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EDITORIAL COMMENT

Epicardial Targets With Endocardial Ablation

Risks for the Unseen*

Samuel J. Asirvatham, MD, FHRS,[a,b,c,d] Martin van Zyl, MBBCH,[a] Fatima Ali-Ahmed, MD[a]

Endocardial ablation for cardiac arrhythmias ideally creates transmural myocardial lesions at targeted sites. Inadvertent thermal damage to noncardiac structures such as the esophagus and coronary vessels represents collateral damage that we seek to minimize. However, when the target itself is epicardial, then ablation is necessary beyond the cardiac wall, and preventing unwanted damage becomes a matter purely of location rather than methods of controlling the delivery of ablation energy. Cardioneural ablation, a promising technique for managing cardioinhibitory syncope and atrial fibrillation, is such a situation where the epicardially located ganglionated plexi (GP) are targeted via endocardial ablation.

In this issue of *JACC: Case Reports,* Scanavacca et al[1] provide a thought-provoking and well-illustrated report of two patients who experienced sinus node (SN) dysfunction when radiofrequency-based GP ablation was done. This led the authors to investigate further into the mechanism of SN injury and possible ways to prevent this complication.

To appreciate the significance and suggestions from the discussion by Scanavacca et al,[1] we must understand the exact anatomical location of the SN, the arterial supply to the SN, colocalization with nodal ganglia, and the vagaries of thermal damage with radiofrequency ablation.

ANATOMY OF THE SINUS NODE AND ITS ARTERIAL SUPPLY

The SN is a group of subepicardial cells with intrinsic automaticity located in the region of the sulcus terminalis at the junction of the embryonic sinus venosus and primordial atrium. The SN cells span from more dense superior locations inferiorly along the sulcus terminalis, sometimes up to the right atrial vestibule.[2] Similarly, the arterial supply to the SN is also varied but typically involves a branch from the right coronary artery in more than half of individuals, the left circumflex in a third, and uncommon branching from the aorta and bronchial arteries in the remainder (**Figure 1**).[3,4] As the authors emphasize, regardless of the sinoatrial pattern of origin, most variants involve a course at the atriocaval and aortocaval junction regions, which is the location targeted when the right superior ganglion is ablated.

More pattern-specific damage to the SN arterial supply may occur with other ablative approaches, such as superior vena cava isolation, left atrial roof ablation (where on the Bachman bundle, the SN artery from the left circumflex traverses), or automatic roof atrial tachycardia ablation (**Figure 2**).[5]

COLOCALIZATION

A now largely defunct procedure was SN ablation for inappropriate sinus tachycardia. Electrophysiologists remember how difficult it was to permanently ablate the SN even to a modifying extent because of its epicardial diffuse position. By contrast, arterial damage as far away as the left endocardial ridge or

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From the [a]Division of Cardiovascular Diseases, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA; [b]Department of Pediatrics and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota; [c]Department of Biomedical Engineering, Mayo Clinic, Rochester, Minnesota, USA; and the [d]Department of Clinical Anatomy, Mayo Clinic, Rochester, Minnesota, USA.

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vein of Marshall in patients who have a left-sided origin for the SN artery can be immediate and dramatic. Regardless of the origin of the artery, it eventually supplies nearly all of the SN complex and the closely related cardiac ganglia. Is such anatomical proximity and exactness in supply a coincidence? During cardiac development, as the heart invaginates into the pericardial sac, structures that leave or enter the heart must do so through gaps or convolutional sinuses in the pericardial space. Thus, the developing SN from the migrating secondary heart field, the epicardially derived arterial supply, and the migrating neural crest cells into the cardiac ganglia share a common method of entry and location by virtue of their developmental migration.[6]

RECOGNITION OF SN INJURY

The 2 cases reported by Scanavacca et al[1] come from a larger series of 42 patients undergoing GP ablation for cardioinhibitory syncope, thus representing a moderate incidence of about 5%. The authors recognized injury when sinus pauses or junctional beats were noted during ablation. Unknown, however, are gradations of injury where presumably ischemia or late sinus injury may manifest either later in the procedure or for variable times after discharge.

AVOIDING SN INJURY WITH ENDOCARDIAL CARDIONEURAL ABLATION

Since cardioneural ablation is performed for life-altering but not life-threatening conditions, even modest rates of complications may preclude more widespread acceptance. As such, a thorough exploration of possible ways of preventing collateral damage with these procedures is required.

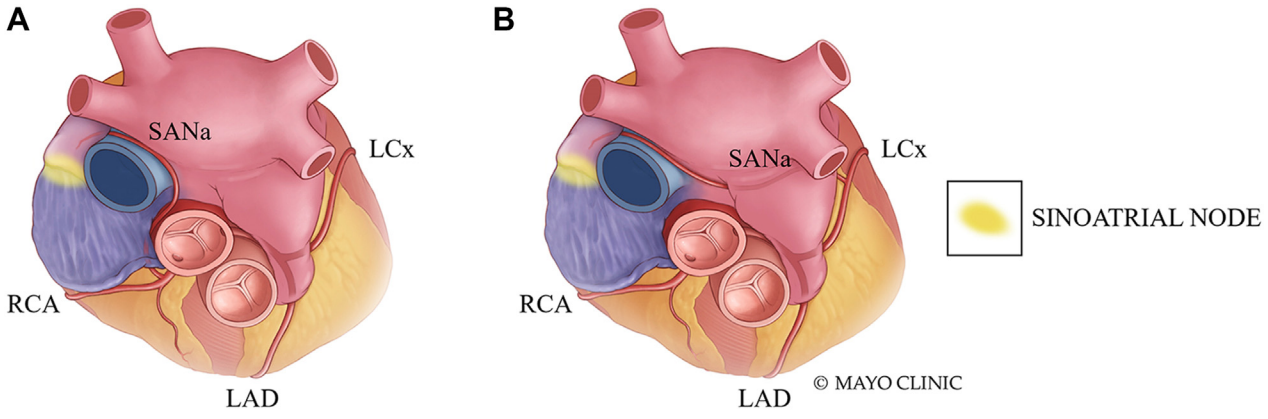
IMAGING. The authors propose high-quality CT angiography before ablation to understand the course of the SN artery and the relationship to known targeted ganglia sites. This imaging can be challenging and requires meticulous contrast phasing and gating to the cardiac cycle. Coregistered CT and angiographic images with created 3-dimensional maps would likely be helpful and add to the complexity of the procedure.

IMPROVING SPECIFICITY. Although there may be an inherent risk to the SN artery when targeting the ganglia, stimulatory maneuvers to document the presence of ganglia may limit ablation sites and quantitatively decrease the likelihood of collateral damage.

EPICARDIAL APPROACHES. Paradoxically ablating in the epicardium may be safer in some instances because limited ablation may reduce thermal effects as a result of being in contact with the epicardially located GP.

HIERARCHY APPROACHES. It is unclear in the science of cardioneural ablation at this point whether complete deganglionation in a nonindividualized manner is necessary for benefit, because certain ganglia predominantly affect the atrioventricular (AV) node, atrial node, or SN, and interganglia effects may be patterned only ablating GP relevant for the

FIGURE 1 Common Anatomical Variations of the Sinoatrial Nodal Artery



(A) Superior view of the heart illustrating two common variants of the SANa origin as it courses towards the sinoatrial node region. The most common configuration in over one half of patients is an origin from the proximal RCA coursing over the interatrial septum and around the superior vena cava to the superior sulcus terminalis. **(B)** In one third, the SANa arises from the LCx and may travel through the left lateral ridge, over the roof of the left atrium to reach the superior vena cava. LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery; SANa = sinoatrial nodal artery.

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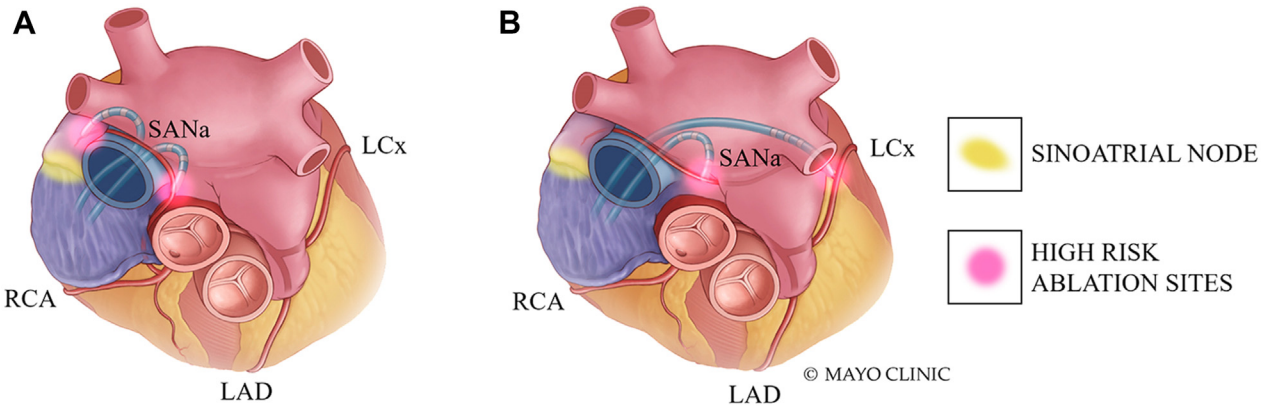
SEPTEMBER 21, 2022:1176–1179

FIGURE 2 Sites of Vulnerability for Sinoatrial Nodal Artery Injury



(A) When the SANa arises from the proximal RCA, the SANa can be injured by ablation at sites either septal or lateral to the superior vena cava depending on its anatomical course. **(B)** When the SANa originates from the LCx, injury to the SANa may also occur with ablation in the left atrium on the superior septum, left atrial roof, or at the left lateral ridge. Abbreviations as in Figure 1.

condition being treated (neurocardiogenic syndrome versus AV block versus atrial fibrillation) may minimize collateral effects better.

ELECTROPORATION (PULSED-FIELD ABLATION). Radiofrequency ablation, like to laser ablation, cryoablation, and microwave ablation, relies on thermal effects. Transmission of heat is difficult to control and may equally ablate arterial tissue, neural tissue, and myocardial tissue based on the temperature reached. Pulsed-field ablation has the potential to ablate tissue without heating or cooling in a manner limited to the area between the electrodes used for delivering the direct current pulses. Although not yet definitively established, arterial damage may be less likely with pulsed field ablation. By contrast, myelinated nerves appear to be relatively protected from electroporation. However, experimental data suggest that the ganglia themselves can be ablated if close electrode proximity is assumed.[7-9]

ANATOMICAL CORRELATES. Scanavacca et al[1] explored in their report a possible unique marker for proximity of the right superior ganglia to the SN arteries. They found unusual angulation between the horizontal plane and the ascending aorta. Their finding is in keeping with prior reports exploring this anatomical covariance. However, larger studies will need to be done with blinded observers because the horizontal plane and asymmetrical chamber enlargement may confound this relationship, specifically the impingement of the aortic knuckle onto the atriocaval junction.

CONCLUSIONS

Scanavacca et al[1] should be congratulated on a clear, insightful, well-illustrated report of a complication when performing a promising procedure that is not yet completely understood. The coming together of cardiac development, precise anatomical relationship, physiological validation, and the unique biophysics of new energy sources should challenge and excite a generation of invasive electrophysiologists to bring forward to patients an effective, safe, and impactful procedure.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The Mayo Clinic has pursued protection of intellectual property including in the form of patents and patent applications, naming Dr. Asirvatham as inventor, related to ablation including pulsed field ablation for treatment of arrhythmias including autonomic modulation, and licensed to AtriAN Medical Ltd (Galway, Ireland). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Samuel J. Asirvatham, Mayo Clinic, 200 First Street SW, Rochester, Minnesota 55905, USA. E-mail: asirvatham.samuel@mayo.edu.

REFERENCES

1. Scanavacca M, Rivarola E, Torres R, et al. Sinus node artery occlusion during cardiac denervation procedures. *J Am Coll Cardiol Case Rep*. 2022;4:1169–1175.

2. Boullin J, Morgan JM. The development of cardiac rhythm. *Heart*. 2005;91:874–875.

3. Ozturk E, Saglam M, Bozlar U, et al. Arterial supply of the sinoatrial node: A CT coronary angiographic study. *Int J Cardiovasc Imag*. 2011;27:619–627.

4. Vikse J, Henry BM, Roy J, et al. Anatomical variations in the sinoatrial nodal artery: A meta-analysis and clinical considerations. *PLoS One*. 2016;11:e0148331.

5. Killu AM, Fender EA, Deshmukh AJ, et al. Acute sinus node dysfunction after atrial ablation: Incidence, risk factors, and management. *Pacing Clin Electrophysiol*. 2016;39:1116–1125.

6. Sylva M, van den Hoff MJ, Moorman AF. Development of the human heart. *Am J Med Genet A*. 2014;164A:1347–1371.

7. DeSimone CV, Kapa S, Asirvatham SJ. Electroporation: Past and future of catheter ablation. *Circ Arrhythm Electrophysiol*. 2014;7:573–575.

8. Sugrue A, Vaidya V, Witt C, et al. Irreversible electroporation for catheter-based cardiac ablation: A systematic review of the preclinical experience. *J Interv Card Electrophysiol*. 2019;55:251–265.

9. van Zyl M, Ladejobi AO, Tri JA, et al. Reversible atrioventricular conduction impairment following bipolar nanosecond electroporation of the interventricular septum. *J Am Coll Cardiol EP*. 2021;7:255–257.

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