Central sleep apnea and ventricular arrhythmias in heart failure patients

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The central sleep apnea (CSA) is a chronic respiratory illness branded by fluctuations in respiratory effort, resulting in the pause of respiratory muscle activity and airflow during sleep [1]. Although the prevalence of moderate to severe CSA in the overall population is somewhat, around 3–17% [2], it is common in patients with atrial fibrillation and stroke and is establish in up to 40% heart failure (HF) patients [3–8]. It has reliably been shown to be independently related to a poorer prognosis [4–6,8–11]. At present-day, continuous positive airway pressure (CPAP) is the most used treatment for CSA. Both CPAP [12-15] and a newer type of PAP therapy, adaptive servo-ventilation (ASV) [16-19], primarily presented upgrading in CSA and cardiac function in non-randomized studies. On the other hand, their long-term efficacy in dropping morbidity and mortality is still discussed. Certainly, the recently published results of the Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure Trial (SERVE-HF), a huge randomized multicentre trial evaluating ASV, exposed that ASV was linked with augmented cardiovascular mortality in heart failure patients [New York Heart Association (NYHA) class II (with recent HF hospitalization, III, or IV)] with diminished ejection fraction (≤ 45%) [20,21].

Based on these facts, we intend to correlate the ventricular therapies events recorded by the implantable cardiac defibrillator (ICD) in patients with HF and CSA parameters registered by the polysomnography.

We selected 18 patients with with normal renal function, HF, all of them having an ICD and CSA. The study was piloted in agreement with the Helsinki declaration and approved by the ethics committee of our institution. All patients signed the informed consent term before inclusion. This study was conducted at the Hospital e Clínica São Gonçalo, Rio de Janeiro, Brazil. Patients were recruited from January 2016 till June 2016 from the Arrhythmias and Artificial Cardiac Pacing Service of the same hospital. Patients with the combination of the following criteria were consecutively enrolled: (i) age between 18 and 70 years; (ii) ICD implantation for primary prophylaxis to SCD, without ischemia proved by coronary angiography; (iii) central sleep apnea; (iv) glomerular filtration rate estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI equation, eGFR [20] >60mL/min/1.73m² without microalbuminuria); (v) HF, with functional class defined by NYHA II or III, with reduced left ventricular ejection fraction; and (vi) the capacity to comprehend, and sign the informed consent form and attend the clinical tests. The patients that presented any of the subsequent criteria were excluded: (i) pregnancy; (ii) valvular disease with significant adverse sequelae; (iii) unstable angina, myocardial infarction, transient ischemic attack or stroke within the 6 months before the procedure; (iv) renovascular

abnormalities; (v) psychiatric disease; (vi) the inability to be monitored clinically after the procedure; (vii) a known addiction to drugs or alcohol that affects the intellect; (viii) or a serious health condition that, in the investigator opinion's, may adversely affect the safety and/or efficacy of the participant or the study.

The results are expressed as a mean and standard deviation for normally distributed data and as median with interquartile range otherwise. All statistical tests were two-sided. Comparisons between two-paired values were performed with the paired t-test in cases of a Gaussian distribution and by the Wilcoxon test otherwise. Comparisons between more than two-paired values were made by repeated-measures analysis of variance or by Kruskal–Wallis analysis of variance as appropriate, complemented by a post-hoc test. Categorical variables were compared with Fisher's exact test. A P-value <0.05 was considered significant. Correlations between two variables were performed by Pearson's chi-square test in case of a Gaussian distribution and with the Spearman correlation test otherwise. All statistical analyses were performed using the program Graphpad Prism v 7.0 (Graphpad Software, La Jolla, CA, USA).

The general features of the 18 patients, the chocardiographic parameters, renal function, 24-hour ambulatory blood pressure measurements, ICD therapies and all the polysomnography parameters are displayed in Table 1. We observed significant correlation between anti-tachycardia pacing (ATP) events with apnea–hypopnea index (Pearson: r=0.9514, 95% Confidence Interval [95%CI] from 0.8718 to 0.9821, P<0.0001, as shown in Figure 1A), central apnea index (Pearson: r=0.9604, 95%CI from 0.8948 to 0.9854, P<0.0001, as shown in Figure 1B), and 4% oxygen desaturation index (Pearson: r=0.9099, 95%CI from 0.7703 to 0.9663, P<0.0001, as shown in Figure 1C). And also a significant correlation between shock events with apnea–hypopnea index (Pearson: r=0.9363, 95%CI from 0.8339 to 0.9764, P<0.0001, as shown in Figure 1A), central apnea index (Pearson: r=0.9255, 95%CI from 0.8075 to 0.9723, P<0.0001, as shown in Figure 1B),

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Table 1. General features of patients at baseline

Feature	Central sleep apnea
N	18
Age, years	64.4 ± 16.5
Body mass index, kg/m²	29.3 ± 4.1
Male sex (%)	12 (67%)
White ethnicity (%)	15 (83%)
Hypertension	18 (100%)
Type 2 Diabetes Mellitus (%)	14 (78%)
Coronary artery disease	15 (83%)
Heart failure	18 (100%)
Functional Class NYHA II	5 (28%)
Functional Class NYHA III	13 (72%)
Implantable cardiac defibrillator implanted	18 (100%)
Anti-tachycardia pacing events	32.9 ± 11.8
Anti-tachycardia pacing events	18 (100%)
Shock events	7.5 ± 6.0
Shock events	12 (67%)
Creatinine, mg/dL	0.91 ± 0.19
Estimated glomerular filtration rate, mL/min/1.73m² (CKD-EPI)	105.2 ± 23.6
Albumin:creatinine ratio, mg/g	22.4 ± 6.3
Mean 24-hour systolic/diastolic ABPM, mmHg	120.3 ± 4.8/75.0 ± 3.6
Echocardiographic parameters	
Left ventricular mass, g/m²	166.7 ± 23.5
Left ventricular ejection fraction (Simpson), %	29.4 ± 8.1
Left ventricular internal dimension at the end of diastole, mm	68.0 ± 6.7
Left ventricular internal dimension at the end of systole, mm	49.8 ± 3.9
Antiarrhythmic agent	
Amiodarone	18 (100%)
Antihypertensive Agents	
ACE inhibitors/ARB	18 (100%)
β-blockers	18 (100%)
Spironolactone	18 (100%)
Polysomnography parameters	
Apnea–hypopnea index, events/hour	45.2 ± 18.3
Central apnea index, events/hour	33.9 ± 13.9
Mixed apnea index, events/hour	5.4 ± 4.2
Hypopnea index, events/hour	22.5 ± 10.8
Obstructive apnea index, events/hour	3.3 ± 3.1
4% oxygen desaturation index, events/hour	51.2 ± 17.4
SpO$_2$ <90%, min	45.9 ± 39.1
Arousal index, events/hour	42.0 ± 16.5
Sleep efficiency, %	58.7 ± 18.4
Rapid eye movement sleep, %	9.7 ± 4.9

Values are presented as Mean ± SD or %; ABPM, ambulatory blood pressure measurements; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; N, number of patients.
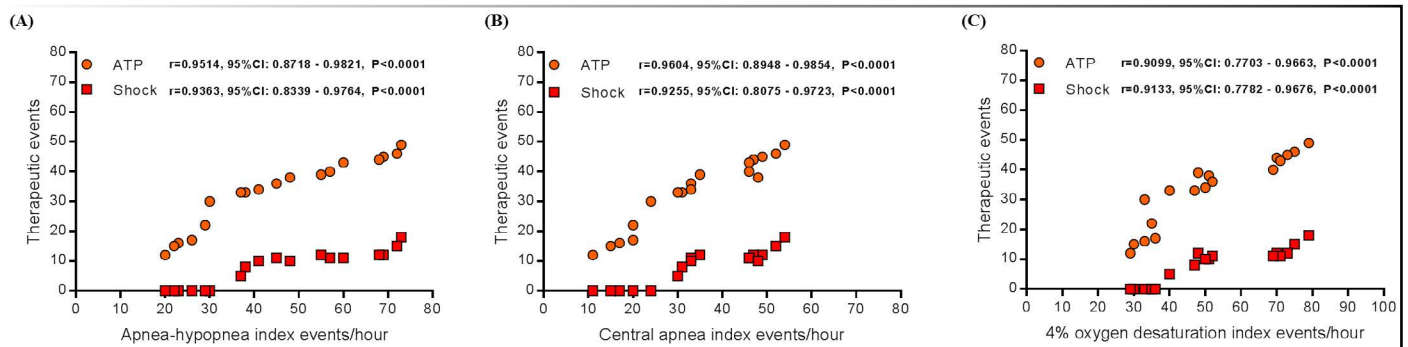

Figure 1. We observed a significant correlation between anti-tachycardia pacing (ATP) and shock events with apnea–hypopnea index (A), central apnea index (B), and 4% oxygen desaturation index (C); 95% CI, 95% confidence interval; n=18.

and 4% oxygen desaturation index (Pearson: r=0.9133, 95%CI from 0.7782 to 0.9676, P<0.0001, as shown in Figure 1C). Our data show that in patients with CSA and HF that have ICD implanted there was a significant correlation between ICD therapies and apnea–hypopnea index, central apnea index, and 4% oxygen desaturation index.

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