Sleep-disordered breathing predicts sinus node dysfunction in persistent atrial fibrillation patients undergoing pulmonary vein isolation

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1. Introduction

Catheter ablation is an efficient procedure for controlling drugrefractory atrial fibrillation (AF) [1]. The midterm results of catheter ablation for AF have been reported recently, and catheter ablation has been considered useful for treating AF [2,3]. The indications for catheter ablation have been expanded to include persistent AF, and a high degree of sinus rhythm maintenance is enabled by additional linear ablation and pulmonary vein isolation [4]. However, we have implanted pacemakers in patients in whom sick sinus syndrome became clinically evident after persistent AF ablation at a small but relatively constant rate. Elvan et al. reported that chronic AF causes sinus node dysfunction (SND) in animal models and that the SN function slowly recovers after AF was terminated [5]. Some reports have indicated that patients with chronic AF develop SND after undergoing electrical cardioversion [6,7]. AF and SND are closely related but we are unable to estimate SN function under

continued persistent AF. If underlying SND during persistent AF can be predicted, it would be useful for determining the necessity for persistent AF ablation. There are some reports that atrial fibrillation becomes the causative factor of sleep respiratory disorder [8,9]. On another front, it was reported that sleep-disordered breathing (SDB) contributes to the risk for atrial fibrillation and sick sinus syndrome [10]. These factors lead to a vicious cycle and worsen AF and SDB. Therefore treatment intervention for AF by catheter ablation is important to break the vicious cycle. Here, we hypothesized that persistent AF patients with SDB might have SND. The objective of this study was to investigate whether underlying SND can be predicted prior to catheter ablation for persistent AF using the apnea/hypopnea index (AHI).

2. Methods

2.1. Study population

Catheter ablation for persistent atrial fibrillation was performed in a total of 103 patients at Hiroshima University Hospital between January 2010 and July 2011. The type of AF was defined according to generally accepted guidelines [11]. From 103 patients, patients with significant valvular disease requiring surgery, patients with underlying diseases such as thyroid dysfunction, patients with heart failure, patients who were diagnosed with sick sinus syndrome in the past, and patients who had terminated AF by pharmacologic or electrical cardioversion were excluded and the remaining 87 consecutive patients with persistent AF and longstanding persistent AF were registered in this study (mean age, 60.6 ± 8.7 years; 71 [81%] male). All antiarrhythmic agents were generally

discontinued at least five half-lives before electrophysiologic studies [12]. Adequate oral anticoagulation therapy (international normalized ratio, 2.0–3.0) was administered not less than 1 month before the procedure and was continued throughout the periprocedural period without interruption as previously described [13]. Patients underwent transesophageal echocardiography to exclude any left atrial (LA) thrombi; they also underwent transthoracic echocardiography and cardiac computed tomography prior to ablation. This study was approved by the Institutional Review Board at Hiroshima University Hospital. Written informed consent was obtained from all patients when they were recruited to the study.

2.2. Sleep study and polysomnography scoring

Nocturnal polysomnography (Alice 4; Philips Respironics GK, Tokyo, Japan) was performed for all patients 1 day before the catheter ablation; it included electroencephalography, electrooculography, and submental and tibialis anterior electromyography for sleep staging, according to a previous report [14]. Apnea was defined as the absence of airflow for >10 s despite persistent respiratory efforts. Hypopnea was defined as a >50% reduction in the amplitude of respiratory efforts for at least 10 s along with a fall in arterial oxyhemoglobin saturation of at least 3%. The total duration of arterial desaturation was quantified as total time with an arterial oxyhemoglobin saturation of <90%. The AHI was defined as the number of episodes of apnea and hypopnea per hour of sleep. The threshold for a diagnosis of sleep-disordered breathing (SDB) was an AHI > 5, and that criterion was used to classify patients into SDB or non SDB groups. We categorized sleep apnea using standard clinical

cutoff points for severity (moderate to severe SDB:AHI ≥ 15) [15]. Therefore, the relationship between AHI and SND was assessed by classifying patients on the basis of an AHI ≥ 15 in the multivariate analysis.

2.3. Cardiac parameter evaluation

We measured the end-systolic LA diameter, left ventricular parameters, and ejection fraction with two-dimensional (2D) transthoracic echocardiography. LA appendage area and LA appendage flow were measured by 2D transesophageal echocardiography 1 day before the catheter ablation.

2.4. Catheter ablation

We performed the double Lasso catheter and electroanatomical mapping-guided extensive encircling pulmonary vein isolation (EEPVI) method. Briefly, a 6-Fr decapolar catheter with 2–5–2 mm interelectrode spacing (St. Jude Medical, St. Paul, MN, USA) was positioned in the coronary sinus. After transseptal catheterization, two 7-Fr decapolar Lasso catheters (Biosense Webster, Diamond Bar, CA, USA) were placed within the ipsilateral superior and inferior pulmonary veins (PVs) guided by selective PV angiography. After constructing three-dimensional electroanatomical maps using a nonfluoroscopic navigation system (Carto, Biosense Webster), continuous circumferential ablation lines were created around the left- and right-sided PVs using a 3.5-mm tip irrigated catheter (ThermoCool, Biosense Webster) at a maximum power of 30 W for 40 s at each site. Temperature was limited to 50 ◦C. The EEPVI endpoint was the creation of a bidirectional conduction block from

LA to PVs. Subsequently, an additional linear lesion connecting the superior aspects of the left and right upper PV isolation lesions was created. If AF was still present after LA ablation, external cardioversion was performed to restore sinus rhythm. Finally, the cavotricuspid isthmus was ablated with an endpoint of a bidirectional conduction block using a 4.0-mm tip, temperature-controlled, nonirrigated catheter (EPT; Boston Scientific Corporation, Natick, MA, USA) at a maximum power of 50 W and a maximum electrode–tissue interface temperature of 60 ◦C. Intravenous heparin was administered to maintain an activated clotting time of 250–350 s during the procedure. The intraoperative sedation depended on only thiamylal sodium just before EEPVI. If sedation did not seem to be obtained or recovered, we supplemented with thiamylal sodium as needed and did not use other sedatives.

2.5. Electrophysiological study and 24-h electrocardiographic monitoring

After a stable sinus rhythm was established by catheter ablation, quadripolar diagnostic catheters (St. Jude Medical) were placed at the His bundle and at the superior right atrium. Subsequently, autonomic blockade was induced by administering 0.04 mg/kg atropine and 0.2 mg/kg propranolol, and the electrophysiological study was performed within 1 h. AA, AH, and HV intervals were measured with a baseline electrocardiogram. The sinus node recovery time (SNRT), evaluated by 30-s burst pacing trains every 50 ms from 600 to 300 ms, was determined as the longest time from the stimulus artifact to the earliest atrial activity. Corrected SNRT (CSNRT) was defined as the recovery interval in excess of the sinus cycle (max SNRT-sinus cycle length) [16]. According to the 2006

guidelines for clinical cardiac electrophysiological studies of the Japanese Circulation Society and a previous report [17], SND was defined as a CSNRT of ≥550 ms. AV node function was evaluated by measuring the AH interval, HV interval, the point of Wenckebach block (AVN1:1 conduction) and the effective refractory period of the AV node (AVNERP). The Wenckebach point of the AV node was determined by increasing atrial pacing from just above the sinus rate with increases of 10 impulses/min per 10 s. The anterograde AV nodal effective refractory period (AVNERP) was measured using an eight-beat drive at a cycle length equal to the sinus cycle length of 100 ms, followed by a single premature atrial stimulus introduced decrementally at 10-ms intervals. AVNERP was defined as the longest coupled premature atrial stimuli interval that failed to propagate to the His bundle. After catheter ablation, the subjects wore 24-h electrocardiographic monitoring devices, from which total beats, maximum heart rate, and minimum heart rate were obtained. Heart rate variability such as low-frequency (LF) power, high-frequency (HF) power, and the LF/HF ratio were also calculated using frequency domain analysis [18].

2.6. Statistical analysis

Continuous variables are presented as the mean ± SD, and the Student's t-test was used for comparison. Categorical variables are presented as the number of data and percent, and compared employing the χ^2 test. Multivariate analysis was used to determine the independent risk factors for SND. Potential predictors with p-values < 0.20 on the univariate analysis were included in a multivariate logistic regression analysis. Odds ratios and 95% confidence intervals were calculated.

p-values of < 0.05 were regarded as significant. All statistical analyses were performed using JMP version 8.0.2 (SAS Institute, Cary, NC, USA).

3. Results

In total, 42 patients (48%) had SND (SND group), and the remaining patients had normal sinus node function (NSN group). Table 1 shows the patient characteristics. Age in the SND group was significantly higher than that in the NSN group (62 ± 7.6 vs. 58 ± 9.4; p = 0.04). The other parameters of the patient characteristics were similar in both groups. No difference was observed in the antiarrhythmic agents between the SND and NSN groups pre catheter ablation. No significant differences were observed for the cardiac structural parameters. The sleep disorders of the all cases detected in preoperative polysomnography were obstruction type. AHI and arousal index were significantly higher and SpO2 was significantly lower in the SND group than in the NSN group (AHI: 25.7 ± 12.7 vs. 17.5 ± 11.4; p = 0.0022; arousal index: 23.3 ± 6.8 vs. 34.4 ± 10.1; p = 0.032; SpO2: 83 ± 1.4 vs. 87.9 ± 1.6; p = 0.025) (Table 2). There was a positive correlation between AHI and CSNRT (R: 0.51; p < 0.0001; Fig. 1). Table 3 shows the ablation procedure and electrophysiological parameters after catheter ablation. SNRT of the SND group was significantly longer than that in the NSN group (1874 ± 790 ms vs. 1218 ± 250 ms, respectively; p < 0.0001). CSNRT was also longer in the SND group than in the NSN group (986 ± 109 ms vs. 395 ± 112 ms in the SND and NSN groups, respectively; p < 0.0001). No significant differences were observed for the AH interval, HV interval, the point of Wenckebach block (AVN1:1 conduction), or AVNERP

between the groups. There was no difference in the ablation procedure between either group. The 24-h electrocardiographic monitoring after catheter ablation revealed that total beats in the SND group were significantly lower than that in the NSN group (90,639 ± 15,806 vs. 99,357 ± 16,595; p = 0.025) (Fig. 2). Minimum heart rate and average heart rate during night time in the SND group were also lower than those in the NSN group (minimum heart rate: 63 ± 9.3 vs. 68 ± 10 bpm; p = 0.038; average heart rate during night time: 68 ± 8.1 vs. 78 ± 10 bpm; p = 0.032). No difference was observed in the LF/HF ratio between the SND and NSN groups (Table 4). A multivariate analysis showed that moderate to severe SDB (AHI ≥ 15) was an independent predictor of SND after catheter ablation for persistent AF (Table 5). Two patients required temporary pacemakers (0.023%) after catheter ablation, and one needed a permanent pacemaker. The average AHI of all patients (n = 87) was 21.2 ± 12.6, and 45 patients (51%) had moderate to severe SDB (AHI ≥ 15). Hypertension in patients with moderate to severe SDB was significantly higher than that without (53.9% vs. 23.7%; p = 0.006). C-reactive protein levels in patients with moderate to severe SDB were also higher than those without (0.15 ± 0.04 vs. 0.007 ± 0.01; p = 0.03). LA diameters in patients with moderate to severe SDB were larger than those without (42.5 ± 4.7 vs. 40.4 ± 4.2; p = 0.04). Heart rate variability was similar in patients with and without moderate to severe SDB. In our study, two patients (0.023%) required temporary pacemakers after catheter ablation, and one of them needed a permanent pacemaker. The CSNRT and total beats 24-h electrocardiographic monitoring of the patient with a permanent pacemaker were 2626 ms and 66,302 beats, respectively.

4. Discussion

In this study, 42 patients (48%) showed SND after catheter ablation for persistent AF. We found that SDB was an independent predictor of underlying SND in patients with persistent AF who underwent catheter ablation.

Several reports have indicated that various factors evoked by SDB cause AF. Hypoxemia and hypercapnia have direct adverse effects on cardiac electrical stability and are arrhythmogenic substrates [19,20]. Patients with SDB are susceptible to AF with increased sympathetic nerve activation during sleep [21]. The forceful ventilatory efforts against upper airway obstruction during apnea result in sympathetic vasoconstriction and increased blood pressure. Increases in blood pressure coupled with the increased afterload resulting from sleep apnea-induced vasoconstriction may contribute to an increase in LA dimensions [22]. In addition, the severity of SDB is independently associated with elevated markers of systemic inflammation [23], and C-reactive protein levels are directly associated with the increasing burden of AF [24]. In chronic phase, these acute structural changes may promote AF by triggering stretch-activated atrial ion channels [25]. In our study, as previously reported, the percentage of patients with moderate to severe SDB who had hypertension and elevated C-reactive protein levels was significantly higher than those without. LA diameters in patients with moderate to severe SDB were larger than those without.

Some reports have also indicated that atrial remodeling caused by AF leads to susceptibility to SND. In a study including 12 patients with chronic lone AF, Kumagai et al. [6] assessed SN function on the day after electrical conversion to sinus rhythm. They found that the mean CSNRT of the patients was

significantly longer than that of controls and was abnormal in nine (75%) patients. Similarly, Manios et al. [7] reported that abnormal CSNRT was found in 10/37 (27%) patients with chronic AF after cardioversion to sinus rhythm. In our study, we performed the electrophysiological study within 1 h after the ablation in patients who achieved sinus rhythm by ablation, and SND was found in 42/87 (48%) of patients with persistent AF. In addition, the total number of heart beats from 24-h electrocardiographic monitoring was significantly lower in the SND group than in the NSN group at 24 h after the ablation.

We sometimes experience tachycardia during the ablation of right pulmonary vein (RPV) and bradycardia during the ablation of ridge of left pulmonary vein (LPV). In our study, we performed only EEPVI without additional ganglionated plexus ablation, and there was no difference in the procedure in all the cases. As for the EEPVI in the present study, more than 20% decrease in heart rate during ablation of LPV was found in 22% of NSN group and in 18% of SND group ($p = 0.13$). And, more than 20% increase in heart rate during ablation of RPV was found in 18% of NSN group and in 12% of SND group ($p = 0.15$). The alternation of heart rate during the EEPVI was similar in the two groups. Additionally, LF power, HF power, and the LF/HF ratio in 24-h electrocardiographic monitoring after ablation were also similar in the two groups. In general, sinus node function can be assessed by overdrive suppression test during electrophysiological study and also by 24 h electrocardiographic monitoring. In this study, SNRT (CSNRT) was measured after pharmacologic denervation during catheter ablation procedure, whereas 24 h electrocardiography was recorded after catheter ablation. Then, we cannot deny the influence of denervation to the ganglion plexi or their

fibers by the EEPVI about the 24 h electrocardiography. In our study, Min HR, total beats of 24 h electrocardiography recording and average HR during night time were lower in patients with SND than those in patients with NSD.

AF can lead to changes in connexin patterns, myocyte cellular substructure, interstitial fibrosis, and apoptotic atrial myocyte death [26]. These structural changes may also be the result of SND. In our study, no significant differences in LA diameter were observed between patients with and without SND. The conduction of AV node tended to deteriorate in patients with SND. Antiarrhythmic drugs were discontinued preoperatively. The structural remodeling was also likely to have an adverse impact on AV node conduction.

On another front, it was reported that SDB itself causes deterioration in SN function [10]. SND may easily cause AF and vice versa, as discussed above. Thus, the possibility that SND is caused by SAS and that AF is caused by SND may be valid. These factors such as SDB, SND, and AF may lead to a vicious cycle and worsen the AF and SDB. Therefore, treatment intervention for AF by catheter ablation is very important to break out of the vicious cycle. By expanding catheter ablation for persistent AF, there may be cases that require additional treatment for bradycardia, but unexpected SND after catheter ablation may increase. In this study, we hypothesized that persistent AF patients with SDB might have SND. However, it is difficult to evaluate SN function in patients with persistent AF before conversion to sinus rhythm. The objective of this study was to investigate whether underlying SND can be predicted prior to catheter ablation for persistent AF using the AHI. As a result, SND was found in significantly more cases of the moderate to severe SDB group than that in

the NSN group in the electrophysiological studies after catheter ablation for persistent AF. Our results suggested that the AF patients complicated with SDB were susceptible to SND. Then, we had better intervene in the SDB before and after AF ablation. The improvement of SDB by continuous positive airway pressure or assisted ventilation may bring beneficial change to SND and avoid pacemaker implantation and we positively become able to use an antiarrhythmic drug after the AF ablation. The AF ablation and treatment intervention for the SDB before and after the procedure may be a new hybrid therapy for AF and there is the potential for improving the long-term outcome for sinus node maintenance after the AF ablation

5. Limitations

There are some limitations in this study. We evaluated CSNRT immediately after ablation. AF ablation influenced autonomic tone. Therefore, we evaluated electrophysiological parameters after an autonomic block. In addition, heart rate variability using the frequency domain analysis of 24 h electrocardiographic monitoring was similar in patients with and without SND. The autonomic modification by the pulmonary vein isolation itself may be a study limitation of this study. We only used thiamylal sodium as an anesthetic for the catheter ablation. Effects of the thiamylal sodium on the autonomic nervous system and atrial electrophysiology cannot be ruled out, but we have used this drug in subjects under the same conditions. Additionally, total doses of sedative agent were similar in both groups. In our study, two patients (0.023%) required temporary pacemakers after catheter ablation, and one needed a permanent pacemaker. Patients who required a permanent or temporary

pacemaker had AHI ≥ 15. Because of the small number of subjects enrolled in this study, we were unable to identify patients who needed a permanent pacemaker from those who did not.

Acknowledgment

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Figure legend

Figure. 1 Correlation between AHI and CSNRT There was the positive correlation between AHI and CSNRT

Figure. 2 Total heart beats after catheter ablation The 24-h electrocardiographic monitoring after catheter ablation revealed that total beats in the SND group were significantly lower than that in the NSN group

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Table

Table 1. Patient baseline characteristics and sinus node dysfunction

	NSN (n = 45, 52%)	SND (n = 42, 48%)	P value
Age (years)	58 ± 9.4	62 ± 7.6	0.04
Male (%)	85	72	0.15
Structural heart disease (%)	27	25	0.85
Hypertension (%)	41	36	0.63
Hyperlipidemia (%)	35.5	40.9	0.69
Diabetes mellitus (%)	70	53	0.1
AF duration (months)	70 ± 12	67 ± 12	0.87
ACE or ARB (%)	34.1	41.6	0.5
HANP (pg/ml)	74.8 ± 70	70 ± 30	0.76
CRP pre ablation (mg/dl)	0.12 ± 0.06	0.12 ± 0.08	0.95
Anti-arrhythmic agents before catheter ablation			
Class Ia/Ib/Ic (%)	0/4.9/4.9	2.7/2.8/2.8	0.2/0.6/0.6
Class II/ III/IV (%)	22/25/22	27/33/23	0.6/0.4/0/9
Cardiac structural parameters			
LAA area (cm^2)	5.7 ± 2.0	5.7 ± 1.8	0.89
LAA flow (m/s)	0.45 ± 0.18	0.39 ± 0.18	0.17
LVDd (mm)	47.3 ± 5.0	46.9 ± 3.7	0.69
LVDs (mm)	32.6 ± 4.1	32.6 ± 4.1	0.98
LA diameter (mm)	41.4 ± 5.0	41.6 ± 4	0.83
Ejection fraction (%)	56.1 ± 5.7	57.6 ± 6.4	0.28

Values are presented as mean or percentage ± SD

ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker;

AHI, apnea/hypopnea index; SND, sinus node dysfunction; NSN, normal sinus node

LAA, left atrial appendage; LVDd, LV dimension diastolic;

LVDs, LV dimension systolic; SND, sinus node dysfunction; NSN, normal sinus node

Table 2. Sleep Study and Polysomnography Score

	NSN (n = 45, 52%)	SND (n = 42, 48%)	P Value
AHI	17.5 ± 11.4	25.7 ± 12.7	0.0022
Apnea index	16.7 ± 15.3	23.7 ± 11	0.082
Hypopnea index	16.5 ± 15.2	23.8 ± 11.1	0.067
Mean SpO_2 (%)	97 ± 2.4	96 ± 2.3	0.27
Minmum SpO_2 (%)	87.9 ± 1.6	83 ± 1.4	0.025
Sleep time (min)	517 ± 78	497 ± 52	0.29
Arousal index	23.3 ± 6.8	34.4 ± 10.1	0.032
OSA (%)	100	100	

AHI, apnea/hypopnea index; OSA, Obstructive Sleep Apnea

Table 3. Catheter ablation and Electrophysiological study

	NSN (n = 45, 52%)	SND (n = 42, 48%)	P value
SNRT (ms)	1218 ± 250	1874 ± 790	<0.0001
A-A interval (ms)	820 ± 184	859 ± 137	0.31
CSNRT (ms)	395 ± 112	986 ± 109	<0.0001
AVN1:1 conduction (bpm)	156 ± 24	146 ± 25	0.07
AH interval (ms)	86 ± 19	94 ± 29	0.20
HV interval (ms)	43 ± 9.1	45 ± 15	0.34
AVN–ERP (ms)	296 ± 49	306 ± 69	0.59
LPV Ablation (min)	23.9 ± 15.2	22.6 ± 10.6	0.81
RPV Ablation (min)	26.9 ± 14.6	26.5 ± 19.8	0.93
PVI Time (min)	63.9 ± 22.5	59.9 ± 24.2	0.54
Fluoroscopy time (min)	64.7 ± 17.6	60.4 ± 13.6	0.35
Radiation dosage (mgy)	1462 ± 738	1929 ± 1270	0.12
Ablation Points (Points)	95.8 ± 33.7	89.8 ± 36.3	0.53
Thiamylal sodium (mg)	476.5 ± 162	517.5 ± 222	0.33
Frequency of EC (J)	108.9 ± 27.3	106 ± 21.9	0.67
Number of EC	1.39 ± 0.62	1.52 ± 1.32	0.65

Values are presented as mean or percentage ± SD

SNRT, sinus node recovery time; CSNRT, corrected sinus node recovery time; AVN1:1, the point of the Wenckebach block; AVN-ERP, the effective AV node refractory period; SND, sinus node dysfunction; NSN, normal sinus node; EC, electrical cardioversion

Table 4. Results of the 24-h electrocardiographic monitoring after catheter ablation

	NSN (n = 45, 52%)	SND (n = 42, 48%)	P Value
Total Beats (beats)	99357 ± 16595	90639 ± 15806	0.025
Max HR (bpm)	113 ± 16	107 ± 17	0.14
Min HR (bpm)	68 ± 10	63 ± 9.3	0.038
Average HR (all day)	83 ±8.2	77 ±7.5	0.091
Average HR (day time)	89 ±11	86 ±7.4	0.37
Average HR (night time)	78 ±10	68 ±8.1	0.032
LF	380 ± 158	508 ± 183	0.60
HF	715 ± 341	885 ± 407	0.75
LF/HF	1.58 ± 1.8	1.09 ± 1.0	0.18

Values are presented as mean or percentage ± SD

HR, heart rate; LF, low frequency; HF, high frequency; SND, sinus node dysfunction;

NSN, normal sinus node

Table 5. Predictors of sinus node dysfunction after catheter ablation

	Uni			Multi		
	OR	95% CI	P value	OR	95% CI	P value
Age (>60 years)	1.97	0.83–4.7	0.12	1.2	0.44–3.5	0.69
AF duration (>36 months)	1.4	0.55–3.3	0.51			
Structural heart disease	0.91	0.33–2.53	0.86			
Men	0.45	0.14–1.38	0.16	0.37	0.1–1.35	0.13
Obesity (BMI >24)	1.9	0.62–5.6	0.26			
Moderate to severe SDB	4.8	1.93–12.1	0.001	3.8	1.32–11	0.013
Hypertension	0.79	0.31–2.0	0.63			
Diabetes mellitus	2.1	0.85–5.5	0.11	1.3	0.46–4.0	0.57
ARB or ACE	0.65	0.17–2.5	0.53			
LAA area (>5.0cm^2)	0.98	0.37–2.7	0.98			
LAA flow (<0.3 m/s)	1.6	0.55–4.4	0.41			
LA dimension (>40 mm)	1.0	0.32–3.2	0.98			
Ejection fraction (<55%)	1.7	0.63–4.4	0.30			
CRP preablation (>0.02mg/dl)	1.2	0.40–3.3	0.79			

Uni, univariate analysis; Multi, multivariate logistic regression analysis; OR, odds ratio; CI, confidence interval; BMI, body mass index; AHI, apnea/hypopnea index; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; LAA, left atrial appendage; LA, left atrial

Figure 1

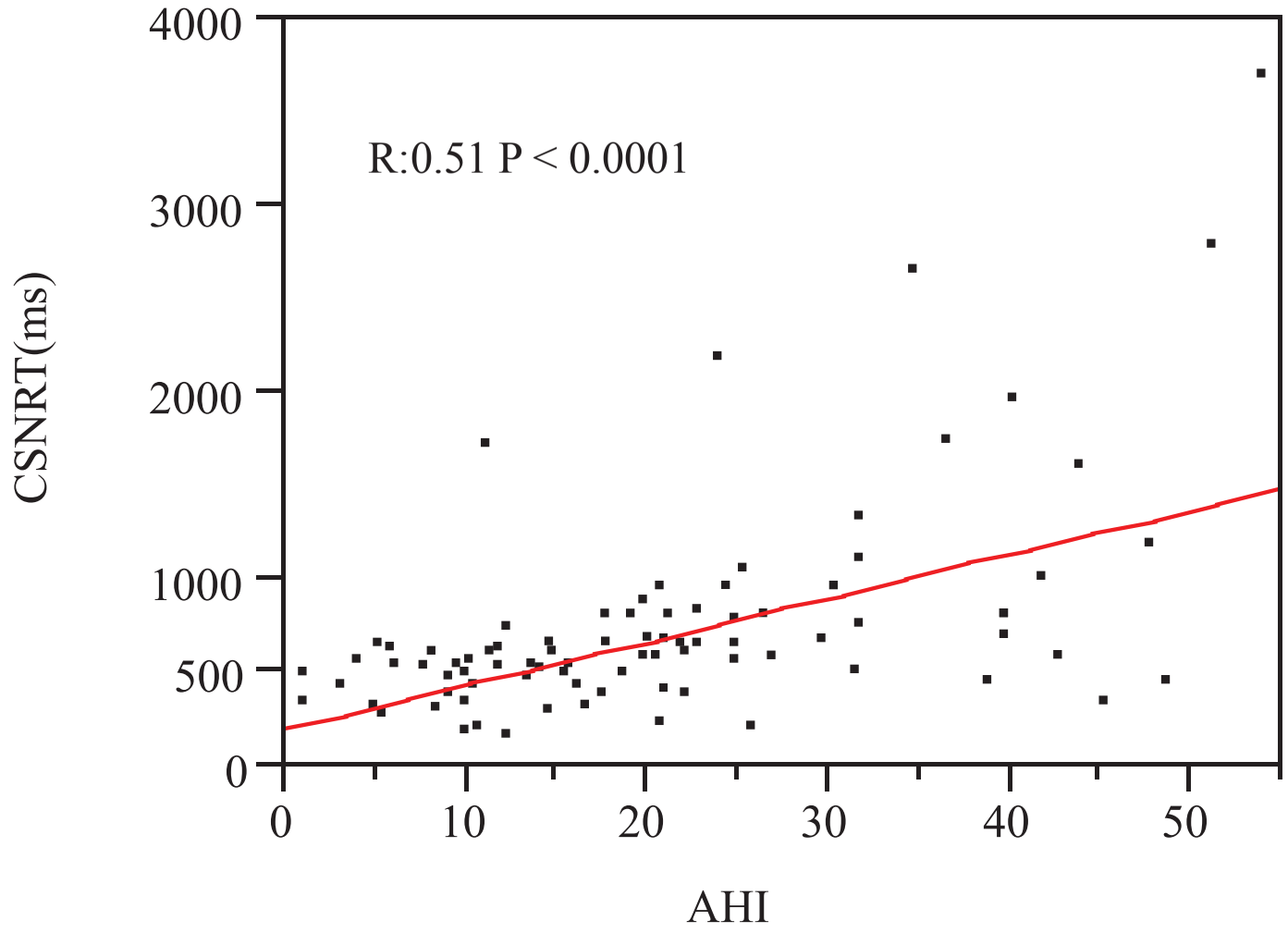
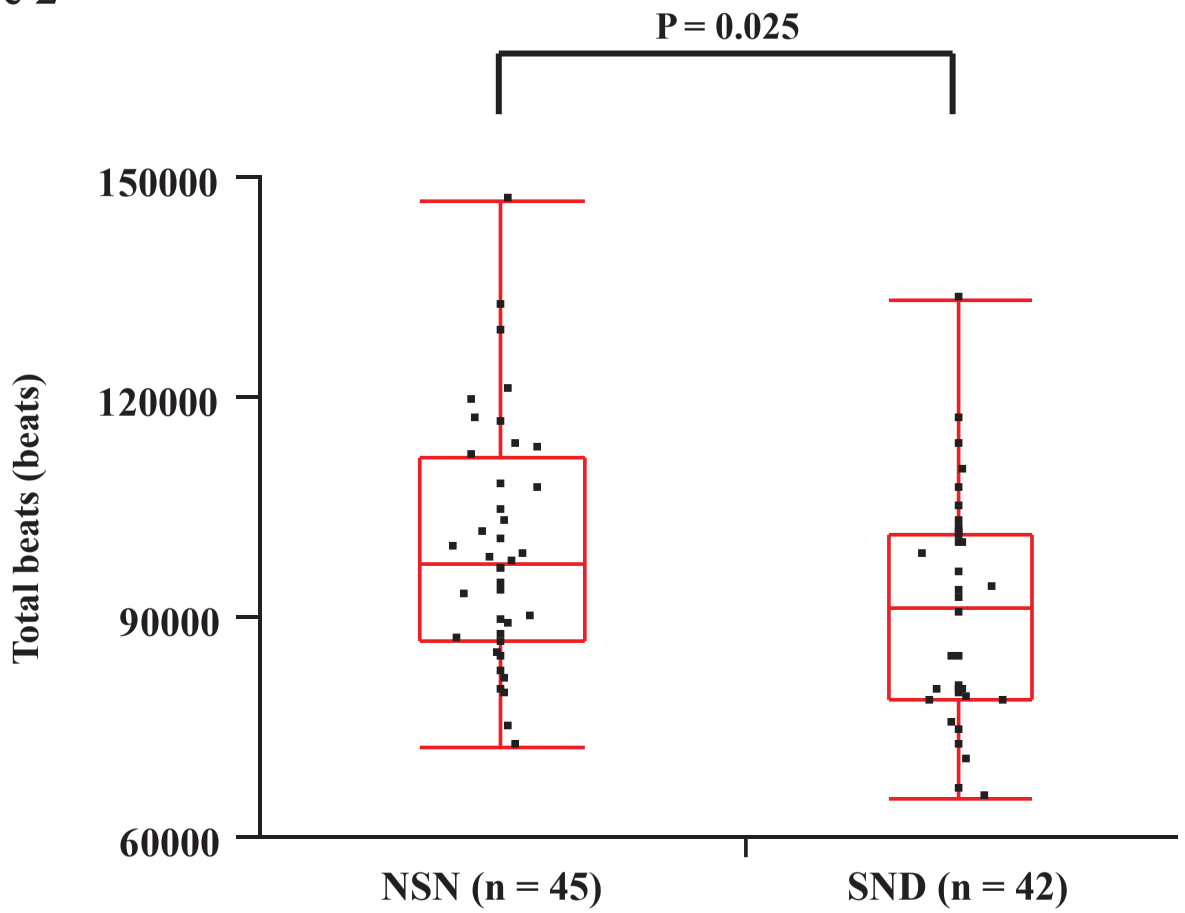

4000
3000
2000
1000
500
0
R:0.51 P < 0.0001
CSNRT(ms)
0
10
20
30
40
50
AHI

Figure 2


P = 0.025
150000
120000
90000
60000
Total beats (beats)
NSN (n = 45)
SND (n = 42)