# ORIGINAL ARTICLE Identification and treatment of sleep-disordered breathing in chronic spinal cord injury

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Study design: A follow up on an ongoing prospective cohort study.

**Objective:** Spinal cord injury or disorder (SCI/D) patients have higher rates of sleep-disordered breathing (SDB) than the general population. The objectives of this study were to examine predictors of SDB diagnosis and to estimate rates of SDB treatment in SCI/D patients.

Setting: A SCI clinical sleep research laboratory.

**Methods:** Twenty-eight SCI/D patients (7 women, age  $42.8 \pm 15.8$  years; 16 cervical and 12 thoracic level injuries) completed a battery of questionnaires (Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin questionnaire (BQ) and fatigue severity scale (FSS)) and had one night of attended laboratory polysomnography (PSG). Participants were then notified of the results of their PSG and were interviewed approximately 1 year later to assess clinical outcomes.

**Results:** The majority of patients reported poor sleep quality on all questionnaires. On the basis of PSG, 22 (79%) patients had SDB (apnea-hypopnea index (AHI)  $\ge$  5 events per hour), and 17 (61%) had moderate/severe SDB (AHI  $\ge$  15 events per hour). Higher ESS scores were associated with a higher risk of AHI  $\ge$  5; however, other questionnaires did not distinguish between those with and without SDB using either AHI cutoff. In follow-up interviews, only 50% of patients had spoken to a health-care provider about SDB and only six patients with SDB were prescribed treatment, four of whom were using the treatment at follow-up.

**Conclusion:** SDB is common and severe among SCI/D patients. Screening questionnaires do not appear to differentiate between those with and without SDB. Even when SDB was recognized, many patients remained untreated. The increased prevalence of cardiovascular disease in SCI/D patients could represent a consequence of untreated SDB, and improving diagnosis and management of SDB has the potential to improve outcomes for these patients.

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# INTRODUCTION

Estimates suggest that 1.9% of the U.S. population or six million people report paralysis and 1 275 000 people have a spinal cord injury or disorder (SCI/D).<sup>1</sup> In fact, SCI/D is the second most common cause for paralysis after stroke.<sup>2</sup> Traumatic injuries (for example, motor vehicle accidents) are responsible for the majority of SCI/D. Today, people with SCI/D are living longer, and approximately 80% are 50 years of age and older.<sup>3</sup> Increased life expectancy of the SCI/D population has been accompanied by an increased prevalence of chronic diseases common in older age including obesity, heart disease and metabolic disease.<sup>4</sup> In fact, about two-thirds of patients with SCI/D are overweight or obese and are, therefore, at increased risk for metabolic disorders, cardiac diseases and sleep-disordered breathing (SDB), as a result.<sup>5</sup>

Studies show that sleep disturbances are prevalent and sleep quality is significantly impaired in SCI/D patients.<sup>5–9</sup> The underlying causes of poor sleep in SCI/D patients include depression, pain, bladder dysfunction, circadian misalignment, use of analgesics/hypnotics and SDB.<sup>9</sup> The net effect is that individuals living with SCI/D suffer from sleep fragmentation, high snoring frequency and overall poorer sleep quality relative to able-bodied individuals. Sleep deficiency is related

to many chronic health problems, including obesity, diabetes, hypertension and cardiovascular disease, all of which are common in SCI/D patients.<sup>10,11</sup> Moreover, poor sleep may exacerbate other symptoms such as depressed mood and impaired cognitive performance, which are potential vulnerabilities in patients with SCI/D.<sup>12</sup> Accordingly, sleep disturbance may be both a cause and a consequence of comorbid symptoms in SCI/D patients. Further research is needed to characterize better the sleep difficulties faced by these patients.

SDB is a common cause of sleep disruption in individuals living with SCI/D. The prevalence of SDB is two to fourfold higher than the general population.<sup>5,13–17</sup> Recent reports have also found that more than half of SCI patients developed SDB in their first year post injury.<sup>18</sup> Therefore, SCI/D may be an independent risk factor for the development of SDB.<sup>15</sup> Nevertheless, the majority of SCI/D patients with SDB remain undiagnosed and untreated despite the established negative consequences of SDB and the high frequency of sleep-related complaints in SCI/D patients.<sup>5,19</sup> One reason that SDB is critically important in these patients is that cardiopulmonary complications are major causes of morbidity and mortality in SCI/D patients because of decreased lung volume, ineffective cough, mucus retention and atelectasis.<sup>14,20</sup> In fact, cardiovascular conditions have superseded

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respiratory causes of death in cervical SCI/D patients and have become the most common cause for mortality in this disabled population.<sup>21</sup> On the basis of the extensive literature linking untreated SDB to cardiovascular mortality, SDB may represent a treatable risk factor among SCI/D patients.<sup>22–24</sup>

The objectives of the current study were (i) to determine predictors of SDB among SCI/D patients based on commonly used sleep questionnaires and (ii) to gather information about clinical followup and positive airway pressure (PAP) therapy among SCI/D patients with SDB, once patients were informed of their diagnosis.

# MATERIALS AND METHODS

# Subjects

The Human Investigation Committee of Wayne State University and the John D. Dingell VA Medical Center (JDDVAMC) approved the study. Written informed consent was obtained from all participants, who completed overnight laboratory screening polysomnography (PSG). We studied adults (>18 years old) with chronic SCI/D if they met the study inclusion and exclusion criteria. Inclusion criteria were (i) non-ventilator-dependent individuals with chronic SCI/D (>6 months post injury) and (ii) American Spinal Injury Association grade A, B, C or D,<sup>25</sup> with injuries at the cervical (C4-C7) or thoracic level (T1-T6). Exclusion criteria were (i) pregnant or lactating females; (ii) advanced heart failure, peripheral vascular disease or stroke; (iii) history of head trauma associated with loss of consciousness; (iv) advanced lung, liver or chronic kidney disease; and (v) extreme obesity, defined as body mass index >38 kg m<sup>-2</sup>. Participants were recruited from local and regional SCI care centers including the JDDVAMC and the Rehabilitation Institute of Michigan.

## Measurements

Every subject who agreed to enroll had a brief history and physical examination and then completed the following questionnaires: Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Berlin questionnaire (BQ) and Fatigue Severity Scale (FSS). The ESS and PSQI are validated self-administered questionnaires to assess daytime sleepiness and sleep quality, respectively.<sup>26-28</sup> The ESS has eight items, and answers are scored 0-3 based on the self-rated likelihood of falling asleep in certain circumstances during the past month. A total score ≥10 is considered clinically abnormal sleepiness. The PSQI is an 18-item index that measures seven areas of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications and daytime dysfunction over the last month.<sup>26,27</sup> Each of these seven domains is composed of a 0-3 scale, whereby 3 reflects the negative extreme on the scale. A total score >5 indicates poor sleep quality. The FSS is a self-administered questionnaire to measure the level of agreement with fatigue symptom statements for the prior week.<sup>29</sup> Scoring of level of agreement is based on a 0-7 scale, whereby 7 reflects strong agreement, and scores  $\ge 2$  indicate significant fatigue. The BQ is a self-administered questionnaire consisting of three categories related to the risk of having sleep apnea. Patients can be classified into 'High Risk' or 'Low Risk' based on their responses. Individuals who endorse two out of the three categories are considered 'high risk' for SDB.30

Standard laboratory PSG was performed according to the standards of the American Academy of Sleep Medicine, and respiratory events were scored using the 2012 AASM recommended scoring criteria.<sup>31</sup> Hypopnea events were scored with EEG arousals even if the 4% desaturation threshold was not reached. SDB was defined as an apnea-hypopnea index (AHI) of  $\ge$  5 events per hour of sleep. In addition to standard full attended PSG (including EEG, EOG and chin EMG), nasal airflow was measured by a pneumotachometer (Hans Rudolph, Inc., Model 3700A, Shawnee, KS, USA) connected to a tight-fitting nasal mask to enhance the quality of the respiratory signals during the recording.

After completing the PSG, all participants with AHI  $\ge$  5 events per hour were notified verbally (personal communication or telephone call from study physician or research coordinator) and were mailed a letter describing their abnormal findings. This is standard practice in our research studies of SDB. Participants with SDB were provided with specific instructions to follow up with their own health-care provider for clinical evaluation and treatment of

#### Table 1 Follow-up survey for patients with sleep-disordered breathing

Question	Answer
Did you report sleep disorders to your physician?	(Yes, No)
If not, what is the reason?	
Did you have a clinical sleep study due to our report?	(Yes, No)
Have you been prescribed positive airway pressure (PAP) therapy?	(Yes, No)
If yes, are you using PAP therapy?	(Yes, No)
If not using PAP therapy why?	

SDB. When possible (and with the patient's permission), the patient's primary care provider was notified. For the purposes of this study, a follow-up phone call was made to all participants with  $AHI \ge 5$  at least 6 months (on average, 12 months) after notifying them of the results of their PSG. The goal of these calls was to assess the outcomes of informing the patient about the presence of SDB using the procedures described above. Of the 22 individuals with SDB, two participants' phones had been disconnected and they could not be reached. One participant stated he did not receive a letter, so it was re-sent. During this follow-up call, a short interview was performed (see Table 1 for a list of interview questions).

## Data analysis

Descriptive statistics, in the form of frequencies (for binary and nominal variables) and means and standard deviations (for continuous variables), were computed for the overall sample, and then separately for those with SDB (AHI  $\geq$  5) vs those without SDB (AHI <5). We also compared individuals with AHI  $\geq$  15 to those with AHI <15. *T*-tests were used for continuous variables and Fisher's exact tests for binary/nominal variables.

Bivariate analyses were performed using two outcome variables. First, we compared those with and without SDB using a cutoff of  $AHI \ge 5$ ) and second we used a cutoff of  $AHI \ge 15$ . The seven core candidate predictors used to predict each outcome were (1) scoring as 'high risk' on the BQ, (2) having a high ESS score ( $\ge 10$ ), (3) ESS total score, (4) having a high PSQI score (> 5), (5) PSQI total score, (6) having a high FSS ( $\ge 2$ ) and (7) FSS total score. Three additional predictors were considered as well, (8) age, (9) body mass index and (10) neck circumference. For the binary predictors (that is, 1, 2, 4 and 6), Fisher's exact tests were performed examining the association between SDB and the predictor. Exact logistic regression analyses were performed for the continuous predictors (that is, 3, 5, 7, 8, 9 and 10). All analyses were performed using Stata version 13.1 (StataCorp. 2013, Stata Statistical Software, College Station, TX, USA) and the exact logistic regression analyses were performed using the 'exlogistic' command.<sup>32</sup>

# RESULTS

#### Participant characteristics

We studied 28 chronic SCI/D participants (21 males; age  $42.8 \pm 15.8$  years; body mass index  $26.2 \pm 4.9$ ; neck circumference  $39.4 \pm 4$ ; 16 cervical and 12 thoracic levels). The etiologies of SCI/D were mainly due to gun shots (36%) or motor vehicle accidents (32%; see Table 2).

#### Patient-reported sleep disturbances

Using four screening sleep health questionnaires (ESS, PSQI, FSS and BQ) the majority of SCI/D patients reported poor sleep quality (see Table 3). Overall, 60.7% had ESS scores of 10 or more (mean  $ESS = 10.5 \pm 4.3$ ) indicating sleepiness, 85.7% had PSQI scores more than 5 (mean  $PSQI = 10.5 \pm 4.3$ ) indicating poor sleep quality, 96.4% had FSS scores of 2 or more (mean  $FSS = 4.5 \pm 1.5$ ) indicating significant fatigue, and 51.9% had high-risk for SDB, based on the BQ.

#### Severity of SDB

On the basis of the attended laboratory PSG, the mean AHI was 29.8 (s.d. = 24.7). Of the 28 patients studied, 79% (n = 22) had SDB

# Table 2 Participant characteristics for the overall sample (overall) and separately for AHI < 5 (vs $AHI \ge 5$ ) and AHI < 15 (vs $AHI \ge 15$ )

	Overall	AHI<5	$AHI \ge 15$	P-value	AHI<15	$AHI \ge 15$	P-value	Ν
Injury location				0.057			0.019	28
Cervical (C4-C7)	57.1% (16)	16.7% (1)	68.2% (15)		27.3% (3)	76.5% (13)		
Thoracic (T1-T6)	42.9% (12)	83.3% (5)	31.8% (7)		72.7% (8)	23.5% (4)		
Age (years)	42.8 (15.8)	31.0 (7.6)	46.0 (16.0)	0.037	36.5 (14.6)	46.9 (15.6)	0.088	28
BMI (kg m <sup>-2</sup> )	26.2 (4.9)	25.9 (3.6)	26.3 (5.3)	0.840	26.4 (4.6)	26.1 (5.3)	0.890	28
Gender (male)	75.0% (21)	50.0% (3)	81.8% (18)	0.144	45.5% (5)	94.1% (16)	0.007	28
NC (cm)	39.4 (4.0)	37.6 (3.1)	39.9 (4.1)	0.210	38.4 (3.2)	40.1 (4.4)	0.267	28
Previous tracheostomy	22.2% (4)	0.0% (0)	26.7% (4)	1.000	12.5% (1)	30.0% (3)	0.588	18
Etiology				0.039			0.077	28
Gun shot	35.7% (10)	83.3% (5)	22.7% (5)		63.6% (7)	17.6% (3)		
Motor vehicle accident	32.1% (9)	0.0% (0)	40.9% (9)		18.2% (2)	41.2% (7)		
Diving/fall	10.7% (3)	0.0% (0)	13.6% (3)		0.0% (0)	17.6% (3)		
Surgical/other	21.4% (6)	16.7% (1)	22.7% (5)		18.2% (2)	23.5% (4)		

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; NC, neck circumference.

Table 3 Comparison of groups using clinical cutoff scores on sleep health questionnaires

	Overall	AHI<5	AHI ≥ 5	P-value	AHI<15	$AHI \ge 15$	P-value	Ν
ESS≥10	60.7% (17)	33.3% (2)	68.2% (15)	0.174	54.5% (6)	64.7% (11)	0.701	28
PSQI > 5	85.71% (24)	100.0% (6)	81.8% (18)	0.549	81.8% (9)	88.2% (15)	1.0	28
FSS≥ 2	96.4% (27)	100.0% (6)	95.5% (21)	1.000	100.0% (11)	94.1% (16)	1.000	28
BQ=high risk	51.9% (14)	16.7% (1)	61.9% (13)	0.077	30.0% (3)	64.7% (11)	0.120	27

Abbreviations: AHI, apnea-hypopnea index; BQ, Berlin questionnaire; ESS, Epworth Sleepiness Scale; FSS, Fatigue Severity Scale; PSQI, Pittsburgh Sleep Quality Index.

 $(AHI \ge 5)$  and 61% (n = 17) had moderate to severe SDB ( $AHI \ge 15$ ). A majority of SCI patients (77.3%, that is, 17/22) with SDB had  $AHI \ge 15$  events per hour indicating a moderate to severe degree of SDB. It is notable that only four participants had previously been diagnosed with SDB before participating in the study.

## Differences between individuals with and without SDB

Table 2 shows comparisons between patients with and without SDB (using an AHI cutoff of 5) and between patients with and without moderate/severe SDB (using an AHI cutoff of 15). There were significant differences between those with  $AHI \ge 5$  vs < 5 in terms of the underlying SCI/D etiology. Second, as we have previously reported those with cervical SCI had a higher prevalence of moderate to severe SDB than those with thoracic injuries, and males were more likely to have moderate to severe SDB than females.<sup>5,15</sup> There were no other significant differences between patients with and without SDB using either AHI cutoff score.

In the series of bivariate analyses predicting the presence vs absence of SDB, 2 of the 10 predictors distinguished between those with and without SDB (AHI $\ge$ 5 vs AHI<5): ESS total score (OR=1.28, P=0.048) and age (OR=1.12, P=0.025). For a one unit increase in ESS score, the odds of having an AHI $\ge$ 5 increased by 28%. A 1-year increase in age was associated with a 12% increase in the odds of having an AHI $\ge$ 5. None of the other eight predictors was significantly associated with SDB (AHI $\ge$ 5 vs AHI<5). Furthermore, none of the 10 predictors was significantly associated with moderate to severe SDB (AHI $\ge$ 15 vs AHI<15).

# Outcomes of SDB diagnosis

Figure 1 depicts rates of PAP therapy acceptance and use among the 18 SCI/D patients who were notified about their SDB diagnosis

using the procedures describe above and the four individuals who were previously diagnosed with SDB (total n=22). Out of the 20 individuals we were able to contact by phone, we found that only 10 (50%) had discussed SDB with a health-care provider. Among those who did not (n=10), the most common reason given was that the patient did not see sleep difficulties as a significant concern worthy of clinical attention (n=6). Furthermore, a clinical PSG was not conducted for 2 out of 10 patients who did speak to a provider because of the patient's perception that he/she would not be able to tolerate PAP therapy. The remaining six individuals were prescribed PAP therapy, and a subset of four reported using it at the time of the follow-up interview. The two individuals not using PAP therapy indicated that it was too uncomfortable to tolerate.

#### DISCUSSION

This study expands our prior work in the area of sleep quality and SDB among patients with SCI/D.<sup>5,15</sup> The main findings of this study are (i) the majority of SCI/D patients reported poor sleep quality on multiple sleep questionnaires; (ii) individuals with SCI/D typically had moderate to severe SDB; (iii) among the sleep questionnaires examined (ESS, PSQI, FSS and BQ), higher ESS scores were associated with elevated risk of SDB, but questionnaires generally did not distinguish between patients with and without SDB; (iv) Even when SDB was diagnosed in patients with SCI/D, clinical management of the disorder remains a challenge.

# Sleep quality is poor for patients living with SCI/D

The majority of patients with SCI/D in our study reported poor sleep quality, regardless of the presence or absence of SDB. Despite the poor sleep quality measured by all four screening sleep health questionnaires (ESS, PSQI, FSS and BQ), only ESS predicted the presence of

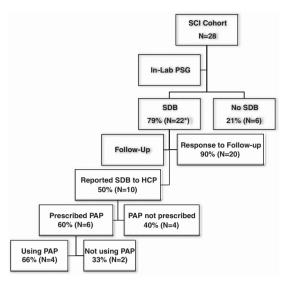


Figure 1 A flow chart to illustrate the rate of PAP therapy acceptance and tolerance in SCI/D patients with SDB diagnosis. HCP: healthcare provider; PAP: positive airway pressure; PSG: polysomnography; SDB: Sleep-disordered breathing.

SDB defined by  $AHI \ge 5$ . The ESS questionnaire is a commonly used measure to determine the presence and severity of subjective excessive daytime sleepiness. It is possible that reported sleepiness is associated with SDB, but other types of sleep-related problems (for example, insomnia) can contribute to sleepiness in SCI/D patients as well. This finding is similar to previous studies in sleep disorders clinic patients using the ESS, which was useful in identified patients with and without SDB in clinical settings;<sup>28</sup> however, unlike prior research, we did not find the cutoff score of 10 to be useful, as approximately one-third of individuals without SDB scored about this threshold, and about onethird of individuals with SDB scored below this threshold. In addition, none of the sleep questionnaires (including ESS) distinguished between those with and without moderate to severe SDB (AHI≥15 vs AHI < 15). This could be because of the fact that the majority of SCI/D patients in our study had moderate or severe SDB, the reported sleep disturbances being so severe, or because of small sample size. The BQ, which is specially designed to identify individuals at high risk for SDB, also misclassified a significant proportion of patients. It appears the BQ is neither sensitive nor specific as a screening tool in SCI/D patients. Future research and larger studies are needed to determine whether sleep health questionnaires can be refined and adapted for use in the SCI/D population.

In contrast to other reports, the rate of SDB found in our study was higher than what has been observed in other studies.<sup>3,13,18</sup> This may be due to several factors. First, we used in-lab attended PSG with pharyngeal catheter and pneumotachometer to accurately detect respiratory events. This may have enabled us to identify more events than were associated using other methodologies for recording respiratory variables during PSG. Second, we scored arousals and associated respiratory events independent of desaturation because patients with SCI/D may experience an arousal in the absence of a desaturation during a respiratory event during sleep. Third, our SCI/D population may have had more long-standing comorbidities than patients studied previously. We also found that moderate to severe SDB was more predominant in men with cervical SCI/D, which is not surprising as male gender and tetraplegia are both considered risk factors for SDB.<sup>15</sup> These are important considerations, as home sleep

testing may be an attractive alternative to laboratory studies in patients with SCI/D; however, the higher rates found in our study suggests that more sophisticated diagnostic testing may enhance sensitivity of testing and enable detection of more subtle forms of SDB.

Although we were not able to clinically follow these patients and make direct referrals to a sleep disorders specialist for clinical management, we did use our standard process for notifying patients (verbally and in writing), and when possible notifying their primary care providers. We also gathered follow-up information via interview from patients about why they did or did not choose to follow-up with their own providers about SDB. Our findings from these semistructured interviews suggest that, even when diagnosed, there are significant barriers to treating SDB among patients with SCI/D. First, patients felt that, given the host of medical conditions with which they were coping, SDB was not sufficiently impactful to warrant attention from their clinical providers. Second, when offered treatment, they experienced the same difficulties commonly reported by able-bodied individuals who are new users of PAP therapy including discomfort from the equipment.<sup>33</sup> Taken together, these findings suggest that targeted patient education combined with support at PAP initiation may be useful for SCI/D patients.

In summary, the rates of SDB are high among patients with SCI/D, and may remain unrecognized and untreated despite the high prevalence of the disease and the known associated cardiovascular risks. It does not appear that routine screening with sleep question-naires can identify individuals with moderate to severe disease, and development of new screening tools may be required. In addition, there are significant challenges to the treatment of patients who are identified as having SDB. Improved screening and detection of SDB should be combined with strategies to increase the acceptability of and adherence to PAP therapy in this particularly vulnerable patient group.<sup>34–37</sup>

# DATA ARCHIVING

There were no data to deposit.

# CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## DISCLOSURE

This was not an industry-supported study.

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