Sleepiness and Sleep in Patients With Both Systolic Heart Failure and Obstructive Sleep Apnea

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Background: Adverse effects of obstructive sleep apnea (OSA), including sleep deprivation, can contribute to the progression of heart failure. The usual indication to diagnose and treat sleep apnea is subjective sleepiness. Previous studies suggest that patients with both heart failure and obstructive sleep apnea often do not complain of sleepiness, albeit their sleep time may be reduced. Therefore, we tested the hypothesis that patients with heart failure have less sleepiness and sleep less compared with subjects without heart failure for a given severity of OSA.

Methods: Sleepiness assessed with the Epworth Sleepiness Scale and sleep structure measured with polysomnography were compared among 155 consecutive patients with heart failure and from a random community sample (n=1139) according to categories of the apnea-hypopnea index (<5, no OSA; 5-14, mild OSA; and ≥15, moderate to severe OSA).

Results: Compared with the community sample, for any given severity of OSA, patients with heart failure had lower mean±SE Epworth Sleepiness Scale scores (7.1±0.4 vs 8.3±0.2 [P=.005]; 6.7±0.7 vs 9.2±0.3 [P<.001]; and 7.8±0.7 vs 9.8±0.4 [P=.01]), indicating less sleepiness despite sleeping less (total sleep time mean±SE [in minutes]: 306±7 vs 384±2, 295±19 vs 384±5, and 285±13 vs 359±7 for no, mild, and moderate to severe OSA, respectively; P<.001 for all comparisons).

Conclusions: Patients with heart failure have less subjective daytime sleepiness compared with individuals from a community sample, despite significantly reduced sleep time, whether or not they have OSA. In patients with heart failure, the absence of subjective sleepiness is not a reliable means of ruling out OSA.

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OBSTRUCTIVE SLEEP APNEA (OSA) can contribute to the progression of heart failure (HF) by exposing the heart to nocturnal hypoxia, elevations in central sympathetic outflow and blood pressure, as well as through oxidative and inflammatory stimuli.[1] Randomized trials have demonstrated that in patients with HF, treatment of coexisting OSA with continuous positive airway pressure decreases sympathetic activity and blood pressure and improves cardiac function.[2,3]

In one of these trials, Kaneko and colleagues[2] made 3 interesting observations. First, patients with HF and OSA generally did not complain of excessive daytime sleepiness (EDS). Second, despite this lack of EDS, patients slept on average for only 5 hours. Third, even though they were not sleepy, treatment of their OSA improved cardiovascular function. Despite these observations, treatment of OSA is not included in guidelines for the management of patients with HF.[4] One reason might be that subjective sleepiness is frequently the main reason for referral to a sleep clinic for diagnosis of sleep apnea in patients without HF. If subjective sleepiness is not a prominent complaint in patients with both HF and OSA, then they may not be referred for assessment of sleep apnea.

Self-reported sleep deprivation has been linked with increased risk of cardiovascular events in several epidemiological studies.[5,6] For example, a prospective analysis of 70 000 women revealed that self-reported sleep time of less than 5 hours per night is associated with significantly increased risk for coronary artery disease, nonfatal myocardial infarction, or cardiovascular death.[5] However, subjects did not undergo polysomnography to confirm self-reported sleep time and sleep deprivation.

Although previous studies[2,7] suggested that patients with both HF and OSA frequently do not complain of EDS and may be sleep deprived, to our knowledge, there have been no studies in which subjective sleepiness and sleep structure

have been compared between subjects with and without HF. We hypothesized that patients with systolic HF have less sleepiness and sleep less compared with subjects without HF for a given severity of OSA.

METHODS

SUBJECTS

Patients With Systolic HF

In a prospective epidemiological study, we approached all patients with HF who were newly referred to the Heart Failure Clinic of the Mount Sinai Hospital (Toronto, Ontario) between 1997 and 2005, to participate. Inclusion criteria were (1) HF due to ischemic, nonischemic, or hypertensive cardiomyopathy with systolic dysfunction (left ventricular ejection fraction [LVEF] ≤45% by echocardiography or radionuclide angiography) and (2) stable clinical status and stable optimal medical therapy for at least 4 weeks. Patients were included regardless of symptoms of, or risk factors for, sleep apnea. Exclusion criteria were (1) unstable angina, myocardial infarction, or cardiac surgery within the previous 3 months; (2) patients with central sleep apnea (defined by ≥5 apneas and hypopneas per hour of sleep, of which ≥50% were central or mixed); (3) pregnancy; and (4) inadequate sleep time less than 4 hours in bed [n=1]). The protocol was approved by the local research ethics board, and all subjects provided written consent prior to enrollment.

Subjects Without History of HF

In this analysis, 1139 participants of the prospective Wisconsin Sleep Cohort Study served as a control group. The Wisconsin Sleep Cohort consists of a stratified random sample of state employees in Wisconsin between the age of 30 and 60 years, as described previously.[8] Exclusion criteria were (1) pregnancy, (2) unstable or decompensated cardiopulmonary disease, (3) airway cancers, (4) recent surgery involving the upper airway, (5) inadequate sleep time (<4 hours in bed), and (6) self-reported physician-diagnosed HF.

POLYSOMNOGRAPHY

Polysomnography was performed in all subjects using the same methods in both centers (Toronto, and Madison, Wis) as previously reported.[8] Thoracoabdominal movements were recorded by respiratory inductance plethysmography and arterial oxyhemoglobin saturation by oximetry. Bedtime (8:30-12 PM) and awakening time (5-8 AM) occurred at the discretion of subjects.

In both centers, apnea was defined as a cessation of airflow for at least 10 seconds, and hypopnea was defined as a 25% or greater decrease in the amplitude in either of the 2 respiratory effort signals, resulting in a decrease of at least 4% in arterial oxyhemoglobin saturation.[8]

To avoid biasing our results because of the different distributions of sleep apnea type between the HF and community samples,[7,9-11] we excluded patients with HF and central sleep apnea. Therefore, in patients with HF, apneas were additionally classified as obstructive or central in the presence or absence of thoracoabdominal motion, respectively, and hypopneas were classified as obstructive or central in the presence or absence of out-of-phase thoracoabdominal motion, respectively.[2,9,12] Mixed apneas were classified as central. Categories of OSA were defined according to the apnea-hypopnea index (AHI) (apneas and hypopneas per hour of sleep: <5, no OSA; 5-14, mild OSA; and ≥15, moderate to severe OSA).

DAYTIME SLEEPINESS

To assess the degree of subjective daytime sleepiness, the Epworth Sleepiness Scale (ESS) was administered to all participants in both centers the evening before polysomnography. The ESS is a validated questionnaire that asks subjects to rate their likelihood of falling asleep in several common situations.[13,14] Scores range from 0 (least sleepy) to 24 (sleepiest). In patients with OSA but without HF, ESS scores correlate directly with the AHI and inversely with sleep-onset latency.[15,16] Excessive daytime sleepiness was defined as a score of 11 or higher.[13]

STATISTICAL ANALYSIS

Data from the HF and community samples were compared retrospectively using SUDAAN software.[17] In all of the analyses, the Wisconsin Sleep Cohort data were weighted back to the original sampling frame.

We calculated mean differences in variables between OSA categories (AHI, <5; AHI, 5-14; and AHI, ≥15) both within and between the HF and community samples. For continuous variables, *t* tests were performed (paired for within-group comparisons and unpaired for between-group comparisons), and β coefficients from linear regressions were used to estimate mean differences. For categorical variables, χ^2 tests were performed and β coefficients from logistic regression were used to estimate odds ratios. Our large sample size allowed us to adjust coefficients for differences in age, sex, and body mass index (BMI) (calculated as weight in kilograms divided by the height in meters squared) when appropriate. Differences between the 2 populations for relationships of OSA categories and outcomes were tested via interaction terms in the regression models. Two-tailed *P* values <.05 indicated significance.

RESULTS

SUBJECTS

We studied 155 patients with HF and 1139 subjects from the community, of whom 76% and 56% were male, respectively. Characteristics of the subjects are given in **Table 1**. More than 85% of apneas and hypopneas were obstructive. In the AHI categories of lower than 5 and between 5 and 14, the mean age ($P=.02$ and $P=.02$, respectively) and the proportion of men ($P<.001$ and $P=.045$, respectively) was significantly higher in patients with HF compared with the community sample. There were no differences in age and proportion of men between subjects with HF and the community sample with an AHI of 15 or higher. Within each AHI category, the AHI values of the patients with HF were similar to those of the community sample; however, among those with no OSA, the AHI of patients with HF was slightly higher compared with the community sample ($P<.001$; Table 1). In the patients with HF with an AHI of lower than 5, between 5 and 14, and 15 or higher, systolic left ventricular function and New York Heart Association (NYHA) functional class were impaired to similar degrees (LVEF [mean±SE], 26%±1%, 26%±2% and 27%±1%, respectively; NYHA functional class, 2.4±0.1, 2.6±0.1 and 2.6±0.1, respectively; $P>.05$ for all comparisons be-

Table 1. Characteristics of Patients With HF and a Community Sample According to the Status of Obstructive Sleep Apnea

Characteristic	AHI, <5		AHI, 5-14		AHI, ≥15	
	Patients With HF (n = 107)	Community Sample (n = 811)	Patients With HF (n = 25)	Community Sample (n = 203)	Patients With HF (n = 23)	Community Sample (n = 125)
Age, mean ± SE, y	53.0 ± 1.4*	49.8 ± 0.3	58.2 ± 2.2*	52.6 ± 0.6	57.3 ± 2.2	54.8 ± 0.9
Male, %	70†	51	84*	65	96	73
AHI, No. per hour of sleep, mean ± SE	1.9 ± 0.1†	1.2 ± 0.1	8.7 ± 0.7	9.0 ± 0.2	30.2 ± 2.1	33.1 ± 1.7

Abbreviations: AHI, apnea-hypopnea index; HF, heart failure.
*Mean value or proportion was significantly different ($P<.05$) between subjects with and without HF.
†Mean value or proportion was significantly different ($P<.001$) between subjects with and without HF.

tween AHI categories). In the patients with HF, there was no significant correlation between the severity of OSA, as assessed by the AHI, and the degree of left ventricular systolic impairment, as assessed by LVEF ($r=-0.006$; $P=.94$).

SUBJECTIVE SLEEPINESS

The patients with HF presented with significantly lower ESS scores compared with subjects from the community in all AHI categories, indicating less sleepiness (mean [95% confidence interval] unadjusted differences: AHI <5, 1.2 [0.4-2.1] [$P=.005$]; AHI between 5 and 14, 2.5 [1.0-4.0] [$P<.001$]; and AHI ≥15, 2.0 [0.4-3.5] [$P=.01$]; **Figure 1**). These differences remained significant after adjusting for age, sex, and BMI ($P<.05$ for all comparisons), indicating that these findings cannot be explained by differences in baseline variables between the HF and community sample. The ESS scores increased significantly with increasing severity of OSA in the community sample but not in the patients with HF (Figure 1). In the community sample, the odds ratio (95% confidence interval) of having pathological EDS (ESS score ≥11) in subjects with, compared with those without, OSA was increased at 1.47 (1.09-2.00) ($P=.01$). In contrast, the odds of having EDS in association with OSA vs no OSA was not increased in the patients with HF (0.96 [0.41-2.22]; $P=.93$). In the patients with HF, there was no significant correlation between LVEF and the ESS score ($r=-0.057$; $P=.48$). Patients with HF were receiving optimal medications (**Table 2**).

SLEEP STRUCTURE

In patients with HF, with an AHI lower than 5 and an AHI of 15 or higher, sleep-onset latency was significantly longer by 8 minutes compared with the community sample in the corresponding AHI categories, indicating less propensity to fall asleep (Figure 1). For subjects with an AHI between 5 and 14, the sleep-onset latency between patients with HF and the community sample was not significant.

In all AHI categories, total sleep times were reduced by more than 1 hour in patients with HF compared with the community sample (mean [95% confidence interval] differences: AHI <5, 78 [62-93] minutes; AHI between 5 and 14, 89 [49-126] minutes; and AHI ≥15, 74 [43-103] minutes; $P<.001$ for all categories; Figure 1). Furthermore, wake time after sleep onset was 31 to 44 minutes longer and sleep efficiency was markedly reduced in the patients with HF compared with the community sample for all AHI categories ($P<.001$ for all comparisons; **Table 3**). The proportions of slow-wave and rapid eye movement sleep were significantly reduced in patients with HF compared with the community sample in those with an AHI lower than 5 (Table 3) but not in those with an AHI between 5 and 14 or 15 or higher. However, among all subjects with OSA (AHI ≥5), patients with HF had less rapid eye movement sleep (mean±SE, 13.2%±1.3% vs 16.6%±0.4%; $P=.01$) but not slow-wave sleep (10.0%±1.1% vs 12.1%±0.6%, $P=.10$) compared with the community sample.

To test whether the observed differences in sleep structure can be attributed to HF, we compared the polysomnographic data of patients with HF and the community sample after adjustment for age, sex, and BMI in those without OSA (AHI <5) (**Table 4**). In the patients with HF, sleep-onset latency and wake time after sleep onset were longer ($P<.001$ for both comparisons), whereas total sleep time was shorter than that in the community sample ($P<.001$). In addition, sleep efficiency and the proportion of rapid eye movement sleep were significantly reduced ($P<.001$) in patients with HF without OSA compared with the community sample, indicating poorer sleep quality. The proportion of slow-wave sleep was not significantly different between the patients with HF and the community sample without OSA.

BODY MASS INDEX

In subjects with an AHI lower than 5 and between 5 and 14, BMI was similar in the HF and community samples (**Figure 2**). However, in those with an AHI of 15 or higher, the mean BMI was lower in subjects with HF than in the community sample (Figure 2). In the community sample, AHI category increased significantly in association with increasing BMI (AHI <5 vs AHI between 5 and 14 [$P=.01$]; AHI <5 vs AHI ≥15 [$P<.001$]) but not in patients with HF ($P>.05$ for all comparisons). We also examined the relative predictive value of obesity (BMI ≥30) for OSA. In both the community sample and the patients with HF, the odds ratio (95% confidence interval) of having OSA associated with obesity was significantly increased at 4.35 (3.23-5.88) ($P<.001$) and 2.27 (1.12-4.54) ($P=.02$), respectively. However, the associa-

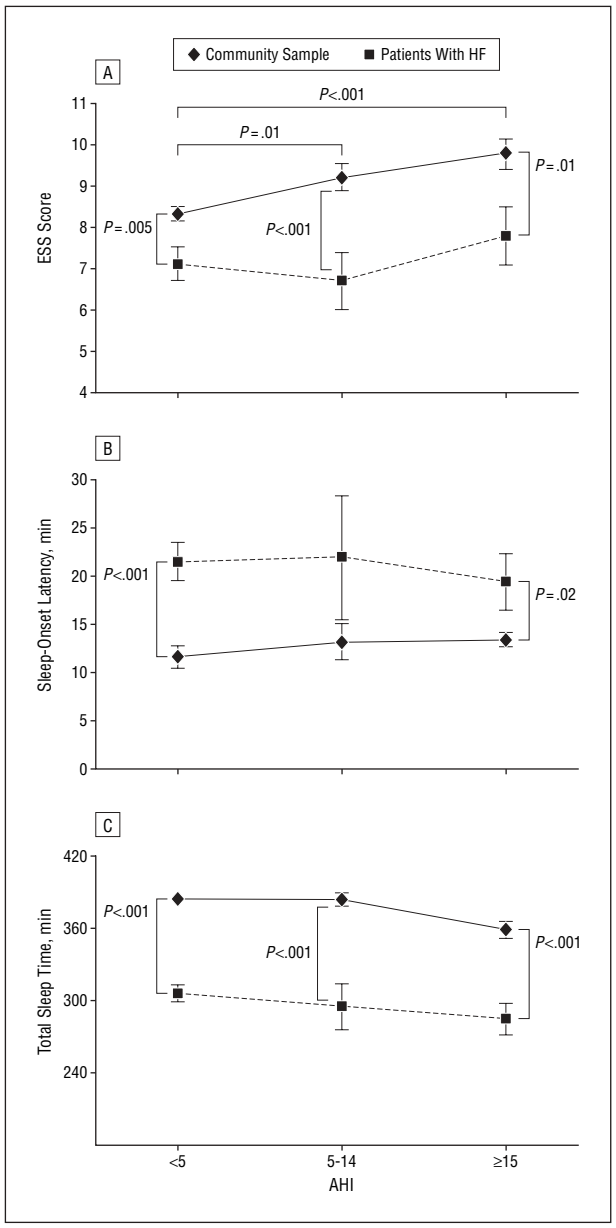

Figure 1. Epworth Sleepiness Scale (ESS) score and sleep structure by apnea-hypopnea index (AHI) categories (<5, 5-14, and ≥15). Patients with heart failure (HF) have lower mean±SE ESS scores (7.1±0.4 vs 8.3±0.2, 6.7±0.7 vs 9.2±0.3, and 7.8±0.7 vs 9.8±0.4, respectively) (A) and longer sleep-onset latencies (21.5±2.0 vs 13.4±0.8 minutes, 21.9±6.5 vs 13.2±1.9 minutes, and 19.4±2.9 vs 11.6±1.1 minutes, respectively) (B) compared with a community sample with no history of HF in all apnea-hypopnea index (AHI) categories indicating less sleepiness despite sleeping less (total sleep time [mean±SE], 306±7 vs 384±2 minutes, 295±19 vs 384±5 minutes, and 285±13 vs 359±7 minutes, respectively) (C). In the community sample, mean ESS scores increased significantly with increasing AHI category. In contrast, there were no significant differences in ESS scores in patients with HF with increasing AHI category.

tion between BMI and AHI was significantly stronger in the community sample than in the patients with HF (*P* for interaction <.001).

COMMENT

This study has given rise to several novel observations. First, patients with HF reported less subjective daytime sleepiness compared with the individuals without a history of HF, whether or not they had OSA. Second, in contrast to individuals from the community sample without HF, there was no association between severity of OSA and ESS score in patients with HF. Third, despite less subjective sleepiness, patients with HF had significantly less sleep time and less sleep efficiency compared with subjects from the community sample in all AHI categories. Finally, compared with the community sample, the association of obesity with OSA was significantly weaker in patients with HF.

Table 2. Cardiac Medication Used by Patients With HF*

Medication	Patients With HF (n = 155)
ACE inhibitors or ARBs	143 (93)
β-Blockers	126 (81)
Loop diuretics	112 (72)
Digoxin	66 (43)

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; HF, heart failure.
*Data are given as number (percentage) of patients.

Previous studies have suggested that patients with both HF and OSA tend not to complain of sleepiness. Javaheri et al[7] identified 9 cases of OSA in a sample of 81 male patients with HF. Only 2 (22%) reported excessive daytime sleepiness. However, because of the small number of patients with OSA and their use of a qualitative rather than quantitative assessment of daytime sleepiness, they could not examine relationships between degree of sleepiness and AHI. In 24 patients with HF and moderate to severe OSA (mean AHI, 41), Kaneko et al[2] found that they generally did not complain of sleepiness (mean ESS score, 6.3). In 84 patients with HF, Rao and colleagues[18] found no difference in ESS score between patients with and without sleep-related breathing disorders. However, sleep-related breathing disorders were assessed with an ambulatory device that did not record sleep and did not distinguish between obstructive and central respiratory events. Moreover, in none of these studies were subjective sleepiness, sleep time, and BMI compared directly with subjects without HF.

Our findings provide strong evidence that patients with HF complain less of sleepiness compared with individuals without HF. First, they presented with lower ESS scores for any given AHI. Second, while we found a significant association between the ESS score and the severity of OSA in the community sample,[15] there was no such relationship in patients with HF. Third, sleep-onset latency was 8 minutes longer in the patients with HF compared with subjects without HF for any given AHI. This finding suggests that the objective propensity to fall asleep is reduced in patients with HF, with or without OSA.

A further intriguing finding was that patients with HF slept at least 1 hour less and had at least 10% lower sleep efficiency compared with the community sample, whether or not they had OSA. Subjects from our HF population slept approximately 5 hours vs 6.5

Table 3. Sleep Structure of Patients With HF and the Community Sample*

Sleep Structure	AHI, <5		AHI, 5-14		AHI, ≥15	
	Patients With HF (n = 107)	Community Sample (n = 811)	Patients With HF (n = 25)	Community Sample (n = 203)	Patients With HF (n = 23)	Community Sample (n = 125)
Wake after sleep onset, min	88 ± 7‡	57 ± 2	101 ± 12‡	60 ± 3	120 ± 12‡	76 ± 5
Sleep efficiency, %	73.6 ± 1.6‡	84.2 ± 0.4	69.6 ± 3.8‡	83.9 ± 0.8	68.2 ± 3.1‡	79.9 ± 1.2
Slow-wave sleep, %	12.3 ± 1.0†	14.6 ± 0.3	10.4 ± 1.6	12.3 ± 0.7	9.6 ± 1.6	11.8 ± 1.0
REM sleep, %	14.3 ± 0.8‡	19.1 ± 0.2	14.4 ± 2.1	18.0 ± 0.5	11.9 ± 1.5	14.0 ± 0.6

Abbreviations: AHI, apnea-hypopnea index; HF, heart failure; REM, rapid eye movement.
*Data are given as unadjusted means ± SE.
†Mean value or proportion of patients with HF was significantly different ($P<.05$) to the community sample.
‡Mean value or proportion of patients with HF was significantly different ($P<.001$) to the community sample.

Table 4. Adjusted Mean Differences in Sleep Architecture Between Patients With HF and the Community Sample Without Sleep Apnea*

Sleep Architecture	Patients With HF vs Community Sample With AHI <5, Mean Difference (95% CI)	*P* Value
Sleep-onset latency, min	8.2 (4.0 to 12.3)	<.001
Total sleep time, min	−68 (−83 to −53)	<.001
Wake after sleep onset, min	21 (8 to 34)	<.001
Sleep efficiency, %	−8.6 (−11.7 to −5.6)	<.001
Slow-wave sleep, % of sleep	−1.0 (−2.9 to 0.9)	>.05
REM sleep, % of sleep	−4.5 (−6.1 to −2.9)	<.001

Abbreviations: AHI, apnea-hypopnea index; CI, confidence interval; HF, heart failure; REM, rapid eye movement.
*Mean differences were adjusted for age sex and body mass index.

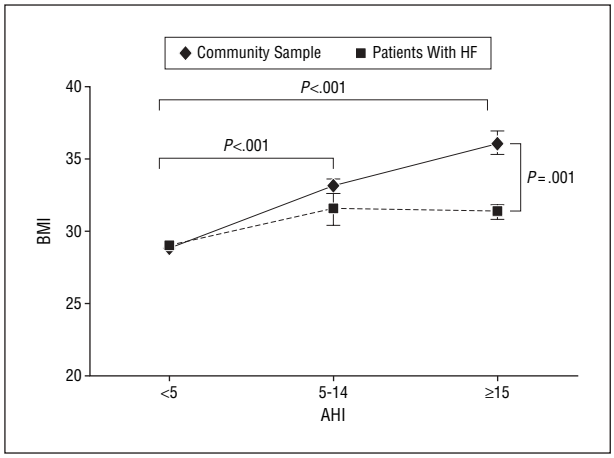

Figure 2. Body mass index (BMI) (calculated as weight in kilograms divided by the height in meters squared) by apnea-hypopnea index (AHI) categories (<5, 5-14, and ≥15). In the community sample, the AHI category increased significantly in association with increasing mean±SE BMI (28.9±0.2, 33.1±0.5, and 36.1±0.8, respectively). In contrast, in patients with heart failure (HF) there was no significant increase in the AHI category with increasing BMI (29.0±0.5, 31.5±1.1, and 31.3±1.2, respectively). In those with an AHI of 15 or higher, BMI was significantly greater in the community sample compared with the patients with HF.

hours in the community sample in all AHI groups (Figure 1). Our findings are similar to those reported in HF patients with and without central or OSA[2,7] and therefore are likely to be representative of patients with HF in general.

In the context of the markedly reduced sleep time and efficiency, the lack of subjective sleepiness in patients with HF is all the more remarkable because reduced sleep time in subjects without cardiovascular diseases is associated with increased daytime sleepiness and reduced sleep-onset latency.[15,16] One possible explanation for this is increased sympathetic nervous system activity in patients with HF compared with healthy subjects[19,20] that is further augmented by the superimposition of OSA.[18,21] Aggarwal and colleagues[20] have demonstrated that patients with HF have elevated suprabulbar subcortical noradrenergic activity that could suppress daytime sleepiness by stimulating alertness. This might neutralize the sleepiness-inducing effects of sleep deprivation and sleep fragmentation.

Another possibility is that patients with HF slept more in the daytime compared with subjects from the community sample. However, this is unlikely because a recent report on 39 HF patients with and without sleep-related breathing disorders, in which lack of physical activity on actigraphy was used as a surrogate for daytime napping, found no differences in presumed nap time between HF patients with and without sleep-related breathing disorders (0.43 vs 0.33 hours; $P=.36$).[22] Moreover, self-reported nap time in those patients with HF was similar to that reported in the entire Wisconsin Sleep Cohort (0.21 hours). Therefore, these data suggest that the low ESS score in HF patients with and without OSA cannot be fully explained by an increase in daytime napping.

The ESS relies on the self-perception of sleepiness and is therefore a subjective means of assessing sleepiness that in subjects without HF correlates modestly, but significantly, with both the AHI and objective measures of sleepiness. When patients present to medical clinics, it is subjective EDS that frequently leads to a sleep study: objective sleepiness can only be assessed by multiple sleep latency tests once a sleep study has been performed and does not correlate any better with AHI than does the ESS.[23] The lack of subjective EDS in the HF group is also consistent with their prolonged sleep-onset latency.

In the patients with HF, we did not find any significant relationship between the degree of left ventricular

systolic dysfunction, assessed by LVEF, and either the AHI or ESS. Thus, there does not appear to be a significant relationship between the severity of left ventricular systolic dysfunction and severity of either OSA or of subjective sleepiness. Because we did not measure LVEF in our community sample, these relationships could not be assessed in them.

The differences in sleep structure between patients with HF and the community sample are independent of other factors that can affect sleep structure such as age, sex, BMI, and OSA.[24,25] Therefore, the impaired sleep time and quality in patients with HF is most likely related to HF. Symptoms or comorbid conditions such as orthopnea and depression associated with HF[26] may contribute to shortened sleep time and impaired sleep efficiency. On the other hand, sleep deprivation has acute adverse cardiovascular effects, including increased sympathetic activity and effects on blood pressure and heart rate,[27] suggesting that sleep deprivation may contribute to the development of HF. Indeed, prospective epidemiological studies demonstrate an increased risk for cardiovascular disease and mortality in subjects with self-reported sleep times of less than 5 hours.[5,6]

Although we found increased odds for having OSA associated with obesity (odds ratio, 2.27; 95% confidence interval, 1.12-4.54), the association of BMI to AHI was significantly weaker in patients with HF than in the subjects without HF. Thus, it appears that obesity is of less importance in the pathogenesis of OSA in patients with HF than in subjects without HF.

A particular strength of this report is that we used a large sample of subjects from the community as a control group rather than sleep clinic patients in whom EDS is frequently the main complaint leading to referral. We therefore avoided this referral bias. Indeed, population studies of screen-detected OSA have found associations of OSA severity and sleepiness that are weaker than in sleep clinic populations.[8,15] Because we studied only subjects with systolic HF, our findings cannot be extrapolated to patients with diastolic HF or patients with OSA and subclinical diastolic dysfunction.[28,29]

In conclusion, our findings suggest that, in patients with systolic HF, the presence or absence of subjective sleepiness and obesity is not a reliable indicator of who does or does not have OSA. In view of recent evidence that OSA may increase the risk for hypertension,[30] atherosclerosis,[31] and cardiovascular events[32,33] and that its treatment with continuous positive airway pressure can lower blood pressure and improve cardiovascular function in patients with HF who do not complain of sleepiness,[2] relief of sleepiness may not be the primary target of treatment for OSA in patients with HF. However, it remains to be seen whether short-term improvement of cardiovascular function induced by treatment of OSA in patients with HF will translate into reduction in long-term morbidity and mortality. Nevertheless, the absence of subjective sleepiness and obesity should not deter one from performing sleep studies in patients with HF to diagnose OSA because its treatment may improve other clinically important outcomes such as symptoms of HF.[3]

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Correction

Incorrect Total Number of Patients in the Abstract. In the Original Investigation titled "Associations Between the Age at Diagnosis and Location of Colorectal Cancer and the Use of Alcohol and Tobacco" by Zisman et al published in the March 27th issue of the ARCHIVES (2006; 166:629-634) the total number of patients in the "Results" section of the abstract on page 629 was incorrect. The first sentence should have read as follows: "Our data set consisted of 166 172 patients with CRC."