# Sinus Node Sparing Novel Hybrid Approach for Treatment of Inappropriate Sinus Tachycardia/Postural Orthostatic Sinus Tachycardia With New Electrophysiological Finding

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**The ideal treatment of Inappropriate Sinus Tachycardia (IST) and Postural Orthostatic Tachycardia Syndrome (POTS) still needs to be defined. Medical treatment yields suboptimal results, endocardial ablation of the sinus node (SN) may risk phrenic nerve damage and open heart surgery may be accompanied by unjustified invasive risks. We describe our first experience of 50 consecutive patients (41 females, 22.83 ± 3.91 years) having undergone a novel hybrid thoracoscopic ablation for drug resistant IST (n = 39, 78%) or POTS (n = 11, 22%). The SN was identified with the help of 3D mapping. Surgery was performed through 3 (5 mm) ports from the right side. A minimally invasive approach with a radio frequency bipolar clamp was utilized to a new target sparing the SN region, to isolate the superior and the inferior caval veins, and a crista terminalis line was made. All lines were interconnected. Normal SR was restored in all patients at the end of the procedure. All patients discontinued medication during the follow-up. After a blanking period of 6 months all patients presented stable SR. At a mean of 28.4 ± 1.2 months, normal SN ruction and chronotropic response to exercise was present. In the 11 patients initially diagnosed with POTS, no syncope occurred. During the follow-up, pericarditis was the most common complication (39 patients; 78%) with complete resolution in all cases. In conclusions the preliminary results of our first experience with a SN sparing novel hybrid ablation of IST/POTS, using surgical thoracoscopic video-assisted epicardial ablation combined with concomitant endocardial 3D mapping may prove an efficient and safe therapeutic option in patients with symptomatic drug resistant IST and POTS. Importantly, in our study all patients had a complete resolution of the symptoms and restored normal SN activity.**  **(Am J Cardiol 2019;124:224−232)**

Postural Orthostatic Tachycardia Syndrome (POTS) is a systemic illness, with postural tachycardia being one of several criteria. It is usually characterized by frequent symptoms that occur with standing, such as light-headedness, palpitations, tremor, generalized weakness, blurred vision, exercise intolerance, and fatigue. These symptoms are associated with an increase in heart rate (HR) of >30 beats/min when moving from a recumbent to a standing position (or >40 beats/min in patients 12 to 19 years of age); and the absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure). The standing (or orthostatic) HR of patients with POTS is often >120 beats/min and increases more in the morning than in the evening.[1] Inappropriate Sinus Tachycardia (IST) is defined as a sinus HR >100 beats/min at rest (with a mean 24-hour HR > 90 beats/min not due to primary causes) and is associated with distressing symptoms of palpitations. The prevalence in a middle-aged population of men and women is 1.2%, including both symptomatic and asymptomatic patients. IST is believed to be a chronic condition, but whether and how quickly patients improve, is unknown. Patients with IST and POTS require significant care and attention, due to the nearly ubiquitous psychosocial distress and the complexity of their problems.

Medical treatment of IST or POTS has shown suboptimal results. If $\beta$ blockers and calcium channel blockers are ineffective; Ivabradine, an inhibitor of the hyperpolarizing sodium current, may be an option.[2]

Radio-frequency sinus node (SN) modification for POTS is not recommended. It often worsens symptoms and occasionally results in the patient requiring a pacemaker, permanent phrenic nerve (PN) paralysis or transient superior vena cava syndrome. SN modification, surgical ablation, and sympathetic denervation are not recommended as a part of routine care for patients with IST. Several groups have described modification or ablation of the SN in IST. In

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Table 1
Autonomic function assessment in patient with IST, POTS, and controls

| Variable | IST (n = 39) | POTS (n = 11) |
|---|---|---|
| Tests reflecting mainly parasympathetic function | | |
| Heart rate response to Valsalva Maneuvers (Valsalva ratio) | 1.71 ± 0.25 | 1.10 ± 0.20 |
| Heart rate variation (RRI) during deep breathing (6 breaths per minute) | 13 ± 3 bpm | 10 ± 2 bpm |
| Heart rate response to standing (30:15 ratio) | 0.90 | 0.85 |
| Tests reflecting mainly sympathetic function | | |
| Blood pressure response to standing (fall in systolic blood pressure − mm Hg) | 5 ± 4 | 32 ± 5 |
| Blood pressure response to sustained handgrip (increase in diastolic blood pressure − mm Hg) | 14 ± 7 | 10 ± 5 |

general, acute success rates are reasonably good, but there is a high rate of symptom recurrence, and with significant complication rates. In addition, SN modification or ablation does not relieve all IST-associated symptoms. There is also no agreement on the optimal interventional approach; modification or ablation, open chest versus conventional intravascular access, and mapping methods. Finally, there is no long-term evidence of symptomatic improvement. Patients and referring physicians need to be aware that despite the potentially invalidating symptoms and the patients' high motivation, the consequences of open heart surgery therapy might seriously outweigh any potential benefit.[1]

We describe a possible novel substrate for POTS and IST and a novel hybrid ablation technique targeting this substrate.

## Methods

From June 2015 until December 2016, 50 consecutive patients underwent a novel hybrid ablation for IST or POTS in a single tertiary center. The diagnosis of IST or POTS was made following the HRS Expert Consensus Document on POT/IST the patients were evaluate from a cardiologist together with a neurologist both expert of IST and POTS.[1] Primary causes of sinus tachycardia were ruled out, as were other mechanisms of supraventricular tachycardia. Every patient underwent 12-lead ECG to confirm normal P-wave morphology, and Holter 24-hour ECG to evaluate the heart rate variability (HRV) and the circadian variation. Additional evaluations included baseline blood testing (complete metabolic panel, thyroid function, blood count, renal function, electrolytes, drug testing, and serum and urine catecholamine) and some of the autonomic testing or long-term monitoring (Loop Holter, implantable Reveal). Autonomic tests were performed according to standard protocols using the Nexfin HD monitor (BMEYE, Amsterdam, The Netherlands) for continuous noninvasive blood pressure measurement. Six cardiovascular reflex tests were collected in the following order with 15 minutes of recovery time between recordings: (1) expiration-to-inspiration ratio of RR interval during slow deep breathing (HR variation), (2) maximum-to-minimum 30-to-15 ratio of RR intervals during active standing,[3] systolic blood pressure response to standing, (4) cold face test, (5) maximum-to-minimum ratio of RR intervals during Valsalva maneuvers (Valsalva ratio), and (6) blood pressure response to sustained handgrip (handgrip ratio). Methodologies as well as databases of normal values for healthy patients of these tests have been described in detail elsewhere[4]. Normal, borderline, and abnormal values of the tests are summarized in Table 1. Patients who proved refractory to, or intolerant of pharmacologic therapy were offered ablative treatment. Risks, benefits, and alternatives were thoroughly discussed. All patients provided written informed consent before the procedure. Data were reviewed under an institutional review board−approved registry. In patients with IST we consider the capacity of effort to evaluate the severity of symptoms and in patients with POTS the presence of syncope was consider as parameter.

The frequency domain measures of HR variability in the population were analyzed using the methods recommended by the Task Force of the European Society of Cardiology.[3] Spectral power was quantified by fast Fourier transform analysis in 2 frequency bands 0.01e0.15 Hz (low frequency [LF]) and 0.15e0.40 Hz (high frequency [HF]).[5,6] The LF and HF components during the 15-minute period in supine and sitting positions and standardized walking were calculated as absolute units. LF/HF ratio was used as the index of sympathovagal balance. In all patients with an implantable cardiac loop recording system (Reveal Linq LNQ11, Medtronic Minneapolis) we obtained long-term monitoring of HRV and HR.

A Holter electrocardiogram was digitalized to 12-bit data at 128 Hz with a scanner (MARS-PC; GE Company, Fairfield, Connecticut), on which ecg parameters (QRS) complexes were collected automatically. The results were reviewed and any errors in QRS labeling were edited manually. The patients with implantable loop recording were analyzed automatically by dedicated internal software (Medtronic, Minneapolis, Minnesota). Computations of HRV measurements were performed using ad hoc analytical software (Kubios HRV freeware). Time-domain variables included the mean normal-to-normal RR intervals, standard deviations of the normal-to-normal RR intervals, standard deviations of 5-minute averages of normal RR intervals, and root mean square of differences between adjacent normal RR intervals. For frequency domain analysis, the power spectrum was quantified by fast Fourier transformation for the following frequency bands: 0.0033 to <0.04 Hz (very-low frequency), 0.04 to <0.15 Hz (LF), and 0.15 to 0.4 Hz (HF). LF/HF was also calculated. Frequency domain measurements of HRV were transformed to natural logarithms for their skewed distribution.[3]

The right chest is accessed with three 5-mm working ports. A port for the camera access at the midaxillary line, a 5-mm port for instruments in the third intercostal space at

the anterior axillary line, and a 5-mm port for instruments in the seventh intercostal space at the anterior axillary line. After placement of the camera port, $CO_2$ insufflation is started at a pressure of 8 mm Hg. This has the purpose to increase the working space by pushing the diaphragm down and the heart toward the left. Based on the patient's morphology and the cardiac anatomy, the location of these ports may vary. In women the lateral mammary fold is used. The pericardium was opened with an endoscopic coagulation hook and/or scissors longitudinally, 2 cm anterior to the PN toward the superior caval vein (SVC) and inferior caval vein (IVC) (Figure 1). To improve visualization and facilitate the dissection of the pericardial reflection of the IVC (to gain access to the oblique sinus), the posterior part of the pericardium is retracted with 2 sutures that are pulled outside the chest posterior to the camera port. The pericardial reflection of the IVC is bluntly dissected until the opening of the oblique sinus. After endocardial mapping of the SN, a bipolar bi-directional radio frequency (RF} clamping device (EMR, Atricure Inc., Mason, Ohio) is positioned over the SVC at the junction with the right atrium (RA) (Figure 1). The SVC has to be free of endovascular electrodes and of the central venous line to avoid damage during clamping and ablation. Three applications are performed at this level. This usually reduces the HR by around 30% acutely, but the rate will recover partially after a few minutes. The same clamping is performed over the IVC. To complete the ablation, the posterior jaw of the clamp is positioned in the oblique sinus and the anterior jaw over the Waterstone groove, covering the crista terminalis. The distal end of the clamp crosses the line over the SVC and the border of the SN. Six applications are performed. This will often create a junctional rhythm, which will recover to slow sinus rhythm after minutes.

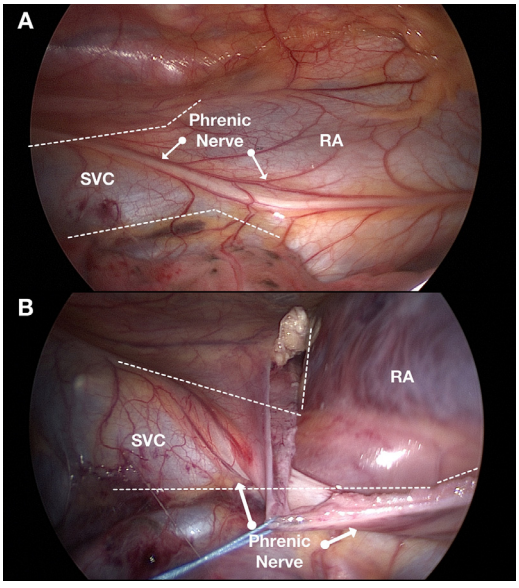


Figure 1. (*A*) Camera view from right thoracoscopic approach, SVC: Superior Vena Cava, RA: Right Atrium Panel A is showing the close pericardium view, the schema explain the relation between all different structures, Panel B is showing the relations modification between the different structure after opening the pericardium.

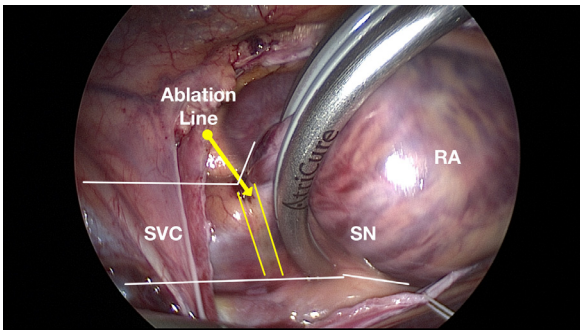


Figure 2. Showing the clamping of superior vena cava (SVC) in relation with sinus node (SN) and right atrium (RA), the yellow line underline the previous ablation line.

The pericardium is closed, and the right lung reinflated. We observed a slowing of the HR during the procedure in all patients immediately after completing the ablations lines. We considered as end point of the ablation a reduction of at least 25% of the HR or fast junctional rhythm (Figure 2).

Patients were studied under general anesthesia without the use of paralytic agents. Antiarrhythmic drugs and $\beta$ blockers were withheld at least 5 half-lives before the procedure. A multipolar catheter was advanced through the right femoral vein into the RA and positioned with its distal 10 poles in the coronary sinus and the proximal poles within the tricuspid annulus. Mapping was performed using a multipolar catheter, either a Penta Array catheter, a circular Optima Catheter, or a Multi Pole Basket. A 3-dimensional activation map was created using the appropriate catheter to each mapping system. CARTO (Biosense − Webster, Diamond Bar, California; n = 12), NavX system (St. Jude Medical, St Paul, Minnesota; n = 34), and Rhythmia mapping system (Rhythmia Medical/Boston Scientific, Marlborough, Massachusetts; n = 4). A baseline electrophysiological study was performed to exclude other mechanisms of supraventricular tachycardia. Bipolar activation mapping identified the earliest site referenced to both an endocardial fiducial point (e.g., coronary sinus electrogram) and the surface P wave. During the mapping, the position of the endocardial catheter was observed by the thoracoscopic video-assistant system. The mapping was performed before and after the ablation. Both maps were obtained during single lung ventilation and open pericardium. The major aim of the mapping was to visualize the SN region and the anatomical relation between SVC, crista terminalis, and IVC and guide the surgeons to preserve the SN from the lesion set. After ablation we remap to confirm the continuity and transmurality of the ablation lines (Figure 3).

Continuous variables are expressed as mean ± SD or median and range as appropriate. Categorical variables are expressed as absolute and relative frequencies. Comparisons of continuous variables were done with a Student's *t* test or the Mann-Whitney *U* test as appropriate. The Chi-square test or the Fisher's exact test was used to compare categorical variables as appropriate. A p value $<0.05$ was considered statistically significant. Statistical analyses were conducted using the SPSS software (SPSS v20, Chicago, Illinois).

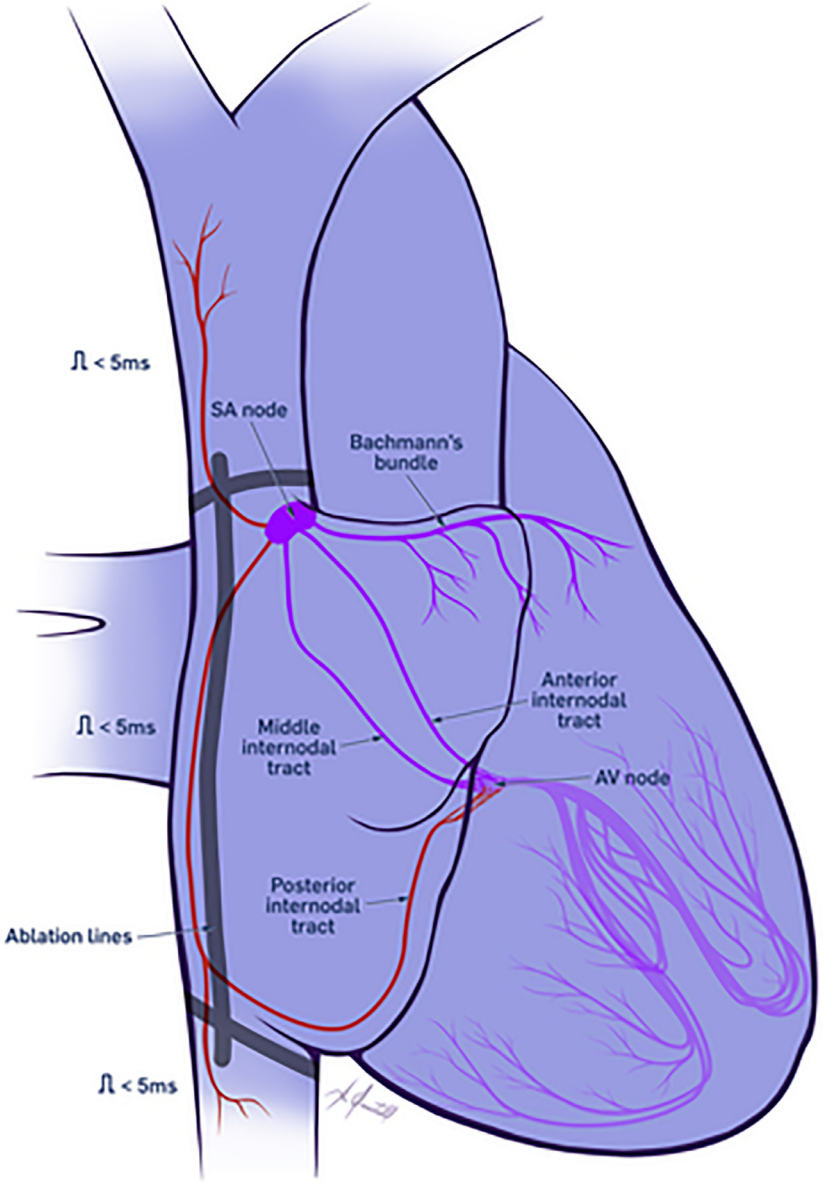


Figure 3. Schema of the right atrium (RA) in red the conduction system targeting during ablation, in blue the conduction system preserved during ablation, with a black discontinued line the schematic orientation of ablation line. Moreover we represented the postpacing interval result in the different location. AV = atrio − ventricular node, IVC = inferior vena cava, RV = right ventricular; SN = sinus node, SVC = superior vena cava. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

## Results

Fifty consecutive patients (age 23 ± 4 years; female 82%) were included in the study; 39 patients were diagnosed with IST (78%) and 11 patients with POTS (22%). The baseline characteristics of the study population together with the symptoms are detailed in Table 2.

Pharmacological treatment was attempted in all patients without benefit. The drugs are detailed in Table 2. Forty-eight (96%) patients underwent a previous electrophysiology (EP) study in another center without diagnosis, 15 patients (30%) underwent a slow pathway ablation for documented Atrio Ventriculair (AV) nodal re-entry tachycardia, 5 patients (10%) underwent a previously typical right flutter ablation, only 1 (2%) patient presenting episodes of atrial fibrillation was treated by PVI. Forty-two patients (84%) received a Reveal Linq (Medtronic, Minneapolis, Minnesota) implantations in other center for unexplained severe cardiac symptoms (Table 1).

All procedures were performed under general anesthesia. Mean total procedural duration was 183 ± 11 minutes; mean 3D mapping time was 12 ± 8 minutes; mean surgical time was 42 ± 16. A mean number of 12.5 ± 1.5 applications per patient was performed with the bipolar radiofrequency clamp. The mean duration of hospitalization was 5.04 ± 0.37 days, mean duration in the intensive care unit was 1.06 ± 0.09 days. All patients had a restored normal sinus function at the end of procedure (Table 5; Figure 4).

Table 2
Baseline characteristics n = 50

| | |
|---|---|
| Women (%) | 41 (82%) |
| Age (years) | 22,83 ± 3.91 |
| Duration of symptoms (months) | 38,10 ± 20,22 |
| Inappropriate sinusale tachycardia (IST) (%) | 39 (78%) |
| Postural orthostatic tachycardia (POTS) (%) | 11 (22%) |
| Left ventricular ejection fraction (%) | 55.71 ± 1.29 |
| Body mass index (kg/m$^2$) | 20.3 ± 4.1 |
| Symptoms | |
| Palpitation | 47 (94%) |
| Syncope with POTS | 11 (22%) |
| Presyncope without POTS | 14 (28%) |
| Dizziness | 40 (80%) |
| Dyspnoea | 23 (46%) |
| Fatigue | 48 (96%) |
| Therapies attempts | |
| Ivabradine (%) | 47 (94%) |
| *discontinued due to intolerance* | *43 (86%)* |
| Calcium channel blockers (%) | 46 (92%) |
| *discontinued due to intolerance* | *46 (92%)* |
| IC class anti-arrhythmic drugs (%) | 46 (96%) |
| *discontinued due to intolerance* | *46 (92%)* |
| Beta blockers Bisoprolol (%) | 50 (100%) |
| *discontinued due to intolerance* | 49 (98%) |
| Beta blockers Metoprolol (%) | 47 (94%) |
| *discontinued due to intolerance* | *47 (94%)* |
| Beta blockers Nebivol (%) | 2 (4%) |
| *discontinued due to intolerance* | *2 (4%)* |
| III class antiarrhythmic drugs Sotalol (%) | 5 (10%) |
| *discontinued due to intolerance* | *5 (10%)* |

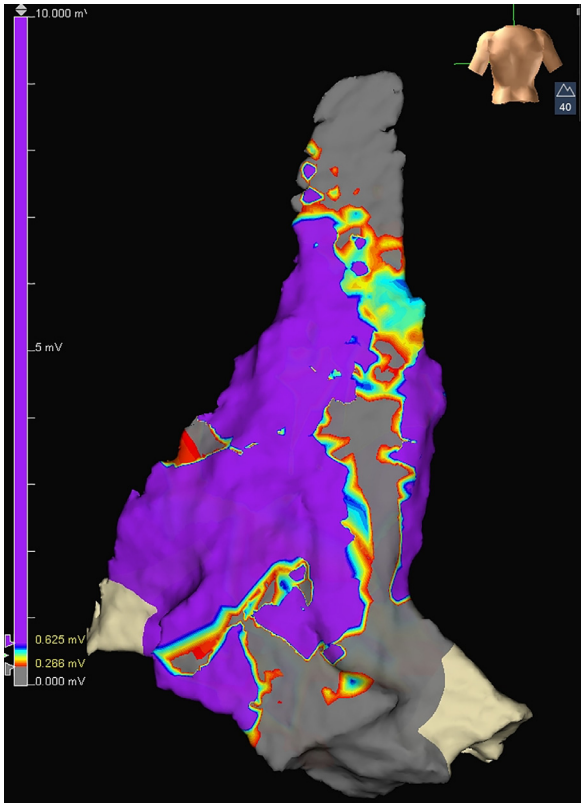


Figure 4. Example of postablation electroanatomical mapping. We can appreciate the isolation of the superior and inferior cava veins and the lateral line.

Interestingly the P-wave morphology during tachycardia recorded by 12-lead ECG was nearly identical to that in sinus rhythm. At the beginning of the procedure all patients with IST presented sinus tachycardia, no changes were observed during the induction of general anesthesia. In patients diagnosed with POTS, Isoprenaline was administered in order to increase the sinus rhythm to 75% of maximal HR following the Sheffield formula (220-age/100)*75 beats/min.[7] We performed simultaneous recordings and measurements with multielectrodes catheters from the SN in comparison with superior vena, crista terminalis, inferior vena cava, as shown in Figure 3. Remarkably, the electrical activation recorded in all positions resulted on time with the early activation in the SN. Differential pacing from all regions demonstrated a postpace internal of less than 5 ms in all sites investigated. We noted that all regions were activated almost simultaneously to the SN with a delay of only 5 ms, during postpace internal. In our approach we decided to disconnect the SN from the fast conduction system of the crista terminalis and the sleeves deep in the SVC and IVC as describe in the Figure 3.

No complications were reported during the ablation procedure. During the follow-up pericarditis was the most common complication which occurred in 39 patients (78%), and was treated within the first 3 months. In 2 patients (4%) the symptoms continued up to 6 months, standard treatment with metilprednisone, acetylsalicylic acid, colchicine were administrated. Table 4 describes postprocedural complications. No blood transfusion was required.

The mean follow-up after ablation was 28.4 ± 1.2 months. All patients concluded 24 months follow-up. The 8 (16%) patients without implantable loop monitoring where followed with serial Holter 24-hour ECG monitoring every 3 months. After a blanking period of 6 months all 50 patients (100%) showed a significant reduction in HR compared with the preablation period. Specifically, the normal-to-normal parameter increased from a mean 539.30 ± 28.72 ms to 1019.60 ± 173.01 ms. Additionally, the standard deviation of all normal RR intervals before ablation was 98.4 ± 15.07 ms, and improved after ablation to 140.49 ± 40.61 ms. After the blanking period all patients presented with a normal chronotropic response to exercise, before the ablation the patients were achieved the maximal HR during the stress test after 50 W, after 6 months all patients were able to perform a normal stress test based of the age capacity above 150 W. Of note, none of the 11 patients with POTS experienced further syncopal episodes after ablation. All patients discontinued medication during the follow-up (Table 3).

We analyzed all electrocardiogram registrations pre- and postablation. The P-wave duration was shortened, the first component of the P wave (18.8 ± 45 ms) was missing

Table 3
Previouslyelectrophysiological procedures

| | |
|---|---|
| Electrophysiological study without diagnosis (%) | 48 (96%) |
| Reveal implantation (%) | 42 (84%) |
| AVNRT ablation (%) | 15 (30%) |
| Typical right atrial flutter ablation (%) | 5 (10%) |
| PVI with cryoballoon ablation (%) | 1 (2%) |

Table 4
Time domain heart rate variability

| | Definition | Preablation (n.50) | Postablation (n.50) |
|---|---|---|---|
| Mean NN (ms) | Mean of all normal RR intervals (normal to normal coupling interval) | 539.30 ± 28.72 | 1019.60 ± 173.01 |
| SDNN (ms) | Standard deviation of all normal RR intervals (SDRR or CLV) | 98.4 ± 15.07 | 140.49 ± 40.61 |
| SDANN (ms) | Standard deviation of mean RR interval for all 5-minute segments of 24-hour ECG recordings | 72,60 ± 28.71 | 126.60 ± 31.61 |
| SD (ms) | Mean of standard deviations of all normal RR intervals for all 5-minute segments of a 24-hour ECG recording | 22,83 ± 3.91 | 62.68 ± 15.91 |
| rMSSD (ms) | Root mean square successive differences between adjacent normal RR intervals over the entire 24-hour ECG recordings | 15,83 ± 11.51 | 35.42 ± 9.11 |
| pNN50 (%) | Percent of difference between adjacent normal RR intervals that are greater than 50 ms computed over the entire 24-hour ECG recordings | 4 ± 3.9 | 16 ± 9.7 |

postablation (P-wave duration before 115.7 ± 58 ms, P-wave duration postablation 96.8 ± 73 ms) (Figure 5).

## Discussion

Our findings demonstrated the feasibility and safety of a novel hybrid endocardial/epicardial ablation approach in IST/POTS patients in whom previous multiple therapeutic medical attempts were not successful. Due to the failure of medication in many patients affected by IST/POTS, several invasive strategies relying either on endocardial or epicardial ablation approaches to modify the SN have been developed. However, most were hampered by partial success and high rates of complications. Since the SN is not a focal structure[8] in most cases, larger areas of the high RA need to be ablated in order to achieve appropriate HR reduction. Generally, the more superior parts of the SN, which are innervated by sympathetic stimulation, provide higher HRs. Although vagal stimulation has the tendency to activate more inferior portions of the SN resulting in slowing of the HR. The right PN runs laterally or posterior laterally to the superior vena cava and follows the lateral RA to the diaphragm (Figure 1). Therefore, there are multiple potential sites of PN damage during endocardial ablation. To avoid this complication, high output pacing is typically used before radiofrequency application. If PN capture is present, energy delivery is avoided at these sites. The area of PN capture can be quite wide, hence, during the conventional RF procedure, potential PN paralysis significantly limit success rates.[8] In addition, the regional anatomy of the SN and superior vena cava−right atrial (SVC−RA) junction is complex, with endocardial ridges that include the crista terminalis, the pectinate muscles, and the arcuate ridge making endocardial ablation less successful. To overcome these limitations, a combined endo/epicardial approach has been developed, using a percutaneous subxyphoid access to the pericardium and a balloon catheter for PN protection. Jacobson et al, presented a series of 5 patients that underwent combined endo/epicardial procedure after failed endocardial procedure. Four patients were successfully treated and 1 had recurrence which was treated by cryoablation via minithoracotomy. Three patients developed pericarditis after the ablation procedure.[9] Another experience was reported by Shandling et al on thoracoscopic ablation of SN, demonstrated feasibility utilizing microwave energy without electrophysiological mapping.[10] Other nonmedical possibilities for treatment of IST include outdated surgical ("on-pump") RA resection and SN isolation,[11] AV node ablation and pacemaker implantation[12] and minimally invasive surgical approaches (Table 6).[13]

Table 5
Complication, therapies, and follow-up

| | |
|---|---|
| Pericarditis in the first 3 months, n | 39 (78%) |
| Pericarditis after the first 3 months, n | 2 (4%) |
| Ablation atypical right atrial flutter during blanking period, n | 2 (4%) |
| Gastroesophageal reflux symptoms during blanking period, n | 20 (40%) |
| Therapies during pericarditis | |
| Ivabradine, n | 10 (20%) |
| Beta blockers Bisoprolol, n | 2 (4%) |
| Protein pomp inhibitors for 3 months, n | 41 (82%) |
| Metilprednisone, n | 5 (10%) |
| Acetylsalicylic acid, n | 41 (82%) |
| Colchicina, n | 47 (94%) |
| Therapies without pericarditis | |
| Ivabradine, n | 1 (2%) |
| Beta blockers Bisoprolol, n | 1 (2%) |
| Protein pomp inhibitors for 3 months, n | 3 (6%) |
| Follow-up | |
| Follow-up (months) | 28.4 ± 1.2 |
| Mean hospital stay (days) | 5.04 ± 0.37 |
| Mean intensive care unit stay (days) | 1,06 ± 0.09 |

The hybrid approach described has a number of distinct advantages over currently used ablation strategies; (1) minimal invasiveness − other than a femoral venous puncture, only 3 (5 mm) ports are placed on the right chest (2) direct visualization of the structures of interest and better direct energy delivered (3) minimal risk of PN damage, (4) simultaneous endocardial activation mapping allowing SN identification and precise epicardial ablation. To the best of our knowledge, this is the largest series of patients treated for IST/POTS with ablation to date. In our study, all patients at the end of the procedure presented a significant decrease in HR, RR intervals, and HRV. This was maintained during the entire follow-up (mean follow-up of 28.4 months). Considering the strongly debilitating symptoms before ablation, these excellent results justify this minimally invasive approach. Importantly, an epicardial procedure will provide direct visualization of the PN, therefore reducing the potential for injury. Finally, endocardial mapping allows for electrophysiologic guidance to an otherwise "blinded" anatomic approach. Although minimally invasive, our approach may have a higher potential rate of complications

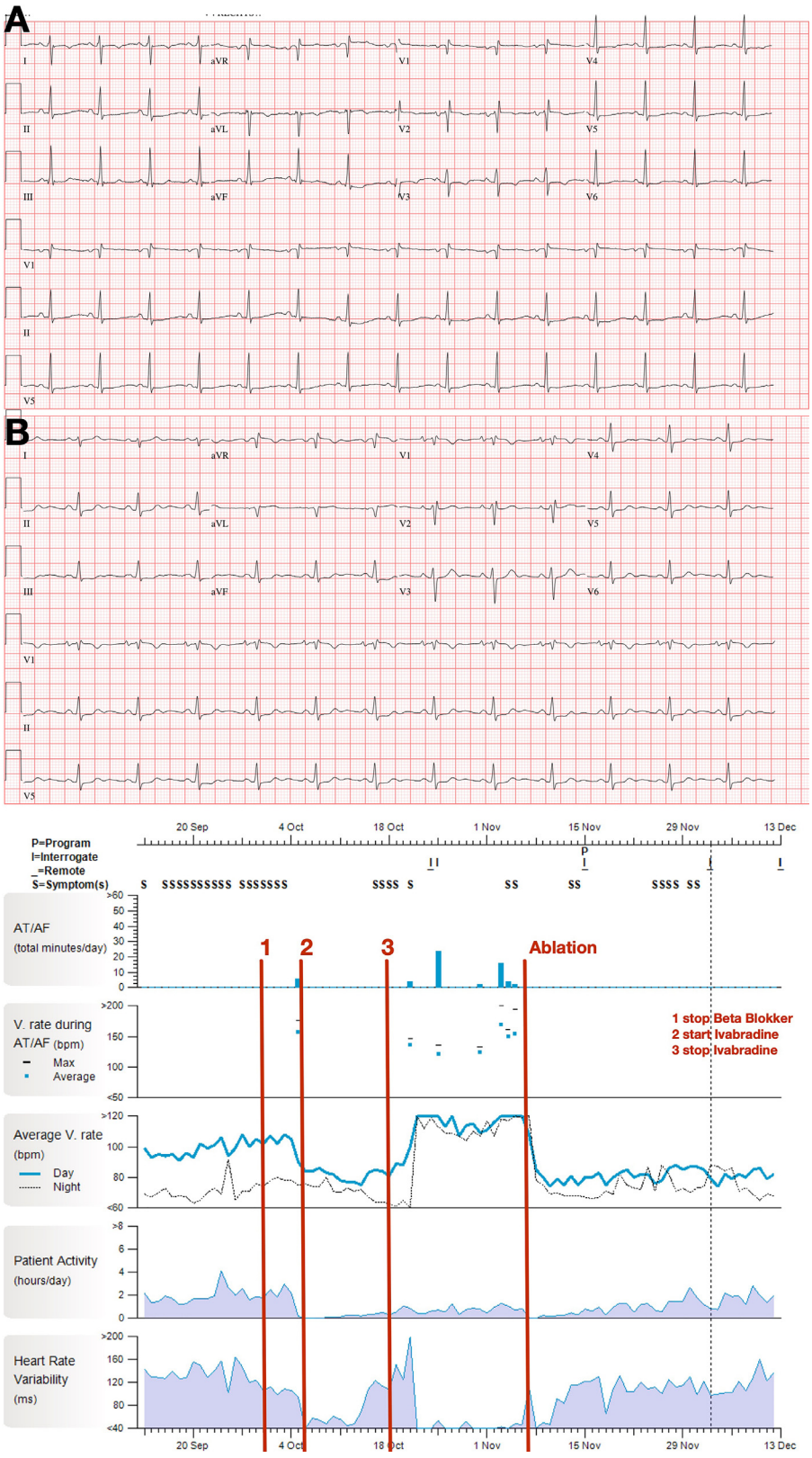


Figure 5. Panel A:Example of electrocardiogram pre (*A*, the patient was under general anaesthesia, heart rate of 95 beats/min) and post (*B*, postprocedure without anaesthesia, heart rate 68 beats/min) procedure. Panel B: example of loop monitoring with different medications, to prove the concept we administrated drugs already failed in advance to record the difference with the ablation therapy.

Table 6
Evolution of the heart rate pre- and postablation and during follow-up

| | IST (n = 39) | POTS (n = 11) |
|---|---|---|
| Pre ablation | 118.5 ± 10.3 | 89.4 ± 11.3 |
| Post ablation (day 1) | 64.7± 12.5 | 72.5 ± 6.5 |
| Post ablation (months 1) | 102.3 ± 25.5 | 90.5 ± 12.5 |
| Post ablation (months 6) | 76.6 ± 5.0 | 63.5 ± 5.9 |
| Post ablation (months 12) | 75.2 ± 3.5 | 60.3 ± 10.5 |
| Post ablation (months 24) | 73.5 ± 8.6 | 61.5 ± 7.5 |

compared with conventional endocardial ablation. There is the risk of general anesthesia, bleeding, pneumothorax, and damage to cardiac and extra-cardiac structures during a thoracoscopic procedure that could result in sternotomy and/or conversion to open heart surgery. These complications have already been described in a larger series of patients who underwent hybrid ablation for AF.[14] Therefore, given the young age of this patient population and the invasive nature of ablations, we do not recommend that they be part of routine care as a first line therapy. Of note, in our procedure, there might be lower incidence of complications when compared with thoracoscopic ablation of other arrhythmias, since only a right-sided approach is used. In addition the procedure is shorter and patients are not anticoagulated. In fact, our patients did not experience any life-threatening complications. The most common adverse event was pericarditis. Although predictable, it could be difficult to treat in some cases. In our cohort, all symptoms of pericarditis resolved with medical treatment. The patients affected, did not bare any sequelae at final follow-up related to this complication. Finally, the procedure was performed by experienced operators with a vast experience of thoracoscopic epicardial AF ablation. Although the complication rate may have been higher in less experienced hands, we believe that hybrid ablation of SN, using surgical thoracoscopic video-assisted epicardial ablation combined with endocardial 3D mapping, may be considered an effective and safe option for patients with symptomatic IST/POTS who have failed medical therapy. Finally, we believe that this approach might lead to a better understanding of the complex structure of the SN, both from an anatomical point of view than from an electrophysiological standpoint. The hypothesis about our ablation strategy is based of consideration regarding the embryological heart development. At early stage of embryogenesis, when the heart is still a tube structure, all cardiomyocytes can automatically initiate impulses. Afterwards, the rest of sinus horn (embriological precursors of the SN, SVC, crista terminalis, and IVC) finally develops into the sinus venous of the RA, a part of superior and inferior vena cava, and the coronary sinus.[15]

Some limitations can be found in our study. The present work was a single-center study. Most of electrocardiographic markers analyzed in the study are dynamic and the real prevalence of these parameters is difficult to evaluate. Larger, prospective, and multicenter studies are needed to confirm our findings. We did not perform any official "quality of life tool."

In conclusion, a novel SN sparing hybrid ablation for treatment of IST/POTS, using surgical thoracoscopic video-assisted epicardial ablation combined with endocardial 3D mapping, appears to be a successful approach. This promising treatment for patients with symptomatic IST and POTS offers a complete restoration of the normal HR and HRV, with a total reduction of all symptoms. Our first experience was free from major complications, including no pacemaker implantation and no PN injury. Interestingly in our cohort, this hybrid treatment has offered an option to patients that have struggled to find any other relief from this debilitating disease, its symptoms, and its psychosocial consequences.

## Disclosures

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