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CLINICAL RESEARCH

Prevalence of sleep-disordered breathing in a 316-patient French cohort of stable congestive heart failure

Prévalence des syndromes d'apnées du sommeil dans une cohorte française de 316 patients insuffisant cardiaques

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KEYWORDS
Sleep apnoea syndromes;Prevalence; Congestive heart failure

Summary
Background. — Heart failure with systolic dysfunction occurs frequently. Studies in North America and Germany have shown a high prevalence of sleep-disordered breathing in patients with heart failure.
Aims. — To assess the prevalence of sleep-disordered breathing and its associated risk factors in French patients with heart failure.

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Methods. — A total of 316 patients with stable heart failure and a left ventricular ejection fraction less or equal to 45% underwent polygraphy prospectively to diagnose sleep apnoea syndrome, defined as an apnoea-hypopnoea index greater or equal to 10 events/h.
Results. — Mean age, left ventricular ejection fraction, and body mass index were 59 ± 13 years, 30 ± 11% and 28 ± 6 kg/m^2, respectively. The prevalence of sleep breathing disorder was 81% (n = 256); 30% of syndromes were classified as central and 70% as obstructive. The mean apnoea-hypopnoea index was high (30 ± 3 events/h) and a large proportion (41%) of syndromes had an apnoea-hypopnoea index greater or equal to 30 events/h. A central sleep apnoea syndrome pattern was associated with more severe heart failure and a more elevated apnoea-hypopnoea index than an obstructive pattern. The prevalence of sleep-disordered breathing was lower in women than in men (64% versus 85%; χ^2 = 0.0003) as was its severity (mean apnoea-hypopnoea index 15 ± 13 events/h versus 27 ± 19 events/h, p = 0.0001).
Conclusion. — The prevalence of sleep-disordered breathing was high in a French heart failure population, with most syndromes having an obstructive pattern. Prevalence and severity were higher in men than in women.

MOTS CLÉS
Syndrome d'apnées du sommeil ;
Risque facteur ;
Insuffisance cardiaque

Résumé
Contexte. — Des études nord américaines et allemande ont démontré une prévalence importante des syndromes d'apnées du sommeil dans l'insuffisance cardiaque. Notre objectif a été de définir la prévalence et les facteurs de risque de ces syndromes dans une cohorte française de patient en insuffisance cardiaque.
Méthodes. — Trois cent seize patients avec une insuffisance cardiaque définie par une fraction d'éjection ventriculaire gauche inférieure ou égale à 45 % ont été dépistés pour le syndrome d'apnées du sommeil par une polygraphie (indice apnée-hypopnée ≥ 10 par heures).
Résultats. — L'âge moyen, la fraction d'éjection ventriculaire gauche, l'index de masse corporelle étaient respectivement 59 ± 13 années, 30 ± 11 % et 28 ± 6 kg/m. La prévalence du syndrome d'apnées du sommeil était de 81 % avec un indice apnée-hypopnée moyen de 30 ± 3 par heures dans ce groupe. Le pourcentage des syndromes d'apnées du sommeil sévères (indice apnée-hypopnée supérieure ou égale à 30 par heures) était de 41 %. Ces syndromes d'apnées du sommeil étaient de type central dans 30 % des cas et dans 70 % obstructifs. Les patients avec un type central étaient plus sévères que les obstructifs (indice apnée-hypopnée = 39 ± 17 par heures versus 26 ± 16 par heures, p < 0,0001). La prévalence et la sévérité du syndrome d'apnées du sommeil étaient moins importantes chez les femmes (respectivement : χ^2 = 0,0003 ; p = 0,0001).
Conclusion. — Dans une population française de patients insuffisants cardiaques, le syndrome d'apnées du sommeil à une prévalence élevée avec une majorité de forme obstructive. Le syndrome d'apnées du sommeil est moins fréquent et moins sévère chez la femme. Ces résultats soulèvent la question la nécessité d'un dépistage systématique des syndromes d'apnées du sommeil dans cette population.

Abbreviations

CHF	congestive heart failure
CSA	central sleep apnoea
LVEF	left ventricular ejection fraction
NYHA	New York Heart Association
OSA	obstructive sleep apnoea
SDB	sleep-disordered breathing

Background

CHF is a leading cause of morbidity and mortality worldwide. Studies in North America [1] and Germany [2] found that SDB was present in as many as 51—76% of patients with CHF, and it has been shown to be associated with ventricular dysfunction and increased mortality in this setting [3,4]. Some studies have suggested that nocturnal ventilation may reduce mortality and morbidity in CHF patients with SDB [5,6]. The prevalence of SDB in a large French CHF population has not been assessed recently, although some data have been published on small groups of patients [7,8] and in other countries [1,2,9—15]. Accordingly, our study aimed to determine the prevalence and characteristics of SDB in a French cohort of patients with stable CHF.

Methods

Study design

Consecutive patients with stable CHF admitted to the cardiology ward of Henri Mondor University Teaching Hospital for a systematic check-up between 2001 and 2007 were included in the study based on the following inclusion criteria: LVEF greater or equal to 45%, stable optimized heart failure therapy and no episode of acute heart failure within the past 4 weeks. Exclusion criteria were the presence of clinical signs of decompensated heart failure, severe chronic obstructive pulmonary disease and known SDB. The study complied with the Declaration of Helsinki and was approved by the local ethics committee. Informed consent was obtained from each patient.

Patient assessment

Clinical and demographic patient characteristics were recorded (age, sex and body mass index). NYHA class was determined and the main cause of CHF was specified (ischaemic or not). The standard CHF therapy was noted for each patient (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, aldosterone antagonists or diuretics) and whether an implantable cardioverter-defibrillator and/or a biventricular assist device had been inserted. A standard 12-lead electrocardiogram was obtained to determine whether the patient was in sinus rhythm or atrial fibrillation.

Polygraphy recording and analysis

The polygraph was recorded overnight in the cardiology ward using a computerized data acquisition system (Embletta™, ResMed, Saint-Priest, France), which recorded oronasal airflow from nasal pressure and mouth thermistance, chest and abdominal effort by inductance plethysmography, pulse oximetry, snoring, actimetry and body position. Regarding trace quality, we took into account only recordings of greater or equal to 4 h duration without any trace missing. A questionnaire related to sleep quality and estimated sleep duration during the night of the recording and the Epworth sleepiness scale was also completed.

According to international recommendations [16], apnoea was defined as a decrease superior to 80% in nasal-airflow lasting greater than 10 s and hypopnoea was defined as a decrease of greater or equal to 30% in nasal-airflow with greater or equal to 4% desaturation. The number of apnoea-hypopnoea events per hour (apnoea-hypopnoea index) was determined after the exclusion of periods with movements, which were considered to be wake periods. A diagnosis of SDB was considered if the apnoea-hypopnoea index was greater or equal to 10 events/h.

Apnoea without chest or abdominal movements, with or without Cheyne-Stokes respiration, was classified as CSA and apnoea with chest and abdominal movements was classified as OSA. As published previously [17], hypopnoeas were considered to be obstructive when there was evidence of upper airway obstruction, such as snoring, paradoxical respiratory band movement or inspiratory flow limitation through the nasal cannula; central hypopnoea, in contrast, was associated with in-phase respiratory movements and no evidence of inspiratory flow limitation. SDB was considered to be central if greater than 50% of apnoea/hypopnoea events were central and obstructive if greater than 50% were obstructive. All recordings were scored manually by two scorers (MS and M-P d'O) who were blinded to the cardiac assessment. If the scorers disagreed about the SDB type (central versus obstructive), the polygraph trace was reread by both scorers together to reach an agreement.

Statistical analysis

Data were expressed as means ± standard deviations (S.D.), unless specified otherwise. Data distributed abnormally (B-type natriuretic peptide concentration, apnoea-hypopnoea index, apnoea index, hypopnoea index, time with saturation less than 90%) were transformed logarithmically to achieve a normal distribution. An unpaired *t* test was used to assess the differences between two groups and a two-way analysis χ^2 test was used to compare proportions. A *p*-value less than 0.05 was considered to be statistically significant. A Bonferroni correction was applied for multiple comparisons; a *p*-value less than 0.0167 was then considered to be significant. Statistical analyses were done using View Statistical Analytical System (SAS, Cary, NC, USA).

Results

Comparison of patients with and without SDB

A total of 316 patients with CHF were included. Most (83%) patients were men and 49% had an ischaemic cardiopathy. Mean NYHA class and LVEF were 2.5 ± 0.8 and 30 ± 11%, respectively. Prevalence of SDB was high overall: 256 (81.2%) patients had SDB defined by an apnoea-hypopnoea index greater or equal to 10 events/h, and nearly 90% of patients had SDB defined by an apnoea-hypopnoea index greater or equal to 5 events/h, as recommended [16]. Further comparisons of patients with SDB and without SDB (non-SDB) were based on the 10 events/h cut-off level. The mean apnoea-hypopnoea index was high (30 ± 18 events/h) in the SDB group. Accordingly, the prevalence of severe SDB (apnoea-hypopnoea index greater or equal to 30 events/h) was high

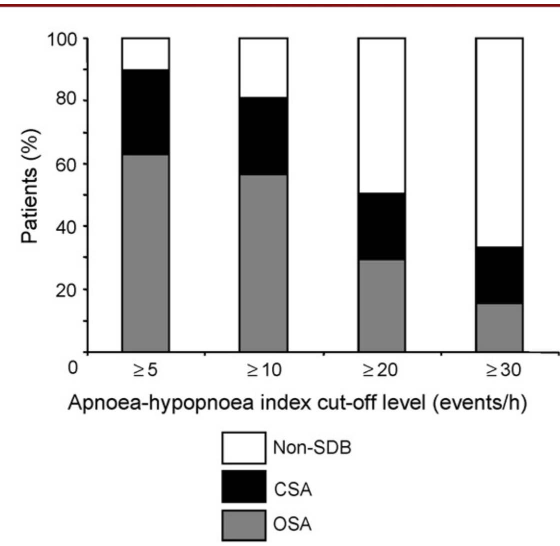

Figure 1. Prevalence of non-SDB, CSA and OSA, using various apnoea-hypopnoea index cut-off levels (5 events/h, 10 events/h, 20 events/h and 30 events/h).

Table 1 Baseline patient characteristics.

Characteristics	All patients ($n=316$)	SDB ($n=256$)	Non-SDB ($n=60$)	CSA ($n=78$)	OSA ($n=178$)
Age (years)	59 ± 3	60 ± 13[a]	55 ± 14	60 ± 13	60 ± 12[c]
Men, n (%)	261 (83)	221 (86)[a]	40 (67)	70 (90)	151 (85)
Body mass index (kg/m^2)	28 ± 6	28 ± 5[a]	25.6 ± 4.4	27.9 ± 5.1[c]	28.3 ± 5.4[c]
NYHA class	2.5 ± 0.8	2.4 ± 0.7	2.3 ± 0.8	2.6 ± 0.8[c]	2.4 ± 0.7
LVEF (%)	30 ± 11	30 ± 10	31 ± 11	26 ± 8[c,d]	31 ± 10
B-type natriuretic peptide (pg/mL)	520 ± 654	547 ± 684[a]	406 ± 501	681 ± 781[c,d]	501 ± 644
Ischaemic, n (%)	156 (49)	133 (52)	23 (38)	39 (50)	94 (53)
Atrial fibrillation, n (%)	66 (21)	59 (23)	7 (12)[b]	23 (29)	36 (20)
Beta-blocker (%)	82	84[a]	73[b]	75	88
Angiotensin-converting enzyme inhibitor (%)	80	79	83	85	76
Angiotensin II receptor blocker (%)	18	19	14	11	22
Spironolactone (%)	58	57	64	70	53
Diuretic (%)	78	82[a]	64[b]	92	79
Cardiac resynchronization, n (%)	37 (12)	28 (11)	9 (15)	10 (13)	18 (10)

[a] $p<0.05$ versus non-SDB.
[b] $\chi^2<0.05$ for OSA, CSA, and non-SDB distribution comparison (%).
[c] $p<0.0167$ versus non-SDB.
[d] $p<0.0167$ versus OSA using Bonferroni correction.

(41% of SDB patients and 33% of the cohort; Fig. 1). SDB patients were more frequently men, older, with a higher prevalence of atrial fibrillation and a higher B-type natriuretic peptide concentration and body mass index compared with non-SDB patients. LVEF and NYHA class were similar in SDB and non-SDB patients. All patients were receiving standard CHF therapy, but a higher proportion of SDB patients were receiving beta-blockers and diuretics.

Comparison of patients with OSA, with CSR and without SDB

Of the total population, 56% were classified as having OSA and 25% as having CSA (Table 1). CSA patients had more severe CHF, with a significantly lower LVEF and higher B-type natriuretic peptide concentration than OSA patients and non-SDB patients. CSA patients also had a more severe sleep apnoea syndrome than OSA patients, with a significantly higher apnoea-hypopnoea index, apnoea index and oxygen desaturation index (Table 2). CSA patients were more often men and more frequently had atrial fibrillation. After adjustment for multiple comparisons between the OSA, CSA and non-SDB groups, both OSA and CSA patients had a higher body mass index than non-SDB patients, but only CSA patients had atrial fibrillation more frequently than non-SDB patients. CSA patients received beta-blockers less frequently (because of intolerance) and diuretics more frequently than OSA patients.

Comparison between sexes

Most patients were men (Tables 1 and 3). Compared with women, men were more often smokers and presented more frequently with ischaemic cardiopathy, whereas body

Table 2 Polygraphic characteristics.

	Non-SDB ($n=60$)	CSA ($n=78$)	OSA ($n=178$)
Epworth score	8 ± 5	7 ± 5	7 ± 5
Apnoea-hypopnoea index (events/h)	4 ± 3	39 ± 17[a,b]	26 ± 16[a]
Apnoea index (events/h)	1 ± 1	20 ± 15[a,b]	10 ± 14[a]
Hypopnoea index (events/h)	4 ± 3	21 ± 33[a]	16 ± 9[a]
Oxygen desaturation index (events/h)	4.4 ± 5	29 ± 20[a,b]	17 ± 16[a]
Lowest oxygen saturation (%)	86 ± 20	74 ± 18[a,b]	81 ± 9
Time in bed with oxygen saturation < 90% (%)	22 ± 55	59 ± 87[a]	42 ± 72

[a] $p<0.0167$ versus non-SDB.
[b] $p<0.0167$ versus OSA using Bonferroni correction.

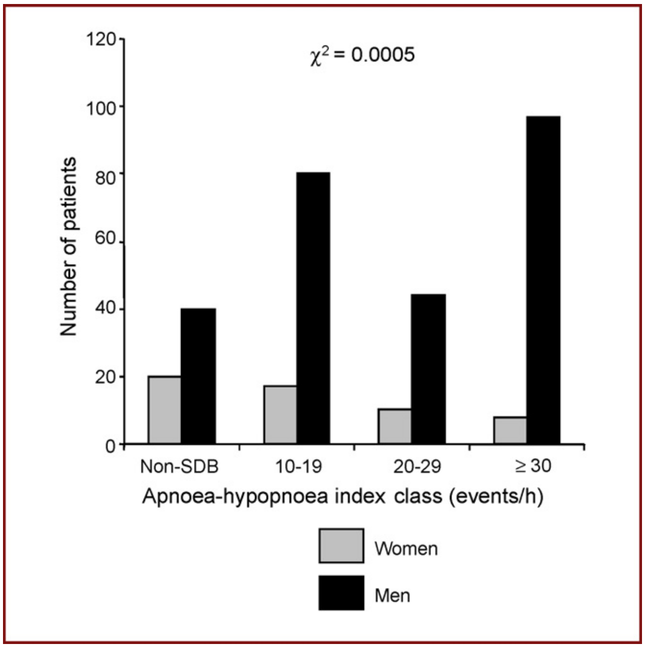

Figure 2. Number of men and women in each apnoea-hypopnoea index class (non-SDB, 10—19 events/h (inclusive), 20—29 events/h (inclusive) and greater or equal to 30 events/h.

mass index, age and presence of hypertension were similar between the sexes (Table 3). Severity of CHF and type of medical treatment were also similar between the sexes, with regard to the entire population and the SDB group (NYHA class, LVEF and B-type natriuretic peptide concentration were not statistically different; Table 3). Women had less frequent and less severe SDB (Tables 1 and 4; Fig. 2) in terms of both apnoea-hypopnoea index (18 ± 9 events/h versus 27 ± 17 events/h in men, p = 0.008) and apnoea index (5 ± 5 events/h versus 11 ± 15 events/h in men, p = 0.03). In the SBD group, the respective proportions of patients with CSA and OSA were similar between the sexes (χ^2 = 0.29).

Discussion

To our knowledge, this study is the first large-scale prospective French study investigating the prevalence of SDB in patients with stable CHF. The major findings of the study were that the prevalence of SDB was high (81%) in CHF patients, the prevalence of severe SDB (apnoea-hypopnoea index greater or equal to 30 events/h) was also high (41% of patients with SDB) and that women with CHF have less frequent and less severe SDB than men with CHF.

The prevalence of SDB in CHF patients is known to be higher than in general population. In the latter, the prevalence varies between 2% and 4% in women and men, respectively, if daytime sleepiness is taken into account to define the sleep apnoea syndrome, but the prevalence increases to 9% and 24%, respectively, if only SDB is considered, irrespective of associated daytime sleepiness [18]. Several factors contribute to the higher prevalence in CHF, including older age, the association of established risk factors such as obesity and smoking habits, and the cardiac pathology itself, which predisposes to CSA. The prevalence in our study is higher than that in most studies published recently [2,9—12], which reported prevalences ranging from 61 [10] to 75% [2] for similar apnoea-hypopnoea index cut-off levels. Selection bias is always a possibility in a single-centre study. In this respect, trace quality and event scoring are key issues. Scoring was done by two different scorers according to international recommendations and in line with other studies [12]. In cases of discrepancy between scorers, the trace was reread to reach agreement. The higher prevalence in our study may also be a French particularity, as

Table 3 Sex-specific patient characteristics.

	Men(n = 261)	Women(n = 55)	p-value
Age (years)	60 ± 13	57 ± 15	0.20
Weight (kg)	83 ± 17	72 ± 15	< 0.0001
Height (cm)	173 ± 8	163 ± 7	< 0.0001
Body mass index (kg/m^2)	28 ± 6	27 ± 32	0.41
Diabetes (%)	20	34	0.046
Cholesterol (%)	54	45	0.25
Hypertension (%)	47	53	0.48
Smoker (%)	72	29	< 0.0001
Ischaemic cardiopathy (%)	54	29	< 0.001
NYHA class	2.4 ± 0.7	2.5 ± 0.8	0.61
LVEF (%)	30 ± 10	30 ± 10	0.67
B-type natriuretic peptide (pg/mL)	524 ± 691	503 ± 488	0.88
Atrial fibrillation, n (%)	13	23	0.10
Beta-blocker (%)	82	83	0.80
Angiotensin-converting enzyme inhibitor (%)	80	74	0.24
Angiotensin II receptor blocker (%)	16	28	0.037
Spironolactone (%)	56	71	0.016
Diuretic (%)	79	75	0.57
Multisite ventricular pacing, n (%)	12	9	0.85

Table 4 Sex-specific polygraphic characteristics.

	Men(n = 261)	Women(n = 55)	p-value
Prevalence of SDB (%)	85	64	< 0.001
Prevalence of CSA (%)	27	15	< 0.001
Prevalence of OSA (%)	58	49	0.002
Epworth score	7 ± 5	8 ± 4	0.56
Apnoea-hypopnoea index (events/h)	30 ± 19	15 ± 14	< 0.001
Apnoea index (events/h)	11 ± 15	6 ± 9	0.008
Hypopnoea index (events/h)	16 ± 20	10 ± 9	0.020
Oxygen desaturation index (events/h)	19 ± 18	10 ± 10	< 0.001
Lowest oxygen saturation (%)	80 ± 19	83 ± 24	0.24
Time in bed with oxygen saturation < 90% (%)	47 ± 79	21 ± 40	0.020

a similar prevalence was found by Tremel et al., although in a smaller group [7]. However, this hypothesis may be confounded by the similarities between our study and other studies in terms of patient characteristics (demographic, anthropometric treatment and CHF aetiology), CHF severity and the screening of consecutive patients irrespective of SDB symptoms, using similar polygraphic ambulatory monitors.

We observed a predominance of OSA over CSA. This result contrasts with previous data that showed similar proportions of both categories of SDB [2,11,15] or a clear predominance of CSA over OSA [9,12,14], but is in line with the recent study by Schulz et al. [10]. In both our study and the study by Schulz et al., most (~90%) patients received beta-blockers. This may have contributed to a decrease in CSA prevalence, as two recent studies have shown that beta-blockers can improve cardiac function and decrease CSA [19,20]. Another potential contributory factor was our inclusion of patients with biventricular pacing, which is also known to reduce CSA [2]. Lastly, a higher body mass index in our cohort compared with others [2] may have contributed to an increase in OSA prevalence. In our study, CSA was associated with men and atrial fibrillation, in line with previous publications, but not with age, in contrast with the study by Sin et al. [15] but in line with the study by Javaheri et al. [1].

We included both men and women in our study, allowing a comparison between the sexes. In accordance with CHF epidemiological characteristics, women represented only 15% of our population [21]. Two important findings of our study were that both CSA and OSA occurred less frequently in women than in men and that SDB was less severe in women in terms of apnoea-hypopnoea index, despite similar degrees of heart dysfunction (as indicated by LVEF, NYHA class, and B-type natriuretic peptide concentration). Several different mechanisms may account for these differences. Firstly, differences in sleep characteristics between the sexes have been described, with men having a greater number of sleep-wake transitions and shorter slow wave sleep; both these factors contribute to unstable sleep, which predisposes to central apnoea [22]. Secondly, studies have shown that progesterone has a positive impact on genioglossus muscle activity, increasing airway luminal calibre and making upper airway closure less frequent during sleep [23,24]. Accordingly, an increase in SDB prevalence has been shown in post-menopausal women in the general population [25].

Limitations

They are several limitations to our study. With regard to OSA sex differences, we did not measure neck circumference; an increase in this variable is an established risk factor for OSA. There were also some methodological issues. Firstly, and in contrast with earlier studies [15], SDB was diagnosed by polygraphy and not by attended polysomnography. The lack of electroencephalographic channels could have led to an underestimation of SDB severity, as the apnoea-hypopnoea index is calculated using recording duration rather than total sleep time. This factor may be crucial, as CHF patients are known to have poor sleep quality, with sleep fragmentation and an increase in waking after sleep onset, either secondary to SDB or to periodic limb movements, or due to the CHF itself [14]. However, exclusion of movement periods measured by actimetry included in the polygraph overcomes this bias partially. Underestimation of the apnoea-hypopnoea index may also come from hypopnoea that is associated with cortical arousals rather than with oxygen desaturation. In the latest American Sleep Disorder Association recommendations [16], measurement of arousal does not appear in the definition of hypopnoea in a routine setting. In addition, however, cortical arousals are associated with autonomic arousals, which are visible as heart rate increases, and with pulse plethysmography modifications; both of these signals are available on the cardio-respiratory polygraph. Another issue is the distinction between obstructive and central events. The gold standard is the measurement of oesophageal pressure that shows an increase in respiratory effort in the case of an obstructive event and a decrease in effort in central hypopnoea. However, this is not feasible in the context of a study such as ours (i.e. a prospective study of consecutive patients in a cardiology ward) and is even contraindicated in the case of CHF patients treated frequently with anticoagulants or antiaggregants. In addition, the measurement of respiratory effort by inductance plethysmography appears in more recent recommendations [16]. Also, in our study, all cardiorespiratory polygraph traces were scored by two independent physicians. In the case of disagreement over the SDB type (central versus obstructive), the two scorers reread the trace together to reach an agreement. This method has caveats, as it does not avoid a centre effect, but it overcomes interscorer variability. Of note, variation in type and severity of SDB in CHF has been studied systematically recently [17], raising the question of whether conventional continuous positive airway pressure or servo-adaptive ventilation is the best treatment [6]. The latter has the advantage in the successful treatment of both central and obstructive components of SDB [26].

Conclusion

In summary, our study showed a high prevalence of SDB in a large prospective French cohort of CHF patients, and differences between the sexes. The results suggest that systematic SDB screening is needed in the CHF population.

Conflicts of interests

None.

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