

Night-to-night Variability in Obstructive Sleep Apnea Severity: Relationship to Overnight Rostral Fluid Shift

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Study Objectives: Overnight rostral fluid shift from the legs to the neck may narrow the pharynx and contribute to obstructive sleep apnea (OSA) pathogenesis. We hypothesized that night-to-night changes in the apnea-hypopnea index (AHI) would be associated with changes in overnight rostral fluid shift.

Methods: Twenty-six patients with OSA (AHI ≥ 10) underwent two polysomnograms 14 days apart with measurement of neck and leg fluid volumes (LFV), neck circumference and upper-airway cross-sectional area before and after sleep.

Results: Although mean AHI did not differ between polysomnograms, 35% of patients had a difference in AHI > 10 , indicating significant intra-individual variability. There were direct correlations between change in non-rapid-eye movement (NREM), but not REM AHI and change in evening LFV between polysomnograms ($r = 0.440$, $p = 0.036$ and $r = 0.005$, $p = 0.982$, respectively) and between change in supine, but not non-supine AHI and change in evening LFV ($r = 0.483$, $p = 0.020$ and $r = 0.269$, $p = 0.280$, respectively). An increase

in evening LFV between polysomnograms was associated with a greater overnight decrease in LFV ($r = 0.560$, $p = 0.005$) and a greater overnight increase in neck fluid volume ($r = 0.498$, $p = 0.016$). Additionally, a greater overnight increase in neck circumference was associated with a greater overnight increase in neck fluid volume between polysomnograms ($r = 0.453$, $p = 0.020$) and a greater overnight decrease in upper-airway cross-sectional area ($r = -0.587$, $p = 0.005$).

Conclusion: Intra-individual variability in OSA severity may be partly explained by day-to-day changes in evening leg fluid volume and overnight rostral fluid shift, which may be most important in the pathogenesis of OSA during NREM and supine sleep.

Keywords: obstructive sleep apnea, rostral fluid shift, upper airway

Citation: White LH, Lyons OD, Yadollahi A, Ryan CM, Bradley TD. Night-to-night variability in obstructive sleep apnea severity: relationship to overnight rostral fluid shift. *J Clin Sleep Med* 2015;11(2):149–156.

Severity of obstructive sleep apnea (OSA) can vary considerably from night to night, but the reasons for this are unclear. Previous studies found a change in the frequency of apneas and hypopneas per hour of sleep (apnea-hypopnea index, AHI) greater than 10 in 18% to 65% of patients undergoing polysomnograms (PSGs) on consecutive nights or one month apart.^{1–4} Furthermore, in one study, 50% of patients undergoing consecutive night PSGs met criteria for OSA diagnosis (AHI ≥ 10) on one PSG but not on the other.³

Few studies have examined the reasons for this AHI variability. While one study found increased variability in patients with higher AHIs, another did not.^{2,5} Changes in rapid-eye movement (REM) or supine sleep times do not explain the AHI differences, as there was also significant variability in the AHI within REM and supine sleep.⁴ One study found that nasal obstruction or a deviated septum was more common in patients with higher AHI variability, but there were no differences in other factors including age, sex, body mass index (BMI), or lung function.⁴

During the daytime, fluid accumulates in the interstitial and intravascular spaces of the legs due to gravity, and on lying down at night, fluid shifts rostrally towards the neck, where

it may narrow the upper airway, predisposing to upper airway collapse and OSA.⁶ In non-obese men, men with heart failure and in hypertensive patients, there are strong relationships between the AHI and the amount of fluid moving out from the legs overnight and with the overnight increase in neck circumference.^{7–9} Diuretics have been shown to reduce the AHI in hypertensive patients with OSA in proportion to the reduction in the amount of fluid shifting out of the legs overnight.¹⁰ Compression stockings also reduced the AHI in patients with venous insufficiency in association with reduced daytime leg fluid accumulation and overnight rostral fluid shift.¹¹ It is

BRIEF SUMMARY

Current Knowledge/Study Rationale: Overnight rostral fluid shift from the legs to the neck may narrow the upper airway and contribute to obstructive sleep apnea (OSA) pathogenesis. Intra-individual night-to-night variability in OSA severity may relate to night-to-night variations in overnight rostral fluid shift.

Study Impact: This study found that intra-individual variability in OSA severity may be partly explained by day-to-day changes in evening leg fluid volume and overnight rostral fluid shift, which may be most important in the pathogenesis of OSA during NREM and supine sleep.

therefore possible that night-to-night variations in rostral fluid shift may lead to night-to-night changes in the AHI. For example, increased time spent sitting increases daytime leg fluid accumulation because of inactivity of the calf muscle pump, and is associated with greater fluid movement out of the legs overnight and a higher AHI.^{8,12}

We therefore sought to examine the spontaneous change in overnight rostral fluid shift and its relationship to the change in AHI in patients undergoing PSGs two weeks apart. We hypothesized that among patients with OSA, night-to-night changes in the AHI would be proportional to changes in daytime leg fluid volume (LFV) and overnight rostral fluid shift.

METHODS

Subjects

Patients aged 18–80 years referred to the sleep laboratory of the University Health Network because of a clinical suspicion of sleep apnea and found to have OSA (AHI > 10 and \geq 50% of events obstructive) were eligible for the study which was part of a larger randomized trial to test the effects of compression stockings on severity of OSA. Twenty-three patients randomized to the control group underwent 2 additional overnight research PSGs 2 weeks apart, with no intervention for their OSA. Additionally, 3 patients who did not meet criteria for the trial (one patient with AHI > 10 on clinical PSG but AHI < 10 on the baseline research PSG, and 2 patients taking diuretics, which was an exclusion for the trial) underwent 2 additional research PSGs and were included in the present study. Exclusion criteria were OSA treated within the last 3 months, tonsillar hypertrophy, heart failure, stroke, and end-stage renal or liver disease. Demographic variables, medical history, and medication use were recorded and physical fitness was assessed using the Duke Activity Status Index.¹³ Patients completed a diary of the number of hours spent sitting during the day of each PSG. The protocol was approved by the Research Ethics Board of the University Health Network and all patients provided written informed consent before participation.

Polysomnography

Overnight PSGs were performed using standard techniques and scoring criteria for sleep stages and arousals.¹⁴ Thoracoabdominal motion was monitored by respiratory inductance plethysmography and nasal airflow by nasal pressure cannulae. Oxyhemoglobin saturation (SaO₂) was monitored by oximetry. Apneas and hypopneas were defined as > 90% and 50% to 90% reduction in tidal volume from baseline, respectively, lasting \geq 10s. They were classified as obstructive if there was out-of-phase thoracoabdominal motion or flow limitation on the nasal pressure tracing and central if there was absent thoracoabdominal motion, or in-phase thoracoabdominal motion without evidence of airflow limitation, during apneas and hypopneas, respectively. Body position was recorded continuously by a video-camera and quantified by a technician. Signals were recorded on a computerized sleep recording system (Sandman, Nellcor Puritan Bennett Ltd, Ottawa, Ontario, Canada) and scored by technicians blind to the measurements of fluid volumes, neck, and calf circumferences, and upper airway

cross-sectional area (UA-XSA). The AHI was quantified. Baseline and follow-up studies were scored by the same technician.

Neck and Leg Fluid Volumes and Circumferences

Body weight was measured before going to bed and within 30 min of awakening the next morning before urinating. Edema of each leg was assessed before sleep on a scale of 0–3.¹⁵ With subjects instrumented for sleep studies, lying awake and supine, LFV and neck fluid volume (NFV) were measured simultaneously using a bioelectrical impedance spectrum analyzer (MP150, Biopac Systems Canada Inc, Montreal, Canada). This technique, which is well-validated, uses the impedance to electrical current within a body segment to measure fluid content.¹⁶ For NFV, electrodes were placed behind the right ear and at the base of the right side of the neck. For LFV, electrodes were placed on the ankle and upper thigh of both legs. Electrodes were secured in place overnight with adhesive tape and the distance between them measured to ensure they were placed the same distance apart at each PSG. Neck circumference was measured just above the cricothyroid cartilage and calf circumferences at their thickest parts using a tape measure. Right and left calf circumference measurements were averaged. Lines were drawn with a marker pen to ensure that measurements before and after sleep were made at the same level. Measurements of NFV, LFV, and neck and calf circumferences were repeated the next morning after awakening and before subjects got out of bed. Differences between measurements made after and before sleep were calculated as the overnight changes in these variables. Measurements were made before PSGs were scored and therefore the experimenter was blind to the AHI.

Upper-Airway Cross-Sectional Area

UA-XSA before and after sleep was measured by acoustic pharyngometry (Eccovision, Hood Laboratories, Pembroke, Massachusetts, USA), with the patient lying supine and the head in the neutral position.¹⁷ UA-XSA was defined as the mean cross-sectional area between the vellum and glottis, and the mean of 4 consecutive recordings was used as previously described.¹⁸ Overnight change in UA-XSA was calculated.

Statistical Analysis

Differences in measurements between PSGs were analyzed using paired t-tests or Wilcoxon tests for normally and non-normally distributed variables, respectively. Bland-Altman analysis was used to assess variability of measurements between PSGs.¹⁹ The limits of agreement were defined as the mean of the differences between measurements \pm 2 standard deviations, with wider limits of agreement indicating greater variability, assuming that 95% of the differences lie within these limits in a normal distribution. Relationships between variables were assessed using Pearson or Spearman correlation coefficients for normally or non-normally distributed variables, respectively. Multiple stepwise linear regression analysis was also undertaken with change in supine and non-REM (NREM) sleep AHI as dependent variables and change in overnight neck and calf circumference changes, change in evening LFV, change in overnight LFV and NFV changes, and change in overnight UA-XSA change as independent variables, with $p < 0.05$ to enter and $p > 0.1$ to remove. A p value < 0.05 was

Table 1—Baseline characteristics.

Age (years)	57.2 ± 10.2
Male sex, n (%)	16 (61.5)
Body mass index (kg/m ²)	32.1 ± 6.3
Hypertension, n (%)	13 (50.0)
Ischemic heart disease, n (%)	4 (15.4)
Diabetes, n (%)	2 (7.7)
Anti-hypertensive medication, n (%)	11 (42.3)
Thiazide diuretic, n (%)	2 (7.7)
Leg edema, 0–3	0.7 ± 0.8
Sitting time (hours/day)	9.1 ± 2.5
Duke Activity Status Index ^a	44.7 ± 14.5

^aMaximum score = 58.2.

considered significant. Statistical analyses were performed by SPSS 20 (SPSS Inc, Chicago, IL).

RESULTS

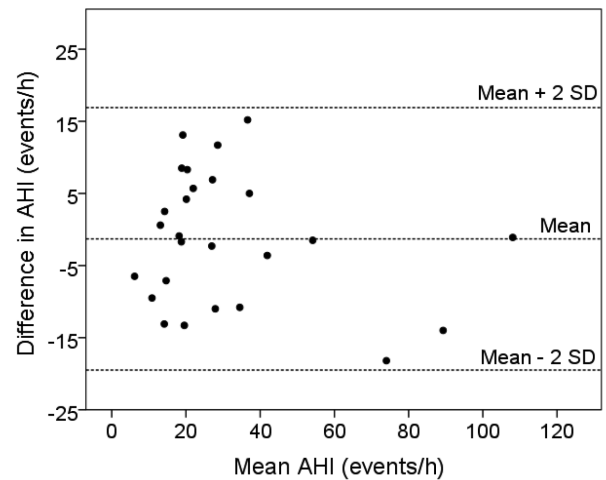
Twenty-six patients participated, whose baseline characteristics are shown in **Table 1**. Patients were middle-aged and obese with minimal edema detectable clinically. They were relatively sedentary as indicated by a sitting time of just over 9 h/day and had reduced physical fitness with a decreased Duke Activity Status Index score. Two patients were taking thiazide diuretics for hypertension, but no patients had changes in medications during the study period.

Apnea-Hypopnea Index Variability

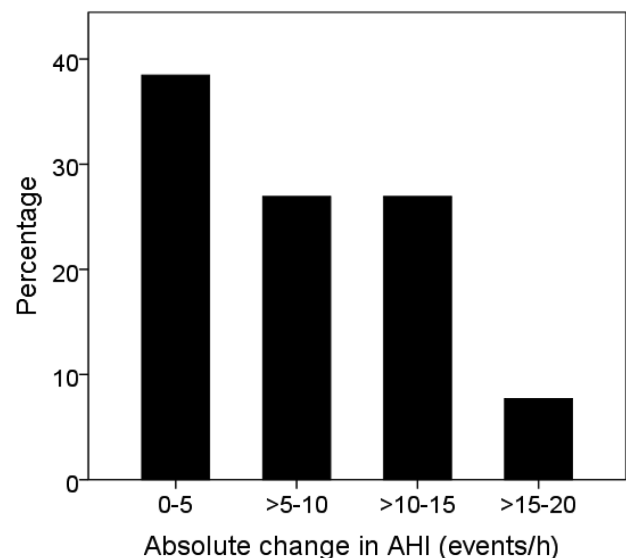
Patients underwent 2 PSGs 14.2 ± 1.5 days apart. The mean AHI did not change significantly between PSGs (32.0 ± 26.1 vs 30.8 ± 24.0, $p = 0.49$), nor did the proportion of obstructive or central apneas and hypopneas (92.3 ± 10.9 vs 93.1 ± 11.2%, $p = 0.71$ and 6.9 ± 9.9 vs 5.9 ± 10.2%, $p = 0.68$, respectively). However, there was considerable intra-individual variability, as there were wide limits of agreement between the studies (mean AHI difference -1.3, limits of agreement -19.5 to 16.9, **Figure 1**). The difference in AHI between sleep studies was > 5 in 63% of patients, > 10 in 35%, and > 15 in 8% (**Figure 2**). There was no relationship between baseline OSA severity and AHI variability ($r = -0.026$, $p = 0.901$ for AHI difference vs mean AHI), nor between change in AHI and change in weight ($r = 0.292$, $p = 0.15$). Despite considerable variation in supine sleep time, there was no relationship between change in AHI and change in absolute time or percentage time spent sleeping supine ($r = 0.247$, $p = 0.22$ and $r = 0.156$, $p = 0.45$, respectively, **Table 2**). Similarly, there was no relationship between change in AHI and change in absolute REM sleep time or percentage time spent in REM sleep ($r = -0.107$, $p = 0.61$ and $r = -0.318$, $p = 0.11$, respectively). This may be because there was also considerable variability when the AHI was divided into supine and non-supine and REM or NREM components (**Table 2**).

Overnight Rostral Fluid Shift

During both PSGs, LFV and calf circumference decreased overnight, and this was accompanied by increases in NFV and

Figure 1—Bland-Altman plot demonstrating differences in AHI between PSG 1 and PSG 2 vs mean AHI of both PSGs.

There was considerable intra-individual variability in the AHI, as demonstrated by the wide limits of agreement (-19.5 to 16.9). AHI, apnea-hypopnea index; PSG, polysomnogram; SD, standard deviation.

Figure 2—Percentage of patients with different degrees of change in AHI between PSG 1 and PSG 2.

AHI, apnea-hypopnea index; PSG, polysomnogram.

neck circumference and a decrease in UA-XSA (**Table 3**). Although there were no mean differences in these measurements between PSGs, there was significant intra-individual variability with wide limits of agreement between measurements.

While there was a direct correlation between change in AHI between PSGs and the change in evening LFV between PSGs within a given individual of borderline significance ($r = 0.401$, $p = 0.058$), there was no correlation between change in AHI and change in overnight decrease in LFV between PSGs ($r = 0.174$, $p = 0.43$). However, when the AHI was subdivided into REM and NREM, and supine and non-supine components, the change in evening LFV correlated significantly with the NREM AHI and the supine AHI but not with the REM AHI

Table 2—Changes in weight, REM and supine sleep variables between polysomnograms.

	PSG 1	PSG 2	p	Mean difference (limits of agreement)
Weight (kg)	92.6 ± 17.5	92.6 ± 17.2	1.00	0.3 (−2.0 to 2.0)
Supine time (minutes)	164 ± 113	151 ± 116	0.46	−14 (−198 to 171)
Supine time (% total sleep time)	57.1 ± 31.3	49.0 ± 31.2	0.09	−8.1 (−54.8 to 38.6)
REM time (minutes) ^a	50 ± 27	47 ± 31	0.49	0 (−36 to 36)
REM time (% total sleep time) ^a	16.4 ± 7.1	14.2 ± 7.9	0.13	−2.2 (−16.5 to 12.1)
Supine AHI	48.7 ± 24.7	47.6 ± 28.2	0.80	−1.1 (−43.9 to 41.7)
Non-supine AHI ^b	22.1 ± 34.3	26.1 ± 36.4	0.77	2.1 (−26.3 to 30.5)
REM AHI ^a	39.3 ± 23.2	41.9 ± 25.7	0.64	2.6 (−49.6 to 54.8)
NREM AHI	29.8 ± 27.9	28.5 ± 25.4	0.44	−1.3 (−22.9 to 20.3)
Obstructive apneas and hypopneas (%)	92.3 ± 10.9	93.1 ± 11.2	0.71	0.88 (−23.7 to 25.5)
Central apneas and hypopneas (%)	6.9 ± 9.9	5.9 ± 10.2	0.68	−0.99 (−25.6 to 23.7)

Limits of agreement = mean difference between PSG 1 and PSG 2 ± 2 standard deviations. ^aREM sleep absent in 2 patients on PSG 2. ^bNon-supine sleep absent in 4 patients on PSG 1 and in 2 patients on PSG 2. REM, rapid eye movement; PSG, polysomnogram; AHI, apnea-hypopnea index; NREM, non rapid eye movement.

Table 3—Changes in fluid volume measurements and sitting time between polysomnograms.

		PSG 1	PSG 2	p	Mean difference (limits of agreement)
Weight (kg)	Evening	92.4 ± 17.3	92.4 ± 17.1	0.85	0.0 (−2.0 to 2.0)
	Morning	91.6 ± 17.4 ^c	91.7 ± 17.0 ^c	0.29	0.2 (−2.0 to 2.0)
	Overnight change	−0.8 ± 0.5	−0.7 ± 0.4	0.06	0.2 (−0.7 to 1.0)
Calf circumference (cm)	Evening	40.4 ± 3.7	40.4 ± 3.7	0.87	0 (−1.0 to 1.0)
	Morning	39.3 ± 3.5 ^c	39.4 ± 3.5 ^c	0.62	0 (−0.8 to 0.8)
	Overnight change	−1.1 ± 0.5	−1.1 ± 0.3	0.58	−0.1 (−0.9 to 0.8)
Leg fluid volume (mL) ^a	Evening	5082 ± 1056	5105 ± 1008	0.80	22 (−796 to 840)
	Morning	4571 ± 968 ^c	4570 ± 899 ^c	0.68	−26 (−620 to 568)
	Overnight change	−553 ± 194	−591 ± 179	0.37	38 (−360 to 436)
Neck circumference (cm)	Evening	44.2 ± 4.3	44.0 ± 4.5	0.33	−0.2 (−2.8 to 2.4)
	Morning	44.7 ± 3.9 ^d	44.4 ± 4.1 ^d	0.20	−0.3 (−2.7 to 2.4)
	Overnight change	0.4 ± 1.1	0.4 ± 1.2	0.93	0 (−2.6 to 2.6)
Neck fluid volume (mL)	Evening	271 ± 90	277 ± 93	0.54	7 (−101 to 115)
	Morning	291 ± 85 ^d	311 ± 109 ^d	0.14	20 (−102 to 142)
	Overnight change	20 ± 37	27 ± 46	0.45	8 (−92 to 107)
UA-XSA (cm ²) ^b	Evening	2.42 ± 0.45	2.31 ± 0.61	0.27	−0.11 (−1.03 to 0.92)
	Morning	2.33 ± 0.51	2.15 ± 0.45	0.03	−0.18 (−0.9 to 0.54)
	Overnight change	−0.09 ± 0.30	−0.16 ± 0.40	0.55	−0.07 (−1.07 to 0.93)
Sitting time (hours/day)		9.1 ± 2.5	9.1 ± 2.8	0.94	−0.2 (−5.2 to 4.8)

Limits of agreement = mean difference between PSG 1 and PSG 2 ± 2 standard deviations. ^aData from 23 patients. ^bData from 21 patients. ^cp < 0.005 vs evening value. ^dp < 0.05 vs evening value. PSG, polysomnogram; UA-XSA, upper-airway cross-sectional area.

or the non-supine AHI (**Figure 3**). No other variables on either univariate or multivariate analyses correlated significantly with the NREM AHI or supine AHI.

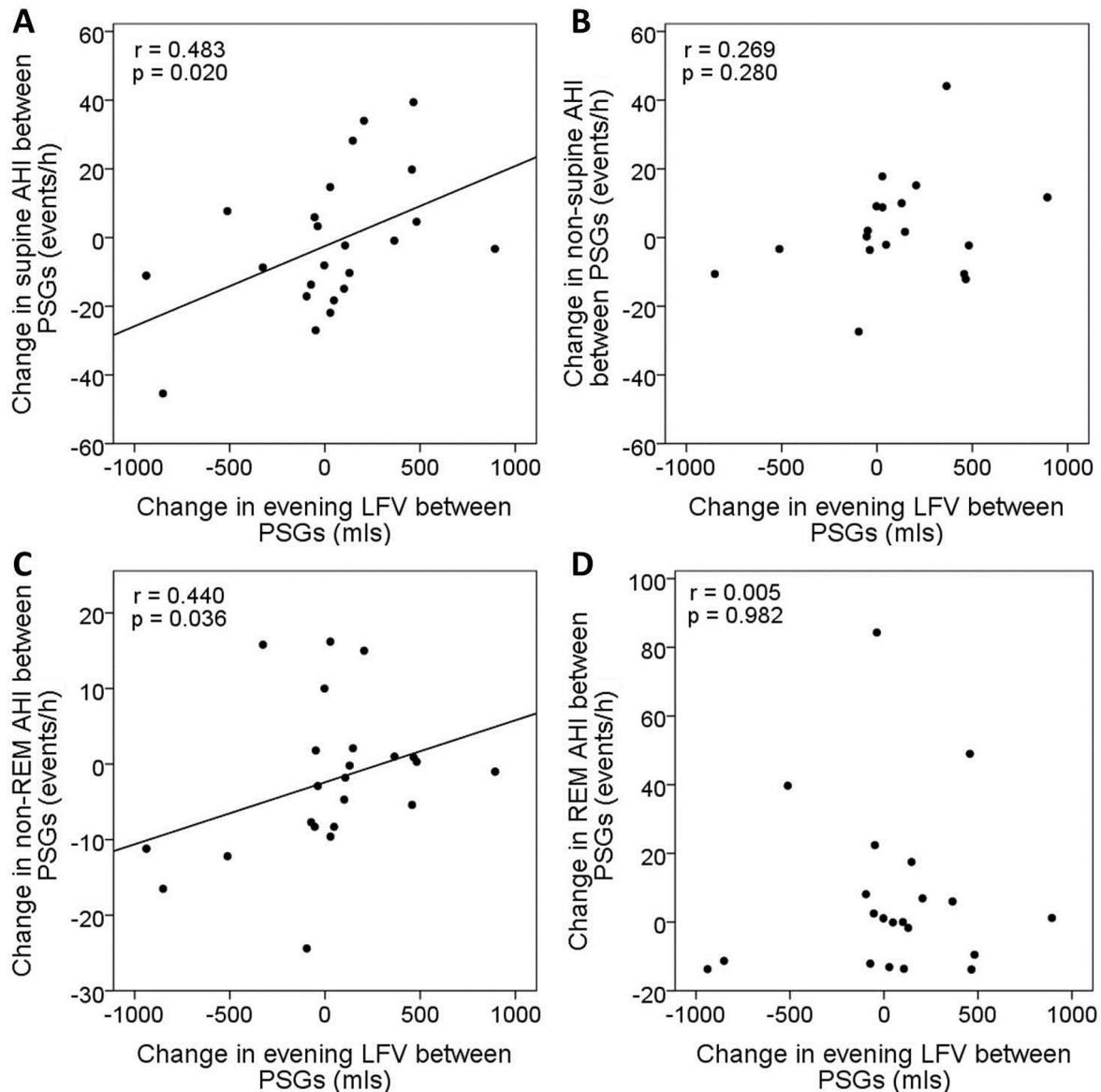
An increase in evening LFV between the 2 PSGs was associated with a greater overnight decrease in LFV (**Figure 4A**) and a greater overnight increase in NFV between PSGs (**Figure 4B**). Additionally, a greater overnight increase in NFV between PSGs was associated with a greater overnight increase in neck circumference (**Figure 4C**) which was in turn associated with a greater overnight decrease in UA-XSA (**Figure 4D**).

Change in AHI and alterations in overnight changes in LFV and NFV did not relate to change in sitting time between PSGs ($r = -0.342$, $p = 0.088$; $r = 0.047$, $p = 0.832$; and $r = 0.215$, $p = 0.293$, respectively).

DISCUSSION

This study has given rise to several novel findings regarding individual night-to-night variability in OSA severity. First, we demonstrated that variability in the AHI, specifically during

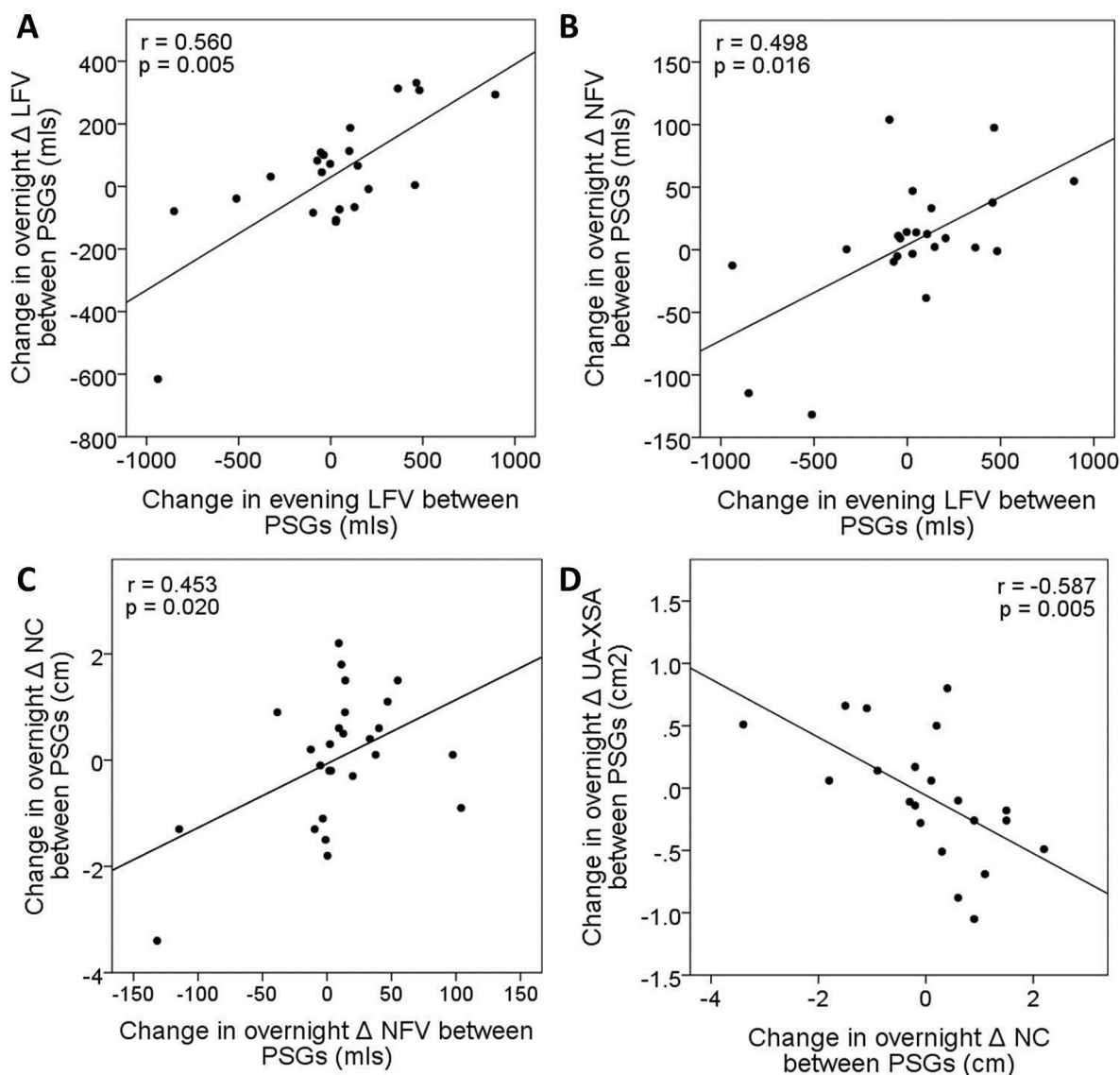
Figure 3—Relationships between change in supine AHI, non-supine AHI, NREM AHI, REM AHI, and change in evening LFV between PSGs.



(A) supine AHI, (B) non-supine AHI, (C) NREM AHI, (D) REM AHI. NREM, non rapid eye movement; AHI, apnea-hypopnea index; REM, rapid eye movement; LFV, leg fluid volume; PSG, polysomnography.

NREM and supine sleep, was related to the change in the volume of fluid accumulated in the legs in the evening. Second, in a given individual, as more fluid accumulated in the legs in the evening, more fluid was redistributed from the legs to the neck overnight and there was a corresponding greater overnight decrease in UA-XSA. Taken together, these findings suggest that variation in the amount of daytime leg fluid accumulation and overnight rostral fluid shift in an individual directly affects upper airway anatomy during sleep and consequently influences night-to-night variation in OSA severity. Finally, the significant relationship between the change in NREM and supine AHI but not REM or non-supine AHI and change in evening LFV suggests that rostral fluid shift is more important in the pathogenesis of OSA during NREM than REM sleep and during supine than non-supine sleep.

These findings expand on our previous work demonstrating a significant relationship between AHI and overnight decrease in LFV on a single night.⁷⁻⁹ However, in the present study, in which fluid volume measurements were repeated during a second PSG, changes in NREM and supine AHI between PSGs correlated with change in evening LFV, rather than change in overnight decrease in LFV between PSGs. Change in the overnight decrease in LFV was, however, strongly correlated with the change in evening LFV between PSGs, as increased daytime leg fluid accumulation resulted in greater fluid movement out of the legs overnight. When measured on multiple nights, AHI may relate more strongly to evening LFV changes than to overnight decrease in LFV because evening LFV is a direct measure of daytime leg fluid accumulation and is possibly more sensitive to changes in overall fluid balance. Accordingly,

Figure 4—Relationships between changes in different variables between PSGs.

(A) Overnight Δ LFW vs change in evening LFW, (B) overnight Δ NFW vs change in evening LFW, (C) overnight Δ NC vs overnight Δ NFW, (D) overnight Δ UA-XSA vs overnight Δ NC. PSG, polysomnography; Δ LFW, change in leg fluid volume; LFW, leg fluid volume; Δ NFW, change in neck fluid volume; Δ NC, change in neck circumference; Δ UA-XSA, change in upper-airway cross-sectional area.

within an individual, an increase in the volume of fluid moving into the neck overnight on PSG 2 was associated with an increase in evening LFW, but not with an increase in the volume of fluid moving out of the legs overnight.

We found that the change in the overnight increase in neck circumference between PSGs was directly related to the change in the overnight increase in NFW between PSGs and inversely related to the alteration in the overnight change in UA-XSA between PSGs, suggesting that in an individual, as more fluid moves into the neck overnight, there is a greater reduction in UA-XSA. Increased fluid present in the intravascular space of the neck may narrow the upper airway by directly increasing extraluminal tissue pressure and increasing capillary hydrostatic pressure, resulting in increased movement of fluid from the intravascular to the interstitial space, which may result in upper airway mucosal edema. For example, in patients with

end-stage renal disease, the AHI correlated directly with the internal jugular vein volume and upper airway mucosal water content measured by magnetic resonance imaging.²⁰ However, in this study we could not determine the exact mechanism of upper airway narrowing in response to neck fluid accumulation. This night-to-night variation in rostral fluid shift and UA-XSA could therefore be one factor accounting for the previously noted night-to-night variation in upper airway collapsibility, and hence AHI.²¹

The relationship between UA-XSA and neck circumference is also consistent with the findings of previous studies in which lower body positive pressure (LBPP) was applied to the legs to rapidly redistribute fluid rostrally. Application of LBPP to healthy subjects and hypertensive patients decreased UA-XSA in association with an increase in neck circumference.^{22,23} Furthermore, in the hypertensive patients the decrease in UA-XSA

and increase in neck circumference were both directly related to the decrease in LFV.²³ In OSA patients, LBPP increased upper airway resistance in association with increased neck circumference.²⁴ Finally, in healthy subjects, LBPP increased upper airway collapsibility in proportion to the decrease in LFV and the increase in neck circumference.²⁵ Taken together, these studies strongly suggest that fluid movement into the neck has anatomical and physiological effects on the upper airway that can predispose to OSA.

The differing relationships between NREM and REM AHI and rostral fluid shift may be due to differences in pharyngeal dilator muscle activity during NREM and REM sleep. During REM sleep there is maximal reduction in pharyngeal dilator muscle activity, which is probably the main mechanism of upper airway collapse.²⁶ Therefore, neck fluid accumulation may not have additional effects on upper airway collapsibility and the AHI during REM because the upper airway is already in its most collapsible state. However, during NREM sleep, when pharyngeal dilator muscle activity is higher and the airway is less collapsible than during REM sleep, narrowing of the upper airway due to neck fluid accumulation is likely to increase its collapsibility. In accordance with these observations, we have demonstrated that rapid intravenous infusion of saline during sleep in men over the age of 40 years induced a marked increase in the AHI in NREM sleep, but not in REM sleep in association with an increase in neck circumference.²⁷

We also found that the supine, but not the non-supine AHI was related to change in evening LFV, suggesting that rostral fluid shift has a greater effect on OSA in the supine position. OSA tends to be worse in the supine position when the upper airway is intrinsically more collapsible, probably because of the effects of gravity.^{28,29} In the supine position, neck fluid accumulation may increase the collapsibility of an already compromised upper airway sufficiently to increase the number of apneas and hypopneas. In contrast, in the non-supine position, when the upper airway is less collapsible, neck fluid accumulation may have a lesser effect on the AHI. There could also be differences in the volume or distribution of fluid in the neck in the supine and lateral positions which result in differing effects on the upper airway, although this could not be determined in the present study.

Reasons for night-to-night variations in rostral fluid shift could include change in activity levels. Increased time spent sitting increases daytime leg fluid accumulation and overnight fluid movement from the legs and is associated with increased AHI.^{8,12} Furthermore, epidemiological studies have demonstrated that decreased exercise levels are associated with increased OSA severity, whereas exercise interventions reduced the AHI independent of changes in body weight.^{30,31} We did not, however, find a relationship between change in AHI and change in sitting time, possibly because habitual sitting time rather than sitting time on a particular day may have a greater influence on LFV and OSA severity.

The degree of intra-individual AHI variability found in this study is consistent with previous studies.¹⁻⁴ We found that 35% of patients had a change in AHI between PSGs of greater than 10, which is comparable to the only other study assessing AHI variability over non-consecutive nights, in which 30% of patients had a change in AHI of greater than 10 between PSGs

performed one month apart.¹ Such AHI variability is clinically relevant, firstly because it could affect treatment decisions which are usually based on the results of one PSG. For example, knowing that the AHI is highly variable from night-to-night might make a physician more inclined to treat a symptomatic patient with a borderline AHI of 5 than if they were unaware of high night-to-night variability. Secondly, since this study demonstrates that AHI variability is related to changes in daytime leg fluid accumulation, interventions targeting rostral fluid shift could be a reasonable treatment strategy for OSA. For example, compression stockings reduced the AHI by 36% in patients with venous insufficiency in association with reductions in evening LFV and the overnight change in LFV.¹¹

This study is subject to some limitations. All but one patient had a baseline AHI > 10, and therefore we could not determine the AHI variability in patients with an AHI < 10 on their first PSG who may have had an AHI ≥ 10 on a second PSG. We also excluded patients with fluid-retaining conditions such as heart failure and end-stage renal failure, who have a high prevalence of OSA and who may have had even greater AHI variability due to alterations in disease activity, fluid retention, or medications.^{9,32} In addition, patients were allowed to get up to pass urine during the night, which could have redistributed fluid back to the legs and affected fluid measurements. However, patients were requested not to void within two hours of the morning fluid volume measurements so that any movement of fluid back into the legs while standing would have been redistributed out of the legs before measurement of fluid volumes in the morning. Furthermore, although the volume of urine voided was not measured, there was no difference in the number of voids/night between PSGs (median [range] 1 [0-2] vs 0 [0-2] voids per night, $p = 0.37$), so it is unlikely that differences in volume of urine voided would have affected the fluid measurements.

In conclusion, this study has provided new insights into the reasons for the well-recognized short-term variability in OSA severity, by demonstrating that changes in NREM and supine AHI relate to spontaneous changes in daytime leg fluid accumulation and overnight rostral fluid shift, lending further support to the concept that overnight rostral fluid shift is involved in the pathogenesis of OSA. Further studies are required to explore the reasons for alterations in rostral fluid shift, such as variations in activity levels, and sitting time, which could in turn provide novel therapeutic targets for the treatment of OSA.

ABBREVIATIONS

AHI, apnea-hypopnea index
 LFV, leg fluid volume
 NFV, neck fluid volume
 OSA, obstructive sleep apnea
 PSG, polysomnogram
 REM, rapid eye movement
 UA-XSA, upper airway cross-sectional area

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication August, 2014

Submitted in final revised form October, 2014

Accepted for publication October, 2014

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DISCLOSURE STATEMENT

This study was funded by a Canadian Institutes of Health Research (CIHR) operating grant MOP-82731. L.H. White was supported by a fellowship from Sleep Country Canada, O.D. Lyons by the Canadian Thoracic Society/European Respiratory Society Peter Macklem Joint Research Fellowship, A. Yadollahi by fellowships from the Toronto Rehabilitation Institute, Mitacs Elevate program and a CIHR Training Grant in Sleep and Biological Rhythms and T.D. Bradley by the Clifford Nordal Chair in Sleep Apnea and Rehabilitation Research. Results based on partial analysis of a clinical trial registered with www.controlled-trials.com (ISRCTN39411395), "Effect of Below-the-knee Compression Stockings on Severity of Obstructive Sleep Apnea: A Randomized Trial." The authors have indicated no financial conflicts of interest.