Intracardiac Echocardiography Guided Anatomical Ablation of the Arcuate Ridge for Drug Refractory Inappropriate Sinus Tachycardia

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Abstract

INTRODUCTION: Inappropriate sinus tachycardia (IST) is a common condition with frequently not tolerated beta-blockers or ivabradine and a high rate of complication in ablation strategy; we describe an alternative anatomical approach of sinus node modulation. **METHODOLOGY:** This retrospective study describes a case series of 6 patients from two centers diagnosed with symptomatic IST undergoing sinus node ablation. **RESULTS:** The mean age was 40.6 ± 13.9 years; five of the six patients were female, 100% of patients reported heart palpitations, and 66% reported dizziness, the average HR on a 24-h Holter was 93.2 ±7.9 bpm. HR during the first stage of a stress test using a standard Bruce protocol was 150 ±70 bpm, The average HR on 24-hour Holter post-ablation was 75 ± 5.6 bpm, the sinus rate HR during stage 1 of a Bruce protocol exercise stress test was 120 ± 10 bpm. **CONCLUSION:** This is the first case series reporting the acute and long-term results of a novel anatomical approach for SNM to treat IST targeting the AR under ICE guidance, The novel anatomic ICE-guided catheter ablation approach aimed to identify the earliest activation at the AR with an extension of RF lesions towards its septal region seems effective and safe to modulate the SN in symptomatic patients with IST refractory to medical treatment.

INTRODUCTION

Inappropriate sinus tachycardia (IST) is a common condition that causes an abnormally high resting heart rate (HR) with an exaggerated chronotropic response during exercise and/or stress, and is associated with debilitating symptoms, exercise intolerance, and near syncope[1]. Pharmacological treatment with B-blockers, calcium channel blockers and/ or Ivabradine are considered first-line therapies for symptomatic patients[2]. However, these medications are frequently not tolerated due to side effects or are ineffective in controlling patient's symptoms[3]. Radiofrequency catheter ablation (RFA) aimed at sinus node modulation (SNM) has been proposed as an alternative therapy for refractory patients, with success rates varying between 23% and 85% in the published literature, and with a variable incidence of procedural related complications (9.5 to 50%) such as phrenic nerve (PN) injury, pericarditis, superior vena cava (SVC) stenosis, cardiac tamponade and iatrogenic sinus node (SN) dysfunction requiring pacemaker implantation[4]. The most common RFA approach for SNM is based on the identification of the upper part ("head") of the SN complex that is activated during higher HR using 3D mapping and is expected to be localized at the lateral aspect of the SVC-right atrium (SVC-RA) junction, according to early anatomic descriptions of sinus node myoarchitecture[5]. In order to activate the higher hierarchy of the SN cells, high doses of isoproterenol are used to increase SN automaticity, and RFA is applied over the earliest activation site. In most cases, additional RFA includes an extension of the RF lesions towards the posteroinferior aspect of the SN complex ("tail") located along the superior aspect of the Crista Terminalis (CT), to achieve clinically significant modulation of the SN activity (Fig. 1a and 1b). An extensive RFA from the "head" to the "tail" in this region could increase the risk for procedural complications from collateral injury of structures such as the PN.

We describe the systematic use of an anatomical approach for SNM to treat IST under intracardiac echography (ICE) guidance, aiming to identify and ablate the earliest activation sites at the arcuate ridge (AR) in the antero-superior SVC-RA junction, and extending the RFA lesion set towards its more septal aspect, at the level of the interatrial septum.

The presented approach is based on the following considerations: 1. ICE is the most accurate real-time imaging technology to delineate the SVC-RA junction[6]. 2. In redo procedures, the extension of ablation from the lateral SVC-RA junction to the AR was needed to obtain final control of HR, as previously reported (Fig. 1c and 1d)[7]. 3. The high doses of isoproterenol required to increase the HR during the procedure are usually poorly tolerated, affecting the accuracy of identifying the most anterosuperior and septal extension of the upper SN region, target for RFA.

LEARNING OBJECTIVES

- Describe the anatomical relationship between the SN and the AR, as an anatomical reference to guide SNM.
- Showcase the use of ICE imaging to identify the relevant anatomy for RFA of IST.
- Discuss the rationale for an anatomical approach that includes ablation of the earliest activation site at the AR, and RFA lesion extension to its more septal rather than lateral portion.
- Present the results of this novel approach for SNM in a case series.

METHODS

PATIENT CHARACTERISTICS

This study describes a case series of 6 patients from two centers with a diagnosis of symptomatic IST based on a 24-hour, 30-day cardiac rhythm monitor and/or implantable cardiac rhythm monitor, and exercise treadmill stress test, which failed pharmacological control of symptoms and tachycardia, who underwent endocardial RFA using a novel anatomical approach guided by ICE. The study was approved by the Institutional Ethics Committees from all participating centers.

PROCEDURE

After obtaining informed consent, all patients underwent an invasive electrophysiologic study (EPS) under moderate sedation with Midazolam and Fentanyl. Programmed electrical stimulation and burst pacing from the high right atrium, coronary sinus, His bundle region, and right ventricle were used to evaluate atrioventricular conduction and exclude other arrhythmias. 3D Electro-anatomic mapping (3DEAM) (Carto 3, Biosense Webster OR EnSite Precision, Abbott) was used in all cases. Femoral venous access was obtained under ultrasound guidance, and an ICE catheter was advanced through femoral access into the RA. From the home view position, the ICE probe was rotated clockwise to visualize the interatrial septum, and then tilted posteriorly to obtain a long-axis view of the SVC[8] (Fig. 2). Slight adjustments using clockwise and counter-clockwise rotation from this position allowed for visualization of the lateral and septal aspects of the AR, identified as a band of atrial myocardium in the region of the SVC–RA junction, typically connecting the CT to the interatrial septum near its superior limbus[7] (Fig. 2). Incremental doses of isoproterenol infusion were used to obtain sinus tachycardia. Once stable sinus tachycardia at the highest tolerated isoproterenol dose (up to 10 mgc/min) was observed, 3DEAM of the SVC-RA region were created using a high-definition multipolar catheter (PENTARAY NAV®, Biosense Webster OR Advisor HD Grid™, Abbott) advanced through a deflectable sheath into the RA. In order to obtain accurate activation points in the AR and avoid point extrapolation, manual annotation was used as deemed necessary, to adjust tags under direct ICE visualization. The course of the right PN was localized by pacing at high output (20 mA/1 ms) and tags were manually annotated on the 3DEAM under ICE visualization when diaphragm stimulation was present (Fig. 3). Local activation times were automatically defined from a stable reference atrial electrogram (EGN), to the maximum negative dV/dT at the local unipolar signal on the mapping catheter. RF applications were performed at the earliest activation location in the AR, using an open irrigated-tip catheter with contact force sensing capabilities (THERMOCOOL SMARTTOUCH SF®, Biosense Webster OR TactiCath™, Ab-

bott). RF power was set at 30 to 40W, with a contact force between 15-20 gm at the operator's discretion. Each RF application was monitored for an impedance drop of at least 10 Ohms, with elimination of local automaticity induced by RFA continued until a 50% reduction in the amplitude of the local bipolar EGM was obtained. The RF applications were anatomically extended from the earliest region at the AR towards its septal aspect, until the elimination of automaticity at this region and/or obtaining a decrease in HR of 25% on Isoproterenol infusion was achieved (Fig. 4 d,e) (usually coinciding with a change of the P-wave axis on the horizontal plane of the ECG). Anatomic extension of the RF lesions towards the septal AR was performed on all study subjects, independent of the local activation times recorded at this location. Repeat activation and voltage maps were performed if a significant decrease in HR was not obtained with initial RFA and additional RF applications were performed on the earliest site at the AR with careful delineation of the PN on the new map. Post-procedure, patients remained in the hospital overnight under continuous ECG monitoring and were discharged the next day if no complications occurred.

Follow-up included an exercise stress test at 3 months, a 24-hour Holter, 30-day cardiac rhythm monitor or interrogation of an implanted cardiac rhythm monitor at 3, 6, and 12 months, and longitudinal clinic visits to assess symptom status and medication adjustments.

STATISTICAL ANALYSIS

Continuous variables are expressed as the mean ± SD values, and categorical variables are expressed as the number and percentage of patients. A Student t-test or Mann-Whitney U test was used, as appropriate, to analyze the differences in the continuous variables, and the chi-square test was used to analyze the differences in the dichotomous variables. All statistical analyses were performed with R version 4.1.0 software.

RESULTS

Patient characteristics

Six prospective patients from 2 centers were included. The mean age was 40.6 ± 13.9 years; five of the six patients were female, 100% of patients reported heart palpitations, and 66% reported dizziness (Table 1). No patients presented with POTS and 2 patients had VVS. Other prevalent diseases included systemic lupus erythematosus (n: 1, 16%), fibromyalgia (16,6%) and anxiety disorder (16,6%). No patients reported other chronic diseases such as hypertension, diabetes or heart failure. 3 patients had undergone previous ablations of other supraventricular tachycardias (atrioventricular accessory pathway, premature atrial contractions and AVNRT). Finally, two patients had undergone previous SNM using the conventional method of high doses of isoproterenol and ablation from the site of maximum precocity extending laterally. Before the procedure, the average HR on a 24-h Holter was 93.2 ±7.9 bpm. HR during the first stage of a stress test using a standard Bruce protocol was 150 ±70 bpm (Table 1).

RESULTS

Procedural data

The average procedural time was 213 ± 60.9 min, and an average radiation dose of 5862,5 mGy. Baseline pre-ablation HR was 100 ± 8.5 bpm, and HR at the maximal tolerated dose of Isoproterenol before RFA was 170 ± 19 bpm. Following RFA, average HR was 74.5 ± 6.5 bpm (p=0.035), and maximal HR with the same pre-ablation Isoproterenol doses was 132 ± 23 bpm (p=0.036). Average HR during 24 h Holter pre was 93.16 ± 7.08 and post RFA 76.66 ± 4.92 (p=0.031).

The area of earliest activation was located at the AR (11 or 12 O'clock landmark from a caudal view of the SVC-RA junction) in all patients. Extension of the RF lesions from the earliest region at the AR towards its more septal region was needed in all the included patients and produced a transitory HR increment before obtaining a significant and sustained HR drop of around 25%. Notably, the activation recorded on the septal aspect of the AR was later compared with the earliest site from its lateral aspect. The mean distance between the RF applications at the earliest region on the AR and the most septal ablated sites was 6 mm (Fig 4 d,e). The distance of the PN to the nearest RF application was 5mm (Fig 4 d,e).

Clinical outcomes

After a mean follow-up of 654 ± 417 days (Table 1), one patient required reinitiating Ivabradine (at a lower dose than pre-ablation) for control of symptoms, and one patient with a history of fibromyalgia complained of mild exercise intolerance, despite no evidence of sinus node dysfunction on post-ablation stress test and heart rhythm monitoring. No patients reported heart palpitations or syncope during follow-up. The average HR on 24-hour Holter post-ablation was 75 ± 5.6 bpm, the sinus rate HR during stage 1 of a Bruce protocol exercise stress test was 120 ± 10 bpm, and the chronotropic response was classified as normal by an independent cardiologist in all the patients. (Table 1).

DISCUSSION

This is the first case series reporting the acute and long-term results of a novel anatomical approach for SNM to treat IST targeting the AR under ICE guidance. The main findings of our study are as follows: 1. ICE allowed real-time visualization of the lateral and septal aspects of the AR at the level of the SVC-RA junction; 2. RF applications at the AR earliest activation site during maximally tolerated isoproterenol infusion (up to 10 mcg/min), produced a suboptimal reduction of the HR in all patients; 3. Extending the ablation lesion set from the earliest site at the AR towards its septal region led to acute and long-term modulation of the SN in all patients without the need to extend the ablation lesion set towards the lateral/posteroinferior extension, thus avoiding risk for PN damage or SN dysfunction.

The importance of the recognition of the AR for SNM by ICE was previously described by Asirvatham et al. who reported a case of a 48-year-old woman with multiple failed ablation procedures for IST performed at the high posterolateral RA earliest site of activation[7]. The patients underwent a repeat procedure showing early activation at the lateral aspect of the SCV-RA. However, detailed 3D mapping under ICE visualization demonstrated an even earlier activation site in the AR area, where RFA was effective and led to definitive control of the patient's arrhythmia and symptoms. In our study, ICE also facilitated the identification of the AR early activation sites, initially masked in all the patients during contact activation mapping, by extrapolation of early activation sites between the SCV and the RA. Our approach included correction of this extrapolation based on tagged points on the surface of the AR, taken with the ablation catheter under ICE guidance, and including those activation points on the corrected anatomy, which included the AR. Based on our case experience and anatomical understanding of this region, we believe AR recognition by ICE increases procedure efficacy and safety, by focusing the mapping and ablation efforts on the AR and preventing unnoticed ablation inside the right atrial appendage. Notably, mapping and ablation of the earliest activation sites alone did not produce the desired HR reduction of around 25%. However, an anatomic extension of the ablation lesion set towards the septal aspect of the AR, performed independently of the local activation times, produced a transient HR increment followed by a significant HR reduction >25% and a change in the P wave axis. These findings suggest that part of the SN complex was located in the septal region, but it was not identified by the activation mapping under the isoproterenol effect. Notably, the reduction of the HR was sustained during follow-up, measured by cardiac monitoring and stress ECG, and associated with symptomatic relief. Despite the encouraging results of this novel anatomic approach to modulate the SN, our investigation does not provide insight into the mechanistic role of the septal aspect of the AR on IST. Furthermore, empirically extending the ablation target to the septal and not the lateral region of the AR, may not achieve the desired HR modulatory effect in some patients, owing to different characteristics in their SN anatomy and extensions. Anatomical studies traditionally describe the SN complex as a crescent-shape structure with a "comma" disposition, in which the "head" lies subepicardial within the terminal groove, formed by the lateral junction of the SCV with RA, and the "tail" extends toward the posteroinferior aspect of the CT reaching the inferior vena cava and RA junction[9,10] (Fig. 1a). This usual "comma" depiction of the SN complex on anatomic drawings, has directed efforts of mapping and ablation for SNM to the lateral SVC-RA junction where the PN resides. Although the "comma" anatomical disposition is the most prevalent, a "horseshoe" arrangement of the SN has also been found in around 12% of hearts[9]. In the "horseshoe" arrangement, the SN complex is situated both medial ("head") and lateral ("tail") to the mid-line of the SCV-RA junction at the AR[10] (Fig. 4 a, b). This anatomic variation of the SN showing

an extension towards the septal aspect of the SCV-RA junction seems to be validated by the first "in situ" 3-D visualization of the human cardiac conduction system performed by means of advanced imaging tools of virtual CT dissection on human cadavers[11](Fig. 4 c). Based on this anatomic variation, it is plausible that the extension of RF ablation from the earliest activation site at the AR towards its septal region could explain the results of our proposed approach described in this study. As mentioned previously, the usual target for SNM is defined as the earliest activation site on the AR under the effect of Isoproterenol. A concept based on physiological studies demonstrating shifting of earliest activation from the "tail" to the "head "of the SN complex under progressive HR increments[4]. However, if patients do not tolerate high doses of Isoproterenol during the procedure, it is possible that the most anterosuperior aspect and septal extension of the SN are not activated, and therefore not targeted, leading to suboptimal results, unless extending the lesion empirically towards the septal AR is performed (electro-anatomical approach). Coincidentally, an electroanatomic analysis of the sinus impulse propagation in normal human atria has shown that the area of earliest activation in the RA has a "spindle" shape in 5 of 7 patients and a "horseshoe" shape in the remaining 2 located between the SCV-RA junction, which could represent the functional characterization of this anatomic SN variation[12]. Finally, it is possible that the extension of RF delivery toward the septal aspect of the SCV-RA junction at the AR in proximity to the interatrial groove could produce a modification of the neural input of the SN with an additive neuromodulatory effect. Interrupting autonomic nervous input to the sinus node by isolating right pulmonary veins, superior vena cava, and ablating fat tissue surrounding the sinus node is an integral part of the surgical treatment of IST[13]. A recently published SN sparing hybrid ablation technique including RF bipolar clamp isolation of the superior and inferior vena cava and lateral ablation line across the Crista terminalis while sparing the SN region (plus adjunct RF endocardial touch-up to complete lesion sets in 46% of cases); was compared to a conventional SNM approach (endocardial and/or epicardial mapping and RF ablation at the site of earliest atrial activation) in 100 consecutive patients (50 in each group)[14]. The SN sparing hybrid ablation group showed a significant acute and long-term improvement in mean daily heart rate and peak 6-minute walk heart rate[15]. These results are consistent with our small study population, but with a much more simplistic approach. As mentioned previously, perhaps the anatomic disposition of the SN complex with a "horseshoe" type and a regional neuromodulatory effect explains why our conservative approach led to excellent acute and long-term results.

Beyond the anatomical explanation of plausibility, it seems that the neuromodulation could play an important role in our results. First, in the body of the sinus node, there is a higher concentration of sympathetic neurons compared to parasympathetic postganglionic neurons[16]. Since the target of our approach is the body of the sinus node, the ratio of sympathetic neurons removed compared to parasympathetic neurons would be greater, with a result of a predominance of the parasympathetic ones. This is a simplistic explanation; however. As we mentioned in our approach, ablation lesions were extended towards the septal region of the AR where the dorsal right atrial ganglionated subplexus (DRAsGP) is located. DRAsGP spread widely into the dorsal and lateral right atrium, including the sinoatrial nodal region and the superior surface of the right atrial appendage[17]. The ablation effect on sympathetic and parasympathetic neurons may explain an improved regulatory effect over the SN hyperactivity seen in IST patients, but this autonomic interaction is more complex than a simple calculation of the number of fibres or GPS ablated.

One question yet to be resolved is why, despite an inadvertent parasympathetic ganglion modulation, a decrease in heart rate was documented in our results. The answer to this question can be addressed by a feature of the sinus node known as functional inhomogeneity, which refers to the difference in the concentration of autonomic receptors along the sinus node, and how 3 areas in the sinus node can be discriminated that have a different response to neurohumoral influences. When performing our ablation approach, the target would be the upper part of the sinus node, leaving cells with a diminished response to neurotransmitters as a guide for the pacemaker. On the contrary, if the conventional ablation method is chosen, it is likely that the target will be cells from the upper zone and transition, leaving cells with a high sensitivity to adrenaline as a subsidiary pacemaker and it could explain why patients could persist with tachycardia[18].

Finally, after explaining our findings from an anatomical and functional point of view, another possible explanation could be the injury to the sinus node artery. Scanavacca et al[19] published a case series, where

they documented injury to the sinus node artery after performing cardiac denervation procedures with a frequency of 4.76%. This was presented and confirmed by CT after performing ablation in the area of the cavo-atrial junction and the area between the SVC and the aorta, the latter is a target for ablation in our approach for modulation of the sinus node, however in none of our patients presented acute signs of sinus dysfunction.

LIMITATIONS

This study constitutes a small sample from 2 different centers. Individuals were only considered for this anatomically based ablation after exhausting all pharmacological and non-pharmacological interventions for control of symptoms and HR. Therefore, our proposed anatomical approach to guide SNM must be evaluated in a larger cohort of patients to determine its reproducibility across a larger number of patients. Nevertheless, our novel approach consistently showed acute and long-term control of HR and proved to be reproducible in all patients, with no complications and

CONCLUSION

The novel anatomic ICE-guided catheter ablation approach aimed to identify the earliest activation at the AR with an extension of RF lesions towards its septal region seems effective and safe to modulate the SN in symptomatic patients with IST refractory to medical treatment. This technique is reproducible and minimally invasive when compared to more complex approaches such as epicardial SNM or surgical/ hybrid ablation procedures. This approach however, needs to be tested in a larger cohort of patients.

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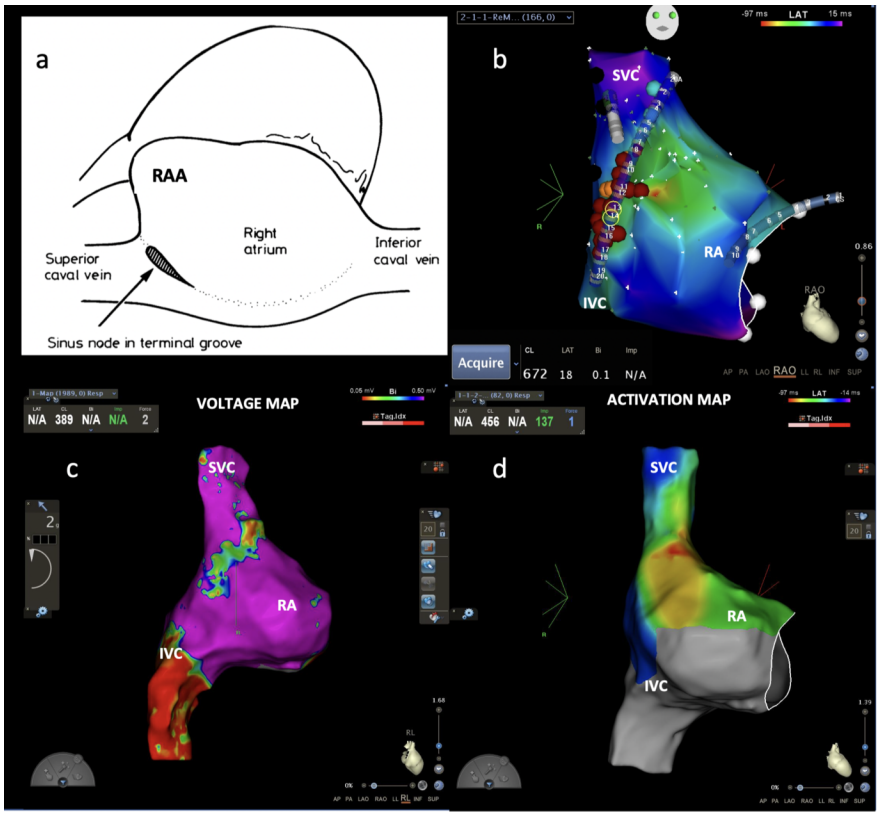

Fig 1. a. Illustration of the RA showing the usual anatomic description of the SN complex represented as a crescent-shape structure with a "comma" disposition in which its "head" is placed at lateral SVC-RA junction and its "tail" extends toward the posteroinferior aspect of the CT. **b** . 3-D activation map of a patient who underwent SNM for IST in which the RF set of lesions was extended from the earliest spot at the lateral SVC-RA junction towards the posteroinferior aspect of the CT crossing next to the PN (dark dots). Note the anatomic extrapolation between the SVC and RA.**c.** 3-D voltage map of a patient who underwent previous SNM for IST at the lateral SVC-RA junction (low voltage zone in green) where earliest activation under isoproterenol was documented. Ablation at this place did not control the HR with the need for an extension to the posteroinferior CT with the same result. **d.** 3-D Activation map of the same patient performed during redo procedure under isoproterenol showing shifting of the earliest activation to the anterosuperior SVC-RA junction at the AR (in red). RA: right atrium, CT: crista terminalis, AR: arcuate ridge, SNM: Sinus Node Modulation, SVC: Superior Vena Cava, IVC: Inferior Vena Cava, HR: Heart rate. PN: phrenic nerve, IST: inappropriate sinus tachycardia. Reproduced from: Anderson RH, Yen SH, Becker AE. The surgical anatomy of the conduction tissues. Thorax. 1983; 38:408–20.

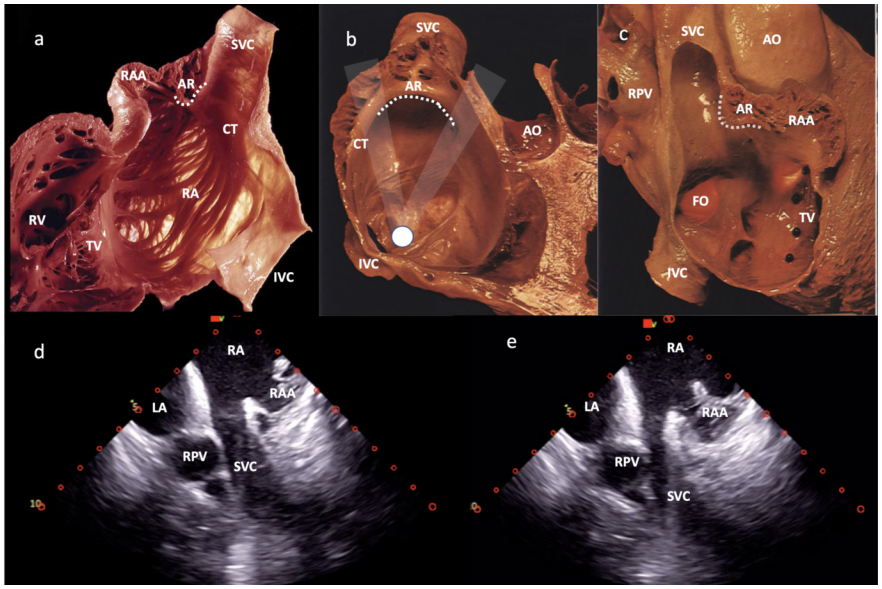

Fig 2. a. Cardiac anatomic specimen from a modified left lateral view in which an oblique vertical transection passing through the SVC posteriorly and the RV anteriorly has been performed to show the lateral half of the SVC-RA junction. In this image, the CT becomes the AR (white dotted line) at the anterosuperior SVC-RA junction. **b.** Cardiac anatomic specimen from an anteroinferior modified view in which the anterior RA and RAA have been removed to show the CT becoming the AR (white dotted line). In this image, the tip of an ICE tilted posteriorly is represented as a white circle from which clock and counterclockwise rotation is performed to obtain a long view of the SVC-RA junction to visualize the lateral, medial, and septal aspects of the AR (represented as white transparent beams). **c.** Cardiac anatomic specimen from a right lateral modified view in which part of the SVC and the lateral half of the posterior RA wall have been removed to show the septal extension of the AR (dotted white line) approaching the interatrial septum next to the Ao. **d** . Long axis ICE view of the SVC-RA junction showing the AR at its lateral portion. **e** . Long axis ICE view of the SVC-RA junction showing the AR at its septal portion (black dotted line) in which a small portion of the Ao is viewed. RA: right atrium, LA: left atrium, AR: arcuate ridge, SVC: Superior Vena Cava, IVC: Inferior Vena Cava, RAA: right atrial appendage, RSPV and RIPV: right superior and inferior pulmonary veins, FO: Foramen ovale, TV: Tricuspid valve, RV: right ventricle, AO: aorta, CT: crista terminalis. Reproduced from: Shivkumar K, Editor Shumpei Mori Kalyanam Shivkumar S. Anatomical basis of cardiac interventions, volume 1 cardiac anatomy. Vol. 1. 2022. 87–96 p.; McAlpine WA. Heart and Coronary Arteries. Vol. 1, Heart, and Coronary Arteries. Springer Berlin Heidelberg; 1975. 97–99 p.

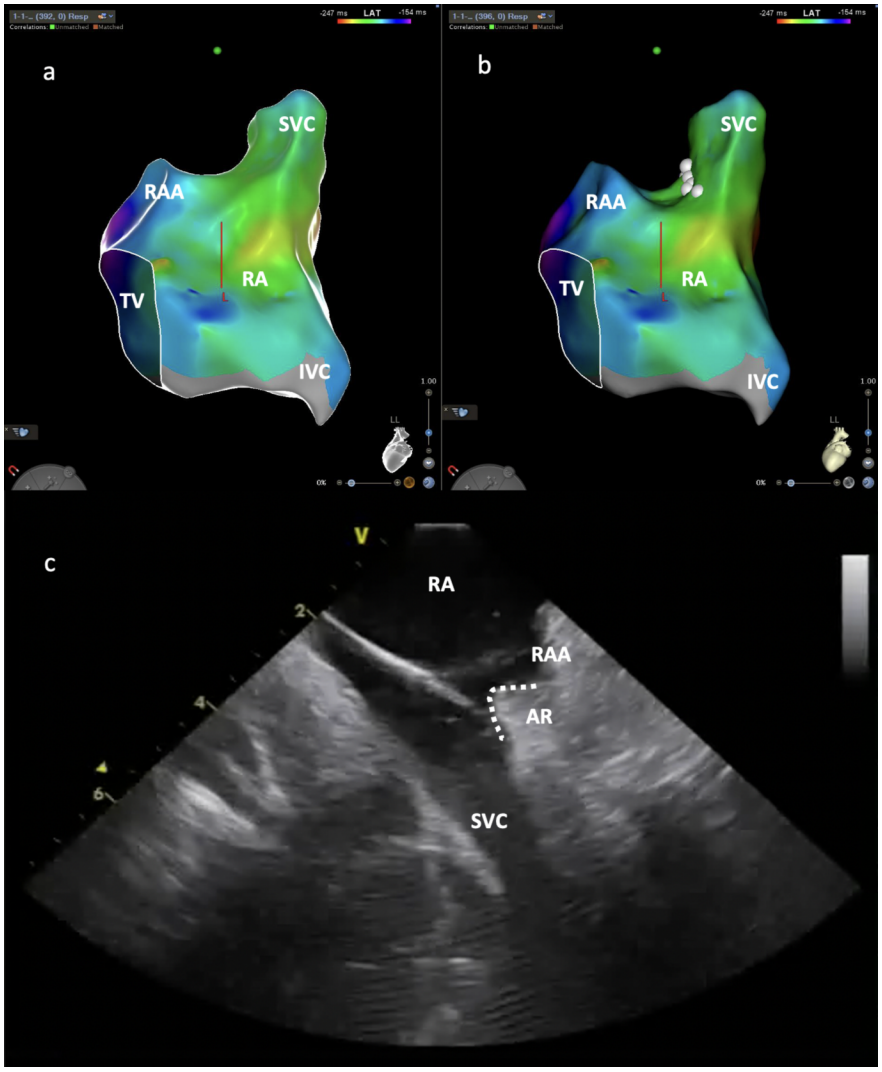

Fig 3. a. 3-D activation map during baseline SR showing anatomic extrapolation between the SVC and the RA and a wide early zone at the high anterolateral aspect of RA. **b.** Same 3-D activation map showing shrinking of the early activation zone that shifted towards a more posterior region after correction of the anatomic extrapolation. The shell was shaved to see the white dots that correspond to anatomic tags taken from the AR under ICE guidance. **c.** Long axis ICE view of the SVC-RA junction showing an ablation catheter in contact with the AR from where anatomical tags were taken. RA: right atrium, AR: arcuate ridge, SVC: Superior Vena Cava, IVC: Inferior Vena Cava, RAA: right atrial appendage, TV: Tricuspid valve.

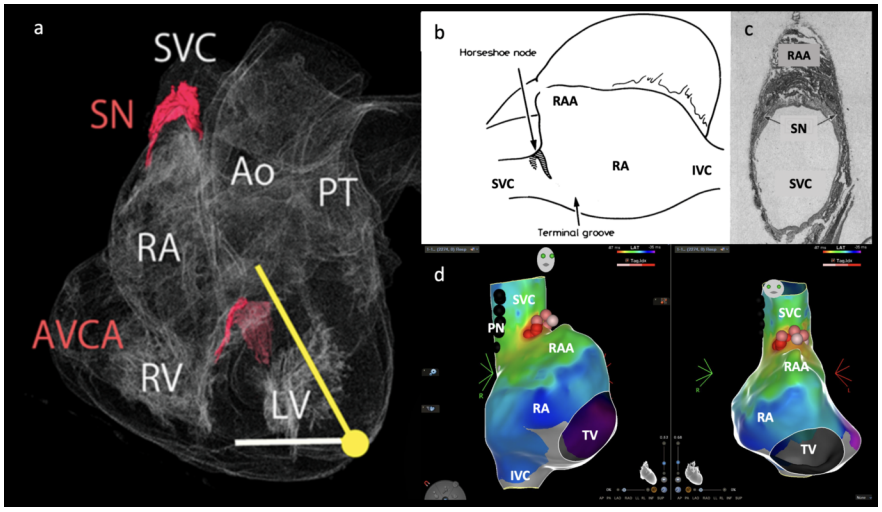

Fig 4. **a.** Illustration of the RA showing the "horseshoe" arrangement of the SN complex in which this structure is situated both medial ("head") and lateral ("tail") to the mid-line of the SCV-RA junction at the AR. **b.** Histological image of a transversal section of the SVC-RA junction viewed from a cephalic view showing a "horseshoe" disposition of the SN complex with medial and lateral extensions along the AR. **d.** 3-D "in-situ" visualization of the human cardiac conduction system performed by means of advanced imaging tools of virtual CT dissection on human cadavers showing extension of the SN complex (in red) from the lateral to the septal SVC-RAA junction. Note the septal extension of the SN coming to the interatrial septum next to the Ao**. d., e.** 3-D activation map of the RA during high HR from RAO and anterosuperior views, respectively. Note the RF lesion set starting at the earliest activation (red ablation dots) at the AR and extended towards its septal portion (pink ablation dots) instead of going to the lateral SVC-RA junction that is relatively next to the PN (dark dots). RA: right atrium, SVC: Superior Vena Cava, IVC: Inferior Vena Cava, RAA: right atrial appendage, TV: Tricuspid valve, PN: Phrenic nerve, Ao: aorta, AVCA: Atrioventricular conduction system, RV: Right ventricle, LV: Left ventricle, PT: Pulmonary trunk. Reproduced from: Kawashima T, Sato F. First in situ 3D visualization of the human cardiac conduction system and its transformation associated with heart contour and inclination. Sci Rep. 2021;11(1):1–15; Anderson RH, Yen SH, Becker AE. The surgical anatomy of the conduction tissues. Thorax. 1983; 38:408–20; Anderson KR, Ho SY, Anderson2 RH. Location and vascular supply of sinus node in human heart. Br Heart J. 1979; 41:28–32.

Table 1.pre and post ablation heart rate variables in patients undergoing SNM in our cohort.

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Lead author	Luis Carlos Saenz
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