Catheter ablation for inappropriate sinus tachycardia:
Clinical outcomes of sinus node ablation

Bruno Reissmann, MD,*‡ Thomas Fink, MD,†‡ Michael Schlüter, PhD,‡ Andreas Metzner, MD,*‡ Feifan Ouyang, MD,‡ Karl-Heinz Kuck, MD, FHRS‡

From the *Department of Cardiology, University Heart Center Hamburg, Hamburg, Germany, †Department of Cardiology, University Heart Center Lübeck, Lübeck, Germany, ‡Department of Cardiology, Asklepios Klinik St. Georg, Hamburg, Germany, and ‡Asklepios proresearch, Hamburg, Germany.

Introduction
Inappropriate sinus tachycardia (IST) is a syndrome defined by unexpectedly fast sinus rates at rest or at minimal physical activity. Symptoms include palpitation, exercise intolerance, incapacity to work, fatigue, dizziness, and presyncope. Pharmacologic therapy is frequently insufficient despite the fact that multiple drugs are simultaneously administered in the majority of patients. Catheter ablation (CA) offers a further treatment option; yet, limited data is available, and the optimal procedural endpoint has not been identified. The aim of this study was to assess clinical outcomes of sinus node (SN) ablation for the treatment of drug-refractory IST.

Case report
Patients
Three consecutive patients (aged 28, 36, and 53 years, all women) with highly symptomatic, drug-refractory IST underwent CA aiming at ablation of the SN. IST was defined as a heart rate of ≥100 beats per minute (bpm) at rest or minimal physical activity. Right atrial activation showed a high-to-low activation sequence that was similar during IST and sinus rhythm at normal heart rate. Atrial pacing did not terminate or change the tachycardia cycle length. No potentially reversible causes for sinus tachycardia were identified.

Within the last 36 months the patients were hospitalized at least 3 (maximum 5) times. Two patients were unable to work because of their IST. Between 3 and 5 antiarrhythmic drugs had failed to provide sufficient symptom control. Two patients had undergone an ablation procedure for the treatment of IST 60 and 62 days, respectively, prior to the current procedure. The procedural endpoint of the preceding ablation procedures was, in contrast to the present approach, modification of the SN, defined by a resting heart rate of <90 bpm and a 20% reduction in heart rate during infusion of isoproterenol. Modification of the SN failed to relieve symptoms in both patients and there was no lasting effect on heart rate, as assessed by 12-lead electrocardiograms (ECGs) and Holter ECGs. Baseline characteristics are given in Table 1. The current study is a retrospective analysis based on our institutional database. The study was approved by our institutional ethical board and was performed in accordance with the Declaration of Helsinki.

Procedures
All procedures were performed with patients under deep sedation using intravenous sufentanil, midazolam, and propofol. After femoral access, 3000 units of heparin were administered. A 7F steerable decapolar catheter (Parahis; Biosense Webster, Inc, Diamond Bar, CA) was positioned in the coronary sinus. Mapping and irrigated radiofrequency (RF) ablation were performed with a 3.5-mm-tip catheter (ThermoCool NaviStar; Biosense Webster, Inc, Diamond Bar, CA). Point-by-point

KEY TEACHING POINTS
- The optimal procedural endpoint of catheter ablation for the treatment of inappropriate sinus tachycardia has not yet been identified.
- Among patients with highly symptomatic inappropriate sinus tachycardia, sinus node ablation aiming at change in P-wave morphology from an inferior to a superior axis appears to be an effective treatment.
- Considering the change in P-wave morphology from an inferior to a superior axis as targeted procedural endpoint can be effective even for patients who did not respond to sinus node modification.

KEYWORDS
Catheter ablation; Clinical outcomes; Follow-up; Inappropriate sinus tachycardia; Sinus node ablation

Address reprint requests and correspondence: Dr Bruno Reissmann, Dept. of Cardiology, University Heart Center Hamburg, Martinistr. 52, 20246 Hamburg, Germany. E-mail address: bruno.reissmann@uke.de.

https://doi.org/10.1016/j.hrcr.2019.10.016
3-dimensional (3D) electroanatomic activation mapping of the right atrium (RA) was performed during sinus rhythm. The junction of superior vena cava (SVC) and RA was identified by selective SVC angiography (Figures 1 and 2). Locations with a potential risk of phrenic nerve injury during CA were identified by pacing. In case of phrenic nerve capture, consequently, no ablation attempt was made at this location. CA was performed at the site of the earliest local bipolar electrogram relative to the surface P wave and guided anatomically by 3D mapping and angiography of the SVC/RA junction. After precise identification of the location of the SN, CA was performed. Prior to each RF application, remapping of the current earliest local activation was performed. Irrigated RF energy was delivered with a maximum power of 30 W and an infusion rate of 20 mL/min. Energy was applied for 30 seconds until the maximal local electrogram amplitude decreased by 70%. The procedural endpoints were a reduction in heart rate to a baseline rate of <90 bpm and successful ablation of the SN, defined as a change in P-wave morphology from an inferior to a superior axis (Figure 3). After CA, isoproterenol was administered to assess chronotropic competence. Previous pharmacologic therapy of IST was discontinued immediately after SN ablation.

### Endpoints

The primary procedural endpoint was ablation of the SN (as described above). Secondary endpoints were procedure-related complications including phrenic nerve palsy.

### Table 1: Baseline patient characteristics

| Patient | Patient | Patient |
|---------|---------|---------|
| #1      | #2      | #3      |
| Age, y  | 36      | 28      | 53      |
| Sex     | Female  | Female  | Female  |
| LV ejection fraction, % | 55      | 60      | 55      |
| Mean heart rate (24h), bpm | 92      | 88      | 87      |
| Maximum heart rate (24h), bpm | 144     | 161     | 153     |
| Insufficient AAD, n | 5       | 3       | 4       |
| Hospitalizations ≤36 months, n | 4       | 5       | 3       |
| Prior attempt at SN modulation, n | 1       | 0       | 1       |
| Time elapsed since prior attempt, days | 60      | –       | 62      |

AAD = antiarrhythmic drugs; bpm = beats per minute; LV = left ventricular; SN = sinus node.
pericardial effusion, pericardial tamponade, and permanent pacemaker implantation.

Follow-up
Clinical follow-up included regular telephone interviews and outpatient clinic visits. In addition, 12-lead ECGs and 24-hour Holter ECGs were performed. In case of symptoms suggestive of recurrent tachycardia, patients were encouraged to contact the investigators.

Acute ablation results
RF energy application was anatomically guided by the 3D reconstruction of the RA and by the earliest local atrial electrogram preceding the surface ECG P wave. Pertinent procedural data are given in Table 2.

In all patients, the location of the SN was found at the lateral aspect of the SVC/RA junction in close proximity to the crista terminalis. During consecutive RF applications, earliest local atrial activation time shifted from a cranial location (lateral aspect of the SVC/RA junction) to a more caudal location (mid-lateral RA). The procedural endpoint was achieved in all 3 patients; accordingly, the P-wave axis changed from inferior to superior. Cycle length increased markedly from 585 to 1130 ms (+93%), 500 to 1210 ms (+142%), and 580 to 1390 ms (+105%). During isoproterenol infusion (at a rate of 1-2 g/min) a chronotropic response was still present with a reduction in cycle length to 595, 610, and 570 ms, respectively. Acute ablation results are given in Table 2.

Before hospital discharge, 24-hour Holter ECGs were recorded in each patient. Mean and maximum heart rate on 24-hour Holter monitoring were markedly reduced after the ablation procedure (mean: 92 to 51 bpm, 88 to 46 bpm, and 87 to 64 bpm; maximum: 144 to 111 bpm, 161 to 92 bpm, and 153 to 106 bpm, respectively).

Complications
In 1 patient, a dual-chamber pacemaker was implanted 6 days after SN ablation. In this patient, SN ablation resulted in an intermittent junctional rhythm with a mean heart rate of 46 bpm. The patient was limited by symptoms of weakness and dizziness. No further complications occurred.

Clinical follow-up
After a mean of 424 ± 136 days, 2 of the 3 patients remained free of recurrent symptoms in the absence of antiarrhythmic drug therapy. The remaining patient, who underwent pacemaker implantation after SN ablation, reported relief of symptoms; however, intermittent palpitation was still present. The 2 patients who were unable to work because of IST resumed work following SN ablation.

Discussion
Main findings
We report on 3 patients with IST who underwent successful SN ablation using the novel procedural endpoint definition of a change in P-wave morphology from an inferior to a superior axis. The approach resulted in (1) significant heart rate reduction; (2) discontinuation of previous pharmacologic therapy; (3) permanent pacemaker implantation in 1 patient; and (4) relief of symptoms and hospitalization, yet complete freedom of symptoms was not categorically achieved.

Pharmacologic therapy for treatment of IST
Patients with IST are frequently treated with a variety of drugs, including ß-blockers, fludrocortisone, phenobarbital, clonidine, and erythropoietin.2,4 The evidence supporting the efficacy of these drugs is poor, since there are no prospective, placebo-controlled clinical trials of any of these drugs.4 As an exception, ivabradine seems to provide a promising pharmacologic treatment option for IST.6,7 However, the duration of medical therapy might be indefinite, and, moreover, there is a considerable number of patients who do not respond well to pharmacologic therapy.3 In the present study, the patients were taking between 3 and 5 antiarrhythmic drugs, including ivabradine in 2 patients, before the ablation procedure. Despite this intensified therapy, our patients did not experience relief of symptoms. The reason why patients do not generally respond to medical therapy remains unknown.

Catheter ablation for the treatment of IST
Data on CA for the treatment of IST are sparse, and there is no consensus on the optimal procedural approach and the procedural endpoint.1 Formatting... please wait

Figure 2
Angiography of the superior vena cava (SVC) and the SVC/right atrium (RA) junction. Contrast medium (CM) is injected through a long sheath (LS) that is positioned in the SVC. DC 1 = diagnostic catheter positioned in the coronary sinus; DC 2 = diagnostic catheter positioned at the His bundle. Fluoroscopic right anterior oblique 30° view.
recurrences following SN modification is consistent with the experience at our center.

Therefore, the aim of the present study was to assess clinical outcomes of SN ablation, defined as a change in P-wave morphology from an inferior to a superior axis, as a novel procedural endpoint. SN ablation was feasible in all of the 3 patients. After a mean follow-up of 424 ± 136 days, 2 patients were free of symptoms. Of note, these patients had previously undergone ineffective CA aiming at SN modification. The remaining patient, who had required permanent pacemaker implantation after SN ablation, reported significant relief of symptoms, yet intermittent palpitation was still present.

IST is a complex disease and the treatment remains challenging. Patients require significant care and attention, yet permanent cure is rare. CA is not considered a treatment on a routine basis. However, CA can provide effective treatment for highly symptomatic, drug-refractory patients. To date, there is no precise procedural endpoint. The establishment of such a generally accepted endpoint should be the objective of further studies.

Complications
Prior studies reported considerably high complications rates.8-13 In the present study, permanent pacemaker implantation occurred as the only complication. Three-dimensional mapping, pacing-guided identification of locations with potential risk of phrenic nerve injury, and an angiography of the SVC are helpful instruments to avoid complications in CA of IST. However, the risk of permanent pacemaker implantation remains a critical aspect that has to be sensitively discussed with the patients.

Limitations
This is an observational, nonrandomized single-center study with only 3 patients. SN ablation might not generally result in a stable rhythm with change in P-wave axis; therefore, the risk of permanent pacemaker implantation might still be

Table 2 Periprocedural data

| Patient | Patient | Patient |
|---------|---------|---------|
| #1      | #2      | #3      |
| RF applications, n | 33 | 29 | 34 |
| Procedure duration, min | 130 | 120 | 140 |
| Fluoroscopy time, min | 5 | 5 | 2 |
| CL before SN ablation, ms | 585 | 500 | 580 |
| CL after SN ablation, ms | 1130 | 1210 | 1390 |
| CL during isoproterenol, ms | 595 | 610 | 570 |
| Mean heart rate (24 h), bpm | 51 | 46 | 64 |
| Maximum heart rate (24 h), bpm | 111 | 92 | 106 |
| Change in mean heart rate (24 h) from baseline, bpm | 41 | 42 | 23 |
| Permanent pacemaker implantation | No | Yes | No |
| Follow-up, d | 609 | 288 | 375 |
| Rehospitalizations, n | 4 | 5 | 3 |

CL = cycle length; RF = radiofrequency; SN = sinus node.
underestimated. In the 2 patients with prior CA aiming at modification of the SN, a potential effect of these procedures on procedural and clinical outcomes should be considered. Further investigations with larger numbers of patients are required to determine the clinical impact of SN ablation for treatment of IST.

Conclusions
Among patients with drug-refractory and symptomatic IST, SN ablation, defined as a change in P-wave morphology from an inferior to a superior axis, can provide effective treatment, even for patients who did not respond to SN modification. The risk of permanent pacemaker implantation must be realized.

References
1. Krahn AD, Yee R, Klein GJ, Morillo C. Inappropriate sinus tachycardia: evaluation and therapy. J Cardiovasc Electrophysiol 1995;6:1124–1128.
2. Olshansky B, Sullivan RM. Inappropriate sinus tachycardia. J Am Coll Cardiol 2013;61:793–801.
3. Rodriguez-Manero M, Kreidieh B, Al Rifai M, et al. Ablation of inappropriate sinus tachycardia: a systematic review of the literature. JACC Clin Electrophysiol 2017;3:253–265.
4. Sheldon RS, Grubb BP, Olshansky B, et al. 2015 Heart Rhythm Society Expert Consensus Statement on the Diagnosis and Treatment of Postural Tachycardia Syndrome, Inappropriate Sinus Tachycardia, and Vasovagal Syncope. Heart Rhythm 2015;12:e41–e63.
5. Shen WK. How to manage patients with inappropriate sinus tachycardia. Heart Rhythm 2005;2:1015–1019.
6. Cappato R, Castelvecchio S, Ricci C, et al. Clinical efficacy of ivabradine in patients with inappropriate sinus tachycardia: a prospective, randomized, placebo-controlled, double-blind, crossover evaluation. J Am Coll Cardiol 2012;60:1323–1329.
7. Ptaszynski P, Kaczmarek K, Ruta J, Klingenhoven T, Cygankiewicz I, Wranicz JK. Ivabradine in combination with metoprolol succinate in the treatment of inappropriate sinus tachycardia. J Cardiovase Pharmacol Ther 2013;18:338–344.
8. Lee RJ, Kalman JM, Fitzpatrick AP, et al. Radiofrequency catheter modification of the sinus node for “inappropriate” sinus tachycardia. Circulation 1995;92:2919–2928.
9. Man KC, Knight B, Tse HF, et al. Radiofrequency catheter ablation of inappropriate sinus tachycardia guided by activation mapping. J Am Coll Cardiol 2000;35:451–457.
10. Marrouche NF, Beheiry S, Tomassoni G, et al. Three-dimensional non-fluoroscopic mapping and ablation of inappropriate sinus tachycardia: Procedural strategies and long-term outcome. J Am Coll Cardiol 2002;39:1046–1054.
11. Frankel DS, Lin D, Anastasio N, et al. Frequent additional tachyarrhythmias in patients with inappropriate sinus tachycardia undergoing sinus node modification: an important cause of symptom recurrence. J Cardiovasc Electrophysiol 2012;23:835–839.
12. Jacobson JT, Kraus A, Lee R, Goldberger JJ. Epicardial/endocardial sinus node ablation after failed endocardial ablation for the treatment of inappropriate sinus tachycardia. J Cardiovase Electrophysiol 2014;25:236–241.
13. Ibarra-Cortez SH, Rodriguez-Manero M, Kreidieh B, Schurrman P, Dave AS, Valderrabano M. Strategies for phrenic nerve preservation during ablation of inappropriate sinus tachycardia. Heart Rhythm 2016;13:1238–1245.