers from other veins such as the vein of Marshall may continue to occur. Ablation in the vein of Marshall itself is unlikely to result in

PNI, but if isolation of this vein in the lateral coronary sinus is contemplated, left PNI is possible^{3, 46}

Phrenic Injury with Non RF Ablation for Atrial Fibrillation

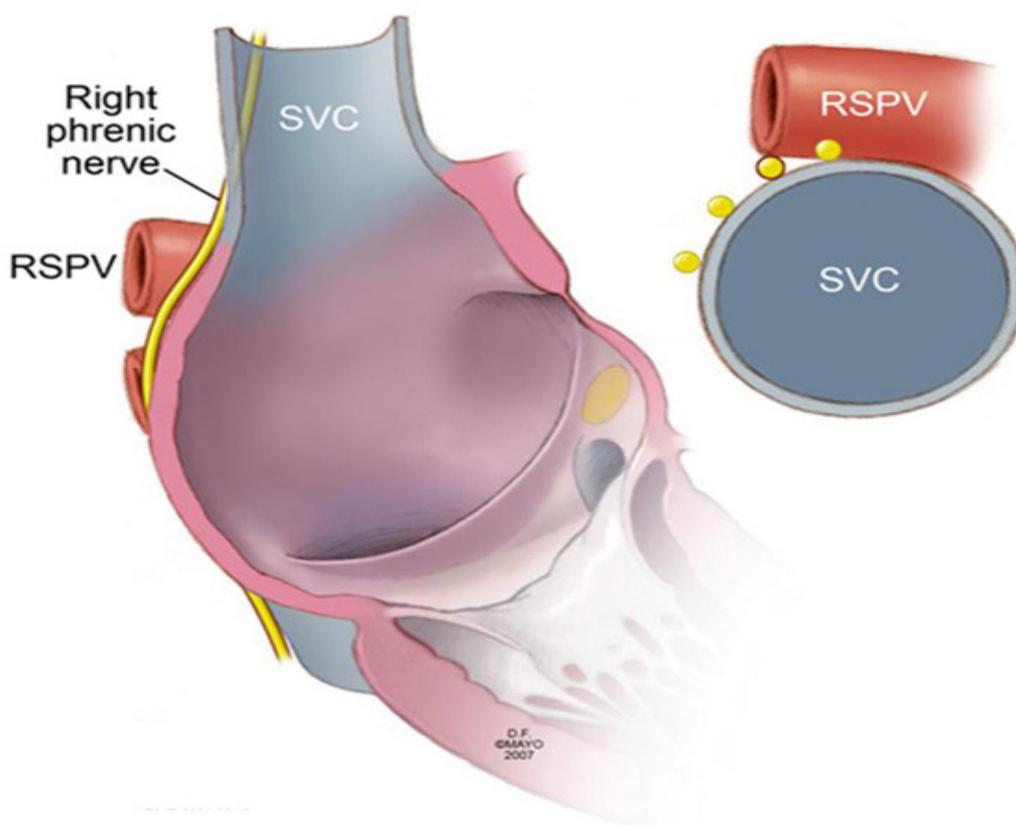
Phrenic nerve injury is a significant limitation to the use of ultrasound-based approaches to ablation in or around the thoracic veins.^{47, 48}

Cryoablation both in the experimental canine model and with clinical ablation has been associated with PNI as well.^{16, 49-51} Okumura et al conducted a study that examined tissue temperatures around pulmonary veins during high intensity focused ultrasound balloon ablation for AF in the

canine model.⁴⁹ Tissue temperatures in eight dogs undergoing 51 right superior pulmonary vein high intensity focused ultrasound ablations were recorded from epicardial thermocouples at right superior pulmonary vein orifice and phrenic nerve. This study disclosed the direct high intensity focused ultrasound ablation effect as the mechanism of PNI occurring within 4-7 mm from the balloon surface.

Tse et al used the CryoCor cryoablation system (CryoCor Inc., San Diego, California) in 52 patients with paroxysmal or persistent AF to isolate the pulmonary vein.⁵⁰ Cryoablation was applied twice at each targeted site (2.5 to 5 min/application). Of these 52 patients, one had transient phrenic nerve

Figure 6: Schematic representation of one technique to avoid diaphragmatic injury. A pacing catheter is placed deep into the SVC. With high output stimulation, persistent phrenic nerve stimulation occurs. Cryoablation is then done close to the ostium. If diaphragmatic movement stops, then cryoenergy delivery is immediately discontinued. If diaphragmatic movement continues, then cooling to an ablative level -70 – (-80°C) is done, thus allowing completion of the SVC isolation procedure. Reproduced with permission from: Bruce CJ et al, J Interv Card Electrophysiol 2008; 22:211-219.



paresis during cryoablation in the right superior pulmonary vein, which resulted in premature procedure termination. The diaphragmatic movement resumed immediately after cryoablation was terminated, and there was no damage or loss of diaphragmatic or pulmonary function at 12-month follow-up.

In another study done by Van Belle et al, a cryothermal balloon approach was used for all consecutive patients who were selected for circumferential pulmonary vein isolation because of paroxysmal AF between August 2005 and August 2007.⁵¹ There were 141 patients included in this study. Of these 141 patients, 4 patients had asymptomatic right PNI persisting at discharge. All 4 patients had recovery of their diaphragmatic movement at 6-month follow-up.

The exact reason why circumferential ablation catheters appear to have a higher propensity to damage the phrenic nerve is unknown. Most likely, however, is that these devices need to be placed slightly into the pulmonary vein for stability. Specifically, when placed deeper into the right upper

pulmonary vein, the risk of phrenic nerve damage would then increase. Other possibilities include resonant frequency ablation occurring with ultrasound systems where energy delivery and heating may occur at a significant distance from where the device has been placed. Future design of pulmonary vein ablation devices will need to incorporate these possibilities, specifically by positioning the energy delivery system outside the pulmonary vein, targeting the perivenous atrial myocardium.

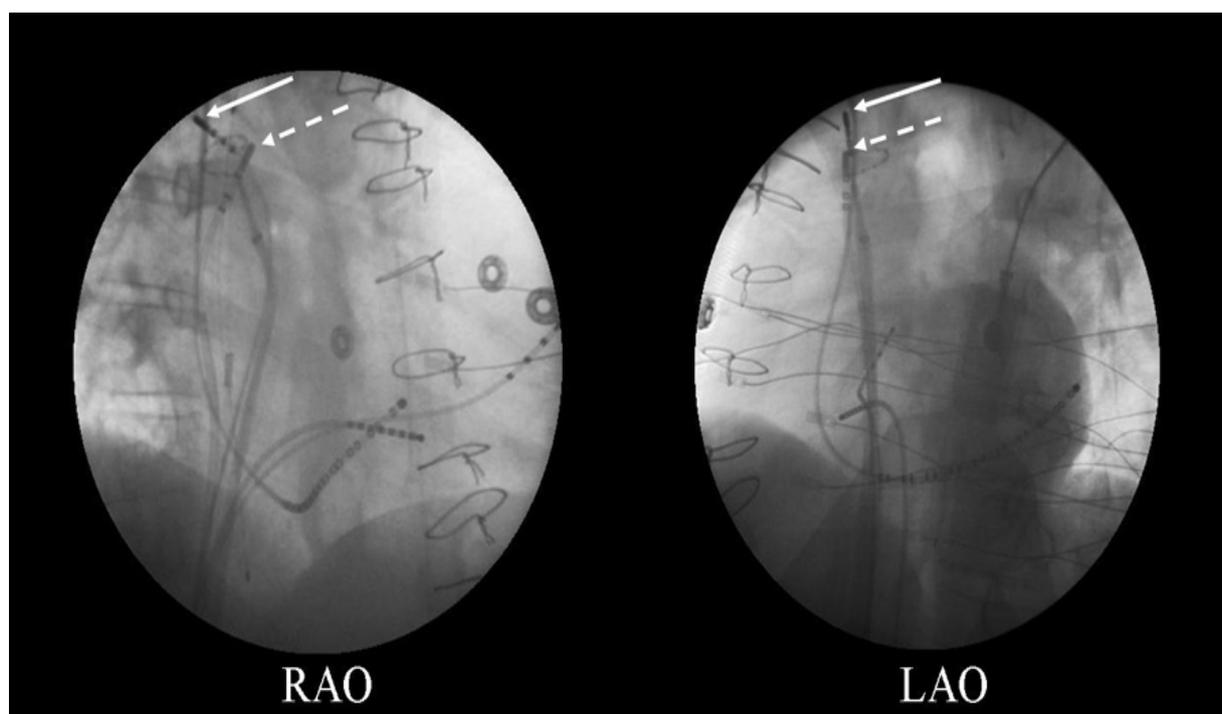
Phrenic Nerve Injury during Adjunctive Procedures Atrial Fibrillation

Phrenic stimulation as well as injury may occur during device implantation. This may be particularly relevant with epicardial device implantation and combined pacing and ablation procedures in patients with a Mustard/Senning procedure with congenital d-transposition of the great arteries.⁵²⁻⁵⁴

Methods to Avoid Phrenic Nerve Injury

With some complications associated with AF ablation, there appears to be definite ways of avoiding

Figure 7: RAO and LAO radiographs with technique of cryoablation exemplified. The circumferential mapping catheter is in the SVC. The pacing catheter (solid arrow) is deep in the SVC at a site where consistent phrenic nerve stimulation is achieved. With continued pacing, cryoenergy is delivered via a catheter placed at the ostium (hatched arrow). Entrance and exit block was achieved in this vein following the procedure.



their occurrence.

Pacing Maneuvers to Identify the Phrenic Nerve Course

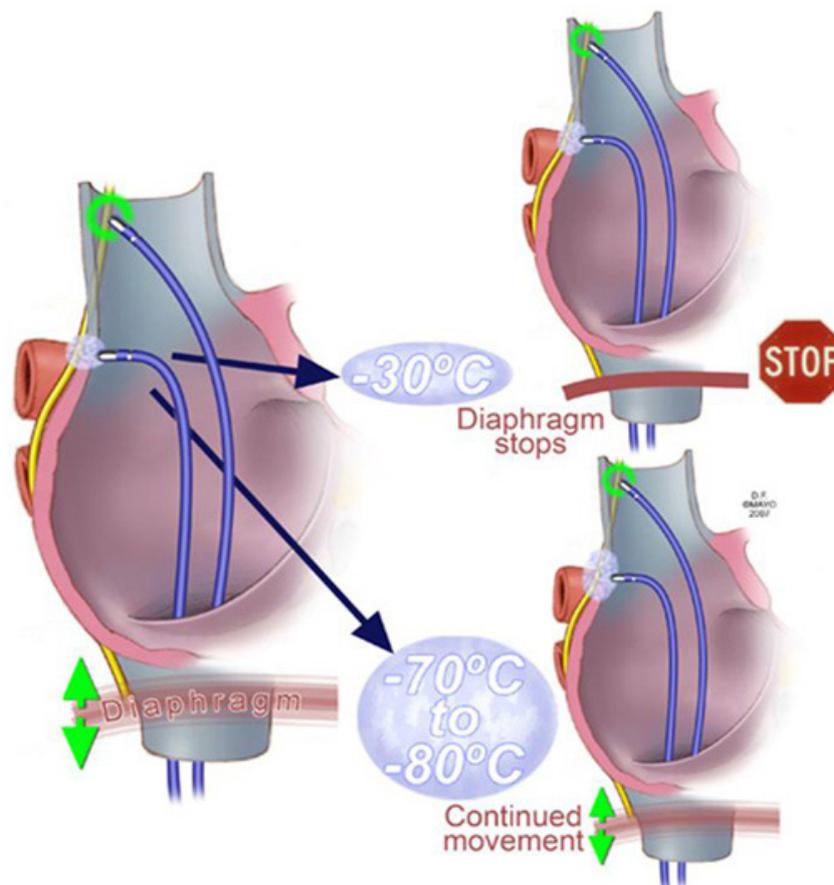
The phrenic nerve can be stimulated when pacing close to the nerve from an endocardial site. Testing for unwanted phrenic nerve stimulation when placing permanent pacemaker leads is routine, and electrophysiologists are familiar with recognizing the characteristic jerky diaphragmatic stimulation when the nerve is captured (Figure 7).

In the setting of radiofrequency ablation, the premise behind this maneuver is that if bipolar pacing done just prior to radiofrequency energy delivery results in phrenic nerve stimulation, then

ablation at that site is likely to damage the nerve. Conversely, if with pacing output, no diaphragmatic stimulation is seen, it is considered safe to deliver radiofrequency energy.

This maneuver has as its advantages - its simplicity, reproducibility, and the fact that the entire course of the nerve can be mapped out and visualized with three-dimensional mapping systems.⁵⁵ Schmidt et al performed three-dimensional electroanatomic mapping in the left and right atriums, SVC, and right pulmonary veins and combined it with a pace mapping technique in order to reconstruct the anatomic course of the right phrenic nerve. Pacing was performed at maximum output with a cycle length of 800 ms, and phrenic nerve capture was defined as either a fluoroscopically

Figure 8: Diagrammatic representation of the typical course of the right phrenic nerve in relation to the SVC and the right superior pulmonary vein (RSPV). Inset shows that while typically (solid circle) the phrenic nerve is in proximity to the distal RSPV, marked variation with no proximity or proximity relatively closer to the base also occurs.



visible or a palpable movement of the right diaphragm. As soon as capture of the phrenic nerve was obtained, the mapping catheter was moved until capture was lost. Each pacing location was marked with a different color according to the pacing response in the electroanatomic map. Hence, a delineation of the phrenic nerve's anatomic course was obtained. From this study, they concluded that pace mapping of the phrenic nerve using three-dimensional mapping can be done in a timely manner and can provide important information on the exact location of the phrenic nerve, which in turn can help prevent PNI.

There are several disadvantages and pitfalls to avoid when utilizing this technique to avoid phrenic nerve damage.

- The optimal pacing output to perform this maneuver is unknown. In one study, high output pacing at 10 V at 2.9 msec⁵⁵ was used and in another at 10 mA at 0.5 msec.⁵⁶ If too low an output is used, phrenic nerve stimulation may not occur despite the proximity of the nerve, and on the other hand, if too high an output is used, ablation may be avoided at multiple sites unnecessarily.

- The propensity to damage the phrenic nerve at

Figure 9: Isolation of the SVC using the cryoablation mapping technique discussed in the text. A circumferential mapping catheter (Lasso 1,2 - LASSO 10) was placed in the SVC. Repeated initiations of AF as well as atrial flutter from this vein were noted. Because of phrenic nerve proximity in the posterolateral portion of the SVC ostium, the cryomapping technique was utilized. Following completion of the ablation, continued rapid tachycardia (arrows) in the SVC occurred intermittently; however, exit block (no conduction to the atrium) was no evident.



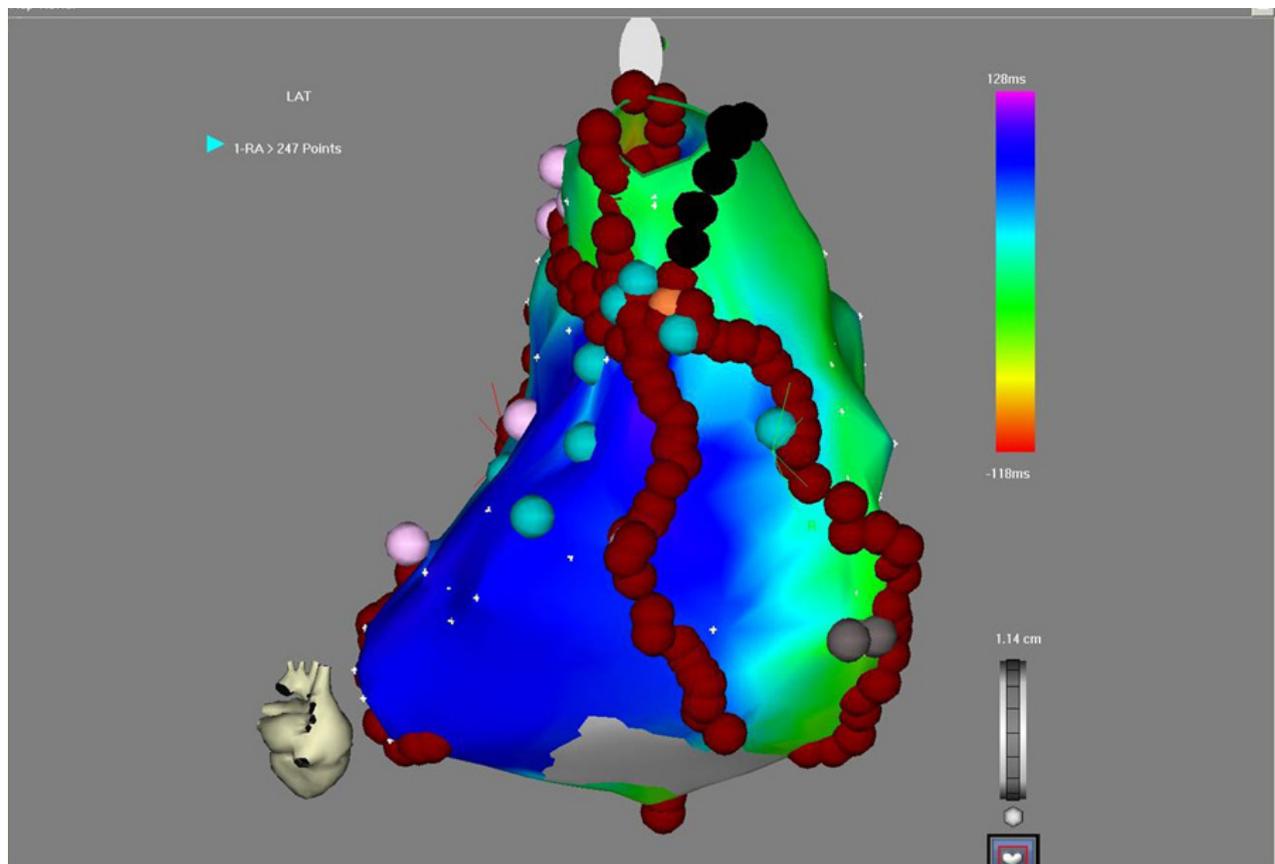
any given location likely varies with the type of catheter (irrigation vs non-irrigation), power delivery, temperature reached, duration of energy delivery, and other factors that affect lesion size. Thus, at a given site in a particular patient, phrenic nerve stimulation at 5 V at 4.5 msec may in fact signify the likelihood of PNI when ablating at 60 W for 120 sec but perhaps not at 30 W for 30 sec. The latter seconds may have been sufficient to complete circumferential isolation of the SVC.

- If the patient is under general anesthesia, a skeletal muscle paralytic agent cannot be used since phrenic stimulation then cannot be recognized whether or not capture occurs with pacing.
- Deep respiration and other movement may

cause phrenic nerve stimulation to be absent at one point in the respiratory cycle, and if ablation energy is delivered at another point, PNI may occur. Thus, care to avoid movement and continued pacing stimulation for at least two full respiratory cycles is required.

- In some instances, the operator may not wish to stimulate the atrial myocardium at the site of planned ablation. For example, ablation may be performed during a tachyarrhythmia to assess the effect of exit block on isolation of a thoracic vein. Pacing may terminate the arrhythmia, and asynchronous pacing may be required when tachycardia rates are high that may result in changing the arrhythmia to AF.
- Finally, the actual etiology of phrenic nerve damage with ablation is not known. While it is pre-

Figure 10: Electroanatomic map of the right atrium, posterior view. The black dots represent areas of phrenic nerve stimulation noted when pacing endocardially with the catheter. The red dots are ablation lesions placed with attempts to avoid proximity to the phrenic nerve while completing an AF procedure (endocardial right atrial maze).



sumed that it is a result of direct heating of the nerve, another possibility is that the blood supply (pericardial phrenic arteries) is damaged, giving rise to ischemic injury to the nerve. In this case, pacing at a site where the arterial supply exists will not result in diaphragmatic stimulation, but ablation at that site will nonetheless damage the nerve.

In summary, because of the above reasons, pacing to identify the phrenic nerve location is not foolproof. Damage to the surrounding artery supplying the phrenic nerve, changes in position, and inappropriately low pacing outputs may all mislead the operator into thinking a particular site of ablation is safe, and yet, PNI results.

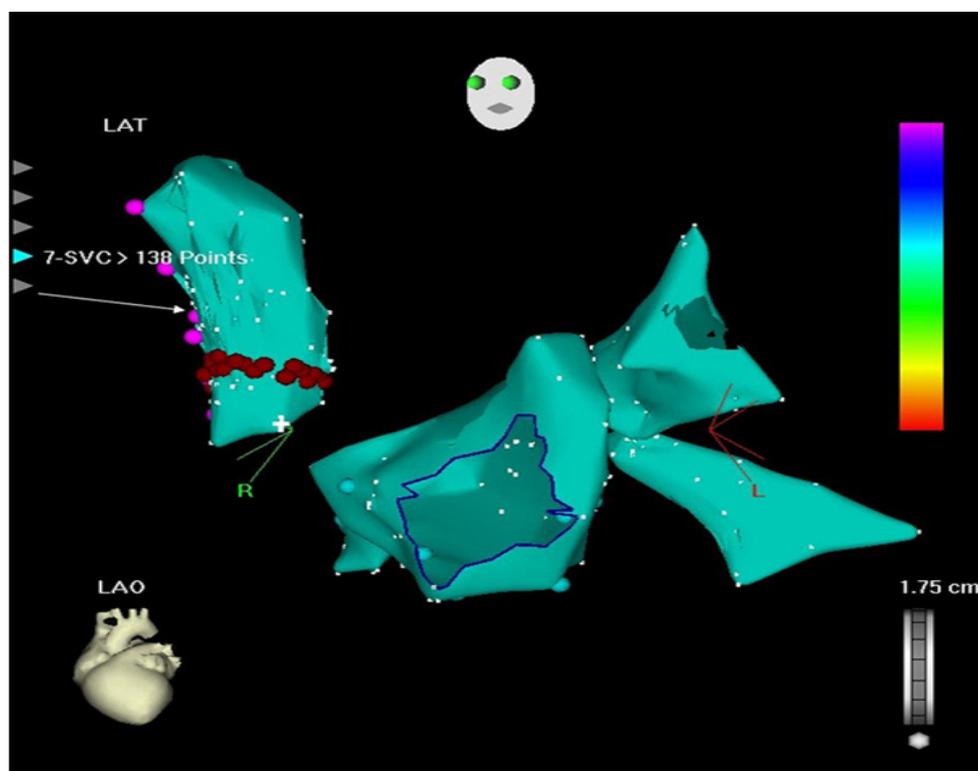
Cryo-mapping Technique

Although cryo energy can result in PNI and, by itself, does not enhance the safety of ablation, a technique has been described with cryo-mapping to avoid PNI⁵⁶ (Figure 8). The key to this maneu-

ver is the characteristic of cryo energy where cooling tissue to a certain level provides a bio-electric effect (slowing of conduction, etc.) that is temporary and can be made permanent if cooled to a more significant level. This technique of cryo-mapping is widely used in electrophysiology, particularly when ablating near the conduction system.^{57,58} For example, when ablating mid septal or anteroseptal accessory pathways, once a suitable site for ablation has been defined (pathway potential, etc.),⁵⁹ cooling to -30 - $(-)$ 35°C is first done. If pathway conduction is lost but AV nodal conduction is still present, then further cooling to -70 - $(-)$ 75°C is performed with the aim of permanently destroying the accessory pathway. In contradistinction, if AV block occurs at -35°C , then cooling is turned off and AV node conduction allowed to return and that site not chosen for further energy delivery.

An analogous maneuver can be done to assess phrenic nerve risk at a given ablation site. Here, a standard electrode catheter is placed high in

Figure 11: Electroanatomic map of the left atrium and the SVC. Following ablation in the left atrium, the SVC continued to trigger arrhythmia. Isolation of this vein was attempted. Care was required to avoid ablation energy delivery near sites of phrenic nerve stimulation (pink dots). Ablation dots are tagged red.



the SVC and the catheter moved until consistent phrenic nerve stimulation at all stages of the respiratory cycle noted. Cryoablation is then performed at a site where radiofrequency energy delivery was considered high risk to cause phrenic damage. If, when cooling to -35°C , diaphragmatic stimulation that had up to that point been observed consistently when pacing within the SVC occurs, then cooling is stopped and ablation not performed. However, if phrenic nerve stimulation continues despite cooling at the questionable site at -35°C , then further cooling to -70 – $(-75)^{\circ}\text{C}$ is undertaken to ablate the tissue and enable the obtaining of entrance block into the SVC (Figure 9).

There are several potential disadvantages with this maneuver.

- It is possible that long-term phrenic nerve damage will occur even when cooling to -35°C .

- If phrenic nerve stimulation stops when ablating at -35°C , cryo energy is simply stopped and no solution of how to isolate the vein is offered. Dib et al developed a new method using cryomapping to successfully ablate at the SVC/right atrium junction despite phrenic nerve proximity [56]. Between January 2001 and January 2007, 110 patients had partial or circumferential radiofrequency ablation at or near the SVC/right atrium junction. Of these 110 patients, 66 had phrenic nerve proximity as ascertained by pacing at 10 mA output. In all but 7, the junction was ablated at points where phrenic nerve proximity was not present. In the remaining 7 patients who had continued arrhythmogenicity despite attempts to modify the substrate, they paced 4 cm into the SVC where consistent phrenic nerve stimulation was obtained. In 1 patient, diaphragmatic stimulation ceased at -30°C , and the energy delivery was stopped. In 6 of 7 patients, with continued diaphragmatic capture, cryoablation at $-70/-80^{\circ}\text{C}$ was then performed.

- Meticulous attention is required to be sure that the pacing site is cephalad to where cryo energy is being delivered. This is because diaphragmatic stimulation will still occur if the phrenic nerve is paced caudal (lower) than where complete transection of the phrenic nerve had occurred.

Electroanatomic Mapping

Three-dimensional electroanatomic mapping is a frequently employed technique during mapping and ablation procedures.^{60,61} Typically, the local electrogram voltage and activation times relative to a standard reference are tagged using this system and a three-dimensional color-coded map rendered.

Pacing maneuvers as described above are performed to identify sites for phrenic nerve stimulation as seen. These points are then tagged on the system as phrenic nerve location sites, and the course of the nerve can be traced out. The ablationist may now be able to design a set of ablation lesions that is likely to result in electrical disconnection of the SVC (or right superior pulmonary vein) without damaging the phrenic nerve (Figures 10 and 11).

Since this maneuver is an extension of the pacing maneuvers to identify phrenic nerve stimulation, the same limitations apply.

Online Imaging of the Phrenic Nerve

Ideally, reliable realtime imaging of the phrenic nerve would allow beat-to-beat assessment of the likelihood of damaging this structure with ablation. Intracardiac ultrasound can occasionally be used to define phrenic nerve location; however, careful imaging is located, and validation with pacing is still needed because of the lack of surety of knowing that another structure is not being imaged.

CT and MRI have been used as diagnostic tools in the assessment of peripheral nerve lesions.³⁴ Although conventional CT visualization of the phrenic nerves, even with high resolution is difficult,³⁵ studies in the past have attempted to identify them based on characteristic clues and by structures within its field.^{34, 62} However, more recently, the use of 64-slice MDCT has enabled clearer visualization and assessment of the phrenic nerves and other mediastinal structures related to cardiac anatomy.⁶³

The proximity of the pericardiophrenic artery and vein to the phrenic nerve has been a useful ana-

tomical indicator in the delineation of the phrenic nerve. Matsumoto uses this consistent relationship to define the right and left pericardiophrenic bundles (RPCB and LPCB).⁶³ The LPCB was visible in 74% of patients with frequent contact on the left atrial appendage. The LPCB was identified most effectively on axial images at the level of the lateral left ventricular wall as a rounded structure with variable density. The RPCB, on the other hand, was detected in only 47% of patients in this study. Visualization of the right and left PCBs are said to be dependent on the amount of adipose tissue within the bundles, flow in the pericardiophrenic vessels, pleural folds, age, sex, and related technical challenges such as minimal contrast differential between RPCB and mediastinal structures.^{62, 63}

In a more recent study, the phrenic nerve has been identified by means of electroanatomic mapping.⁵⁵ In almost 90% of patients, the phrenic nerve was successfully captured. This technique uses 3D mapping and pace mapping over a craniocaudal distance of around 40 mm to trace the anatomic course of the nerve. In addition to being able to identify the course of the right phrenic nerve in a reasonable timeframe in patients, the phrenic nerve relationship with the SVC and the RUPV is also possible with electroanatomic mapping.⁵⁵

However, to date, no direct phrenic nerve visualization using imaging technology is available. The high degree of variability in the course of the phrenic nerves, especially the right phrenic nerve, remains a challenge to the effective characterization of these nerves through imaging.

Management of Patients with PNI

Even with the highest degree of caution and the use of all available maneuvers to identify the phrenic nerve, ablationists must be prepared to manage this condition should it occur. Prompt diagnosis is important despite the lack of availability of any specific treatment since unnecessary evaluation for shortness of breath may otherwise occur. An understanding of the natural history of PNI along with the availability of certain therapeutic interventions that may be considered in specific instances is required. Unfortunately, accurate knowledge for the likelihood and timing of phrenic nerve function recovery and selecting patients for specific interven-

tions is unknown.

Diagnosis

(Phrenic nerve injury is suspected when a patient complains of shortness of breath, often described as difficulty in taking in a deep breath, following ablation. The diagnosis is also often picked up on routine chest x-rays in otherwise asymptomatic individuals. The characteristic finding is elevation of the affected hemidiaphragm (usually right) that was not present prior to ablation. A similar radiologic appearance may result from subdiaphragmatic fluid collections, subpulmonic effusions, or atelectasis following ablation. When doubt exists, a sniff test with cine fluoroscopy is performed when the patient is asked to sniff. Normally, the diaphragm will move down with sniffing, but a paralyzed diaphragm will move paradoxically upward while the normal diaphragm moves down.^{19, 20, 64, 65}

Natural History of PN

Although exact timing of recovery and whether recovery is certain is not presently known, most patients appear to recover phrenic nerve function (following ablation-induced damage) before a 6-12-month timeframe.^{16, 38, 50, 51}

Treatment of Persisting Symptomatic PNI

At present, there is no widely available simple method of restoring phrenic nerve or diaphragmatic function. In certain cases, plication of the diaphragm to avoid elevation of the diaphragm and adverse mechanical impact on respiration can be considered. However, the role of this procedure in adults is not clear as only isolated case reports or small series have been reported.⁶⁶⁻⁶⁹ Phrenic nerve stimulators placed surgically can also be considered in rare cases. Diaphragmatic pacing is the stimulation of the phrenic nerves with electrical current via an implanted pacemaker, resulting in the contraction of the diaphragm.⁷⁰ Dr. Surani and colleagues present a case report of a 60-year-old female with confirmed right hemidiaphragm paralysis. She underwent successful placement of a right diaphragmatic pacemaker, and her symptoms rapidly abated.⁷⁰ Lue et al sought to evaluate the

long-term complications of phrenic nerve pacemakers to see if they were beneficial to patients or not.²¹ They studied three patients who had had phrenic nerve pacemakers for over 20 years. Although pulmonary complications and the surgery itself are a hindrance, the patients' independence and quality of life were greatly improved due to these devices.

Summary

Phrenic nerve injury is a well-recognized complication of radiofrequency ablation procedures for AF. High-risk locations include the ostium of the SVC and within the RUPV. An accurate knowledge of the anatomy of this nerve, its propensity for a variable course, and knowledge of maneuvers that can identify nerve proximity will allow ablationists to perform successful venous isolation with low risk of nerve injury.

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