Sleep Disordered Breathing is Associated with Appropriate Implantable Cardioverter Defibrillator Therapy in Congestive Heart Failure Patients

Address for correspondence:
Luca Tomaello, MD
Department of Biomedical and Surgical Sciences,
University of Verona
P.le L. A. Scuro, 10 - 37134
Verona, Italy
luca.tomaello@libero.it

Luca Tomaello, MD; Luisa Zanolla, MD; Corrado Vassanelli, MD; Vincenzo LoCascio, MD; Marcello Ferrari, MD

Department of Biomedical and Surgical Sciences, University of Verona, Italy

ABSTRACT

Background: Implantable cardioverter defibrillators (ICDs) are increasingly employed in patients affected by congestive heart failure (CHF) and sleep disordered breathing (SDB) is frequent in this population.
Hypothesis: To investigate SDB prevalence and influence on appropriate ICD discharges in CHF patients.
Methods: A total of 22 consecutive ICD patients with systolic CHF (left ventricular ejection fraction [LVEF]<45%) were studied by polysomnography.
Results: A total of 17 (77.2%) showed SDB (apnea-hypopnea index [AHI]_ 10 events/hour). After controlling for LVEF and New York Heart Association (NYHA) class, AHI and severity of hypoxia during sleep results correlated to appropriate ICD discharges ($r = 0.718$; $P < .001$, $r = -0.619$; $P = .003$, respectively).
Conclusions: Sleep disordered breathing is frequent in ICD recipients due to left systolic ventricular dysfunction and may increase the risk of ventricular arrhythmia and appropriate ICD discharges.

Introduction

Sudden cardiac death (SCD) is associated with excess mortality in patients affected by congestive heart failure (CHF) due to ischemic or nonischemic cardiomyopathy.[1] Various trials have refuted the hypothesis that antiarrhythmic drugs are useful to improve survival in patients with systolic dysfunction and implantable cardioverter defibrillators (ICD) are actually employed in the primary prevention of SCD in heart failure patients. Left ventricular ejection fraction (LVEF), alone or in combination with other indicators, is considered the main predictor of arrhythmic death in CHF patients.[1]

It has been recognized that patients with cardiac dysfunction frequently have undiagnosed sleep disordered breathing (SDB).[2]

A recent analysis of postinfarction nondiabetic patients with systolic heart failure has shown that individuals with a body mass index (BMI) $> 30\ kg/m^2$ have a significantly higher risk of appropriate ICD shock therapy. A possible explanation could be the presence of sleep-related malignant arrhythmias given the high prevalence of obstructive sleep apnea in obese individuals. However few studies have been conducted on the relationship between SDB and arrhythmia in ICD patients.[3]

We investigated patients with impaired left ventricular function who received an ICD in primary prevention to evaluate whether the presence of sleep disordered breathing could be associated with appropriate ICD therapies.

Materials and Methods

Between July and October 2007, 22 male consecutive primary prevention ICD recipients gave informed consent to participate in a home-based sleep study. Eligibility criteria included left ventricular systolic dysfunction as evidenced by a rest LVEF $< 45\%$ measured by echocardiography, ischemic or nonischemic etiology, BMI $< 35\ kg/m^2$; exclusion criteria were primary heart valvular disease, history of chronic obstructive pulmonary disease or other pulmonary disease, renal insufficiency (creatinine > 200 mmol/L), unstable angina, myocardial infarction, cardiac surgery, acute heart failure decompensation, or ICD implantation within the previous 3 months. All patients were treated with angiotensin-converting enzyme inhibitors (ACEI) and β-blockers (carvedilol) at the time of ICD implantation and at follow-up visits; all patients were in sinus rhythm.

Respiratory monitoring consisted of a polysomnography performed with a portable device (Embletta Portable Diagnostic System, Medcare, Iceland). Airflows at nose and at mouth were measured by a nasal cannula connected to a pressure sensor and by a thermistor; thoracoabdominal movements were evaluated by stress sensitive belts (piezo crystal transducer Embletta Portable Diagnostic System, Medcare, Iceland) and arterial oxyhemoglobin saturation ($SatO_2$) by a pulse oxymeter Embletta Portable Diagnostic System, Medcare, Iceland. The data were analyzed off-line after manual inspection of the raw polygraph recordings. The following definitions were used to classify abnormal

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breathing patterns. Apnea, an absence of airflow for more than 10 seconds; obstructive apnea, apnea accompanied by paradoxical, out of phase, thoracoabdominal movements; central apnoea, apnea without respiratory movement; hypopnea, a reduction in the amplitude of respiratory movement for more than 10 seconds to less than 50% of the maximum amplitude recorded during the preceding breathing cycle, associated with an oxygen desaturation of 4% or more; hypopneas were further classified as obstructive or central in the presence or absence of out of phase thoracoabdominal movements, respectively. The apnea-hypopnea index (AHI) was defined as the number of episodes of apnea and hypopnea per hour of sleep.

Patients having an AHI $\geqslant 10$ were diagnosed as having sleep disordered breathing (SDB); obstructive sleep apnea-hypopnea (OSAH) was defined as an AHI $\geqslant 10$ events/hour of which $> 50\%$ were obstructive; patients were classified as central sleep apnea-Cheyne-Stokes respiration (CSA-CSR) if they had $> 50\%$ of events as central in origin with typical waxing and waning pattern of tidal volume.

The ICDs were programmed in the standard fashion and the rate of detection of ventricular tachycardia (VT) and ventricular fibrillation (VF) was left to the discretion of the implanting physician according to individual patient's characteristics; all electrograms were reviewed by expert electrophysiologists at approximately 3 month intervals and appropriate ICD therapies for VT or VF were registered. In all patients, a retrospective analysis was conducted to identify ICD interventions and for each patient the frequency of device interventions was calculated as the ratio of the number of appropriate therapies to duration of follow-up (therapies for year of implant for patient [ThYP]).

Patient characteristics were described as mean $\pm$ SD and counts (with percentages); the significance of differences within groups was analyzed with a student t test and association between variables by Pearson correlation test. All measurements were performed using SPPS version 12.0 software (SPSS Inc., Chicago, IL)

Results

Sleep disordered breathing was present in 17 out of 22 patients (77.2%), with a mean AHI of 25 ± 12 events/hour. A total of 11 (64.7%) patients were classified as affected by OSAH and 6 (35.3%) patients as CSA-CSR. Cheyne-Stokes respiration was present in 4 (66.6%) out of 6 patients with CSA. There were no significant differences in terms of age, BMI, cardiomyopathy etiology, LVEF, and New York Heart Association (NYHA) class, between the groups; duration of follow-up appeared to be longer in patients unaffected than in patients affected by SDB (see Table).

As regards device programming, there were no significant differences in any parameters between patients without SDB and those with SDB, including VT detection rate (150.2 ± 14.3 vs 151.3 ± 15.6/min), and VF detection rate (191.3 ± 15.4 vs 190.2 ± 14.2/min).

Table 1. Baseline Characteristics of Patients Included in the Study

Characteristic	Patients Affected by SDB (n = 17)	Patients Unaffected by SDB (n = 5)
Age (yr)	65 ± 8	60 ± 12
Body mass index (kg/m^2)	28 ± 3	27 ± 2
Ischemic etiology (%)	60%	80%
NYHA class	2 ± 0.7	2.2 ± 0.8
Ejection fraction (%)	29 ± 5	26 ± 6
Duration of follow-up (mo)	19 ± 14	26 ± 15

Abbreviations: SDB, sleep disordered breathing.

After a mean follow-up of 19 ± 14 months a total of 22 appropriate ICD discharges were delivered in ICD patients affected by SDB with a mean ThYP of 1.56 ± 3. Patients without SDB experienced a total of 4 shocks during a mean follow-up of 26 ± 15 months, with a mean ThYP of 0.24 ± 0.4. A total of 18 appropriate ICD therapies were delivered in OSAH patients (follow-up of 21 ± 15 mo) with a mean ThYP of 1.8 ± 3.4 whereas a total of 4 shocks was observed in CSA-CSR patients (follow-up of 17 ± 14 mo) with a mean ThYP of 1.2 ± 2. No significant difference in terms of ThYP was appreciated between the groups.

When analyzed as a linear continuous variable, AHI showed to be positively correlated to the number of appropriate ICD therapies; the association persisted after controlling for ejection fraction and NYHA class ($r = 0,718$; $P < .001$, see Figure). On the other hand, ICD events showed to be inversely associated with minimum oxygen saturation during the night (nadir $SatO_2$); the association persisted, although appeared weaker, at multivariate analysis controlling for LVEF and NYHA class ($r = -0.619$ $P = .003$).

Discussion

Although obtained in a small number of patients, our data shows that sleep disordered breathing affects a high proportion of CHF patients with an ICD. The main finding of the study relies on the fact that severity of SDB and the degree of consequent nocturnal hypoxia, appear to be a determinant of appropriate ICD discharges, which stands for life-threatening ventricular arrhythmia, in CHF patients independently from the entity of systolic dysfunction and NYHA class.

We were unable to demonstrate any statistical difference in terms of incidence of ICD discharges among the groups (SDB affected vs unaffected) probably due to the small

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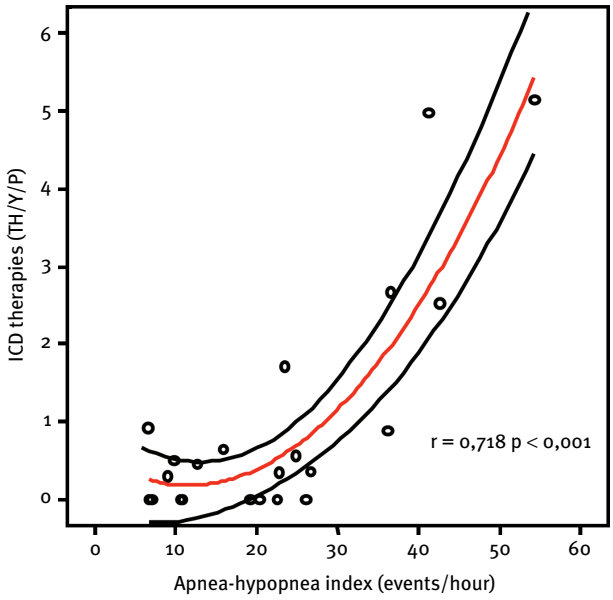

Figure 1. Correlation between apnea-hypopnea index (ev/h) and number of ICD therapies (therapies for year of implant for patient [ThYP]) in patients with CHF.

numbers involved in the study and the large standard deviation among patients. In this series, duration of follow-up appeared longer in subjects without sleep apnea than in patients affected by the disorder; we speculate that a low incidence of therapies during a longer follow-up in controls further suggest that a greater risk of ICD discharges exists in patients with sleep apnea.

Previous works have demonstrated that patients with obstructive sleep apnea are at increased risk of SCD during nighttime and that ventricular arrhythmias occur significantly more often in association with SDB in patients with reduced LVEF treated with ICD in secondary prevention.[4,5] Moreover in the cited study on day-night patterns of SCD it was shown that the severity of obstructive sleep apnea correlated directly with risk of nocturnal sudden death from cardiac causes.[5] Our study was not directed to evaluate a day-night pattern of ICD shocks and a larger cohort of patients is currently under enrollment to prospectively collect data on diurnal variations in the timing of appropriate ICD therapies.

In this primary prevention study, we have observed that increasing severity of SDB is associated with more appropriate ICD discharges in patients at high risk for malignant arrhythmia. These findings essentially agree with a recent report by Serizawa et alshowing patients with heart failure at an increased risk of ICD discharge due to comorbid sleep apnea.[6]

As regards the role of nocturnal hypoxia, our results are indirectly supported by previous studies indicating that hypoxemia may trigger complex ventricular ectopies both in obstructive sleep apnea and in congestive heart failure.[7,8] Moreover, our data provide a further rational basis for the use of nocturnal oxygen therapy in heart failure patients, which has been shown to suppress ventricular ectopies and reduce the incidence of malignant arrhythmia in CHF patients.[9,10] However, our patients were not treated with nocturnal oxygen therapy and no definite conclusion about the role of oxygen administration on ICD discharges can be drawn from the present study. A randomized controlled trial is needed to evaluate efficacy of oxygen to reduce incidence of ICD shocks in this setting.

Despite many published results on predictors of SCD and appropriate shocks in ICD candidates, optimal risk stratification is still open to debate. As a consequence, a consistent number of ICD patients still suffer from frequent appropriate device interventions and are prescribed antiarrhythmic drugs with potentially severe adverse effects.[11] The best predictor of malignant arrhythmia remains LVEF and additional indicators have been used with inconclusive results. We underscore the potential role of sleep studies in order to quantify the risk of sudden cardiac death and ICD shocks.

In conclusion, our study is one of the few that specifically addresses sleep disordered breathing in patients with an implantable cardioverter defibrillator and suggests that (1) SDB is frequent among receivers of ICD in primary prevention due to left ventricular systolic dysfunction and (2) AHI and severity of hypoxia during sleep are predictors of arrhythmic risk and should be considered in the stratification of CHF patients who are candidates for ICD. A larger study is needed to confirm these results and to evaluate the impact of different treatment strategies for sleep disordered breathing on ICD discharges in patients at high risk of sudden cardiac death.

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