Upper airway resistance syndrome (UARS) patients present with complaints of excessive daytime sleepiness and do not have obstructive sleep apnea (OSA) on evaluation by standard nocturnal polysomnography (NPSG).\(^1\) The diagnosis of UARS is made when nocturnal esophageal pressure (Pes) monitoring demonstrates crescendo changes in intrathoracic pressures followed by frequent arousals or microarousals.\(^2\) Alternative methods to Pes monitoring that have been studied for use in the diagnosis of UARS include semiquantitative analysis of transduced nasal pressure waveform\(^3\) and measurement of pharyngeal closing pressure.\(^4\) None of these alternative methods to Pes monitoring are considered to be sufficiently validated as to be recommended for widespread application by a recent consensus group assessing the diagnostic accuracy of techniques for the measurement of sleep-disordered breathing.\(^5\)

Few clinical sleep disorders centers in the United States routinely utilize Pes monitoring to diagnose UARS.\(^6\) Factors preventing the widespread use of this technique include patient refusal or intolerance\(^7\) and the requirement of additional technical expertise and expense. Thus, many patients are diagnosed as having UARS presumptively, without Pes monitoring, on the basis of the qualitative perception of possible respiratory-related arousals from standard...
NPSG. To date and to our knowledge, no studies validate the use of standard NPSG alone as an accurate method for the diagnosis of UARS.

Quantitative respiratory inductive plethysmography (RIP) measurements are based on the detection of changes in volume of the chest and abdomen over the breathing cycle. The sum of these measurements has been demonstrated to provide an estimate of tidal volume if calibration is maintained.\(^9\) Assessment of the degree of asynchrony between chest and abdominal measurements during sleep allows detection of hypopneas, which correlates closely to events detected by pneumotachometer.\(^9\) Based on the obvious need to diagnose UARS without Pes monitoring, the current study seeks to determine if RIP is accurate for this purpose.

**Materials and Methods**

**Patients**

Approval for this study was obtained by the Institutional Review Board and Human Use Committee of the Department of Clinical Investigation at Walter Reed Army Medical Center. Patients with symptoms suggestive of narcolepsy or other likely nonrespiratory sleep disorders were excluded from study participation. Over a 3-month period, 64 adult patients, with a median age of 34 years (range, 18 to 48 years) and median body mass index (BMI) of 27 kg/m\(^2\) (range, 25 to 29 kg/m\(^2\)), received NPSG for the evaluation of complaints of witnessed apnea, snoring, and excessive daytime sleepiness.

**Polysomnography**

All patients received an initial 12-channel NPSG (Somnostar 4100 system; SensorMedics Corp; Yorba Linda, CA) that included the following standard parameters: central and occipital EEG, right and left electro-oculogram, digastric and tibialis electromyogram, continuous airflow by oronasal thermistor, chest wall excursions by thoracic and abdominal inductive plethysmography, heart rate and rhythm by ECG, oxyhemoglobin saturation by pulse oximetry, and acoustic monitoring of snoring sounds. The NPSGs were scored using 30-s epochs following the Rechtschaffen and Kales\(^10\) criteria for sleep/wake determination and sleep-staging. Arousals were defined for the presence of apnea, which was defined as complete absence of oronasal thermistor airflow for at least 10 s. Obstructive hypopnea was defined as \(\geq 50\%\) decrement in oronasal airflow for at least 10 s associated with evidence of increasing respiratory effort as measured by qualitative inductive plethysmography. The requirement of \(> 4\%\) decrease in oxyhemoglobin saturation from baseline was not used because the present study evaluated patients who were less likely to desaturate than typical OSA patients who have decreased lung oxygen stores due to obesity and advanced age.\(^12\) Patients were considered to have OSA if NPSG demonstrated an apnea-hypopnea index (AHI, apneas and hypopneas per hour) \(\geq 10\).

For patients who did not have OSA, the following night a second NPSG was performed, which included the standard 12-channel recording montage along with the additional measurement of Pes with a 2.7-mm-diameter electronic pressure catheter (Gaeltec; Hackensack, NJ) with the tip positioned in the midesophagus by radiograph. Once correctly positioned, the catheter was secured at the nose with adhesive tape. The catheter tip transducer was referenced to atmospheric pressure and calibrated with a water manometer to \(\approx -50\) cm and \(+50\) cm H\(_2\)O. UARS events (RERAs, respiratory effort-related arousals) were identified by observing crescendo changes in Pes followed by an EEG arousal. Events were scored only if the most negative Pes exceeded the baseline wake minimum negative Pes by 50% and was \(\leq -12\) cm H\(_2\)O.\(^8\) The UARS index was defined as the mean number of RERAs per hour over the course of the night. Patients were considered to have UARS if the UARS index was \(\geq 10\) events per hour.

**Quantitative RIP**

Along with Pes monitoring and standard NPSG, RIP was recorded simultaneously (SomnoStar PT; SensorMedics Corp). The input leads for RIP consist of two cloth belts that cover curved wires that encircle the chest and abdomen. Initial calibration of the ribcage and abdominal signals were performed during the first 5 min of operation using the qualitative diagnostic calibration procedure.\(^13\)

A software program (RespiEvents; SensorMedics Corp) allows for the breath-by-breath calculation of the peak inspiratory flow to mean inspiratory flow ratio (PIFMF). The PIFMF value is 1.57 (\(\pi/2 \times \text{radius}\)) when the RIP-derived flow waveform is completely rounded, indicating normal pharyngeal resistance. As the flow waveform flattens, indicating increased pharyngeal resistance, the PIFMF value approaches 1.0. Figure 1 is a diagrammatic representation of these various waveforms and values. For each patient, PIFMF measurements were performed during quiet wakefulness and with 40 randomly selected breaths in the supine position for two conditions: stage 2 sleep, immediately prior to arousals.

**Statistical Analysis**

For supine, stage 2 sleep, portions of the study with \(> 3\) min of this condition were identified. Starting with the second consecutive 30-s epoch of this condition, a random number generator was used (with a range of 5 to 20) to count subsequent breaths and identify these for analysis. For supine breaths prior to an arousal, a random number generator was used to identify 30-s epochs. If the epoch contained an arousal, the breath prior to the arousal was analyzed.

Data are expressed as the mean (\(\pm SD\)) unless otherwise stated. The association of the change in PIFMF (wake-sleep) with the change in Pes for each condition was evaluated using Pearson’s correlation coefficient. Correlation coefficients between the PIFMF (wake-sleep) and Pes were performed using the mean of the Pes nadirs for all 40 breaths for each patient.
under both conditions. The change in PIFMF (wake-sleep) was compared between the UARS and non-UARS groups using the Wilcoxon rank sum test. Receiver operating characteristic analysis was used to determine the sensitivity and specificity at different values for the change in PIFMF (wake-sleep). Statistical significance was accepted for $p \leq 0.05$.

**Results**

**Polysomnographic Characteristics of Patient Groups**

Standard NPSG was diagnostic for OSA in 50 of the 64 patients. The median AHI of the OSA group was 24 (range, 14 to 51). The 14 non-OSA patients had a median AHI of 3 (range, 0 to 6). These 14 patients received a second NPSG with Pes measurement and RIP. Nine of the 14 non-OSA patients met the diagnostic criteria for UARS. Figure 2 illustrates the distribution of the Pes nadir (most negative pressure for the entire study) for the UARS vs non-UARS patients (respective means, $-32 \pm 12$ cm H$_2$O vs $-6 \pm 3$ cm H$_2$O). Figure 3 illustrates the distribution of UARS indexes for the UARS vs non-UARS patients (respective means, $31 \pm 9$ events per hour vs $2 \pm 2$ events per hour). The five non-UARS patients exhibited the least negative Pes nadirs and the lowest UARS indexes, with no evidence of overlap with the UARS patients. The total arousal index was increased in the UARS compared with the non-UARS group ($23 \pm 8$ events per hour vs $12 \pm 5$ events per hour; $p = 0.03$). Sleep stage distributions for the UARS group and non-UARS group are compared in Table 1. The UARS and non-UARS groups were similar with respect to the

**Table 1—Comparison of Demographics for the UARS and Non-UARS Groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age, yr</th>
<th>BMI, kg/m$^2$</th>
<th>Epworth Sleepiness Scale Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>UARS</td>
<td>38 ± 6</td>
<td>27.3 ± 1.7</td>
<td>14 ± 4</td>
</tr>
<tr>
<td>Non-UARS</td>
<td>35 ± 10</td>
<td>27.1 ± 3.1</td>
<td>11 ± 3</td>
</tr>
</tbody>
</table>

*Values expressed as mean ± SD. p Values were not significant for comparisons between groups.
duration of the various sleep stages with the exception of stage 3 or 4 sleep, which was decreased in the UARS group.

Demographic Characteristics of Patient Groups

Table 2 demonstrates that the mean age, BMI, and Epworth Sleepiness Scale scores were similar for the UARS and non-UARS groups. The age and BMI were typical for UARS patients, as these patients tend to be younger and less obese than OSA patients. The Epworth Sleepiness Scale scores suggest both groups perceived excessive daytime sleepiness, as scores in this range are typical for patients with untreated sleep disorders.

Evaluation of RIP for Diagnosis of UARS

The correlations of PIFMF (wake-sleep) and Pes were significant for the combined UARS and non-UARS patient groups during stage 2 sleep \( (r = -0.70, p = 0.035) \) and for breaths occurring immediately prior to arousals \( (r = -0.82, p = 0.016) \). These correlations were performed using the mean of the Pes nadir for all 40 selected breaths for each individual patient under both conditions.

For stage 2 sleep, there was no significant difference between the PIFMF (wake-sleep) for the UARS and non-UARS groups \( (0.161 \pm 0.122 \text{ vs } 0.099 \pm 0.022; p = 0.36) \). For breaths occurring immediately prior to arousals, the PIFMF (wake-sleep) was increased for the UARS group compared with the non-UARS group \( (0.228 \pm 0.098 \text{ vs } 0.099 \pm 0.022; p = 0.001) \). The evaluation of PIFMF (wake-sleep) to detect changes in Pes for either stage 3 or 4 sleep was precluded by the short duration \( (< 5 \text{ min}) \) of these sleep stages in four of the nine UARS patients. Breaths in stage REM sleep were not evaluated because it was expected that tidal breathing would vary appreciably from breath to breath, resulting in decreased utility to distinguish the patient groups.

The sensitivity and specificity of RIP to distinguish UARS from non-UARS patients using the PIFMF (wake-sleep) for stage 2 sleep is presented in Figure 4. The greatest diagnostic accuracy for stage 2 sleep occurs at a cutoff of 0.1 PIFMF (wake-sleep) with a sensitivity of 67% and specificity of 80%. For breaths occurring immediately prior to arousals, PIFMF (wake-sleep) had a greater diagnostic accuracy, with a sensitivity and specificity of 100%. All UARS patients demonstrated a PIFMF (wake-sleep) \( \geq 0.13 \) for breaths occurring immediately prior to arousals and all the non-UARS patients demonstrated a PIFMF (wake-sleep) \( < 0.13 \).

Discussion

This study demonstrates that RIP can accurately distinguish UARS from non-UARS patients using the analysis of PIFMF (wake-sleep). However, the most accurate application of this technique requires analysis of breaths prior to an arousal in the supine position. This application requires that the RIP signal be integrated with EEG signals. It is logical that the PIFMF (wake-sleep) is most useful prior to arousals in UARS patients, because these arousals are typically preceded by RERAs. RERAs are characterized by a crescendo pattern in intrathoracic pressure with a nadir occurring for the breaths immediately preceding an arousal or microarousal. The nadir in intrathoracic pressure is a consequence of increased upper airway resistance, which accentuates the asynchrony between the chest and abdominal components of RIP and results in a RIP-derived flow waveform that suggests flow limitation. Only breaths occurring prior to an arousal, rather than prior to a microarousal, were analyzed because of the potential difficulty in the reproducibility between individual scorers in the detection of microarousals.

Table 2—Percentages of Total Time in Bed for the Various Sleep Stages and Wakefulness in the UARS Group Compared With the Non-UARS Group

<table>
<thead>
<tr>
<th></th>
<th>Wake</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3–4</th>
<th>Stage REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>UARS</td>
<td>8 ± 5</td>
<td>10 ± 6</td>
<td>56 ± 12</td>
<td>8 ± 5†</td>
<td>18 ± 7†</td>
</tr>
<tr>
<td>Non-UARS</td>
<td>5 ± 3</td>
<td>7 ± 3</td>
<td>50 ± 10</td>
<td>17 ± 5†</td>
<td>22 ± 8†</td>
</tr>
</tbody>
</table>

*Values expressed as mean ± SD. REM = rapid eye movement. †p = 0.039.
Whyte et al\textsuperscript{18} demonstrated that there is difficulty in maintaining the calibration of RIP when it is used as a measure of tidal volume over the course of a night of sleep in normal subjects. The current study did not seek to reproduce these findings in UARS patients, hence a pneumotachometer was not used to calibrate the RIP or to document initial wake concordance between specific RIP-derived measures and tidal volume. Berg et al\textsuperscript{19} found that RIP, nasal pressure transduction, and the widely used oronasal thermistor are not adequate in comparison to the direct measurement of minute ventilation when these are utilized to detect hypopneas. However, the current study was designed to determine if a RIP-derived measurement can distinguish UARS from non-UARS patients, although the moderate degree of correlation between individual Pes measurements and PIFMF (wake-sleep) for breaths selected from stage 2 sleep are consistent with prior studies.

Hosselet et al\textsuperscript{20} recently demonstrated in a study of 14 patients that the semiquantitative analysis of nasal pressure waveform contour allowed for nine OSA patients to be distinguished from five non-OSA patients. Nasal pressure waveform contours were qualitatively graded as normal, intermediate, or flattened (flow limited). This study included only one patient who may have had UARS, but Pes was not monitored. The current study uses PIFMF to quantify the degree of waveform contour flattening, although the requirement to select breaths prior to an arousal to obtain optimal accuracy suggests RIP is also a semiquantitative method for identifying the increases in upper airway resistance that occur in UARS patients.

In conclusion, measurement of PIFMF (wake-sleep) for breaths randomly selected immediately prior to an arousal in the supine position allowed for the accurate identification of UARS patients from non-UARS patients. Randomly selected breaths from stage 2 sleep were not as accurate for the identification of UARS patients. Integration of RIP with standard NPSG should allow for the diagnosis of UARS without measurement of Pes.

REFERENCES

7 Chervin RD, Aldrich MS. Effects of esophageal pressure monitoring on sleep architecture. Am J Respir Crit Care Med 1997; 156:881–885