METHODS

Polysomnography

Overnight polysomnography (PSG) was conducted according to the American Academy of Sleep Medicine recommendations and included monitoring of: electroencephalogram (C4-M1, F4-M1 and O2-M1); left and right electrooculograms; submental and tibial electromyograms; electrocardiogram; abdominal and thoracic motion; nasal and oral airflow; nasal pressure; oxygen saturation; body position; and sound. These data were collected on a computerized data acquisition system (Grass Aurora polysomnography systems; Grass Telefactor, West Warwick, RI).

Categorization of sleep stage and respiratory events were performed according to standard criteria.¹ The severity of sleep-disordered breathing was defined by the apnea-hypopnea index (AHI), which is defined as the number of apneas and hypopneas per hour of sleep. An apnea was defined as a reduction in the thermal sensor of 90% lasting >10 s and a hypopnea was defined as a reduction in the nasal pressure signal of 30% or more lasting >10 s and associated with a 4% oxygen desaturation.¹ Total sleep time (TST), sleep efficiency (SE), wake time after sleep onset (WASO), sleep onset latency (SOL), arousal index (ArI, number of arousals per hour of sleep), and proportion of stages N1, N2, N3, and R were also recorded.

The PSG was used to divide the study time into the sleep period and the wake period. Sleep period was defined as the time between sleep onset (first epoch of sleep) and waking in the morning (last epoch of sleep). The wake period incorporates the remainder of the 24-h period.
**Esophageal pH/Impedance Monitoring**

Esophageal pH/impedance monitoring was performed using a pH/impedance catheter (O.D. 2.3 mm, Comfortec Z/pH catheters, Sandhill Scientific, Highlands Ranch, CO) with one pH electrode and 6 impedance sensors spaced 2 cm apart. The catheter was inserted into the esophagus via the nares and positioned so that the pH electrode was 5 cm above the lower esophageal sphincter (LES), the position of which had been determined previously from esophageal manometry. The impedance sensors were 3, 5, 7, 9, 15 and 17 cm above the LES. Prior to insertion the pH electrodes were calibrated against solutions of pH 4 and 7. The catheter was connected to an ambulatory reflux monitor (ZepHr, Sandhill Scientific, Highlands Ranch, CO). The pH signal was also outputted into the PSG system to facilitate synchronization with the sleep parameters.

Liquid reflux episodes were defined as a 50% drop in <2 seconds from the pre-episode mean impedance. In addition, there must have been retrograde bolus movement in the distal two impedance channels. The pH channel was used to classify episodes as acid or non-acid. A pH drop to <4 indicated an acid reflux episode, whereas retrograde bolus movement with either no pH drop or a drop to >4 was defined as a non-acid event. Acid clearance was achieved when the pH returned to >4 for ≥5 seconds. An event was considered proximal if it migrated to >15 cm above the LES.

Reflux parameters were defined as follows:

- **Acid clearance time (pH only).** Proportion of the recording time where the pH was <4 (regardless of whether liquid was detected in the impedance sensors).

- **Longest event.** Length of longest reflux event (with liquid presence indicated by the impedance sensors).
**Acid time (%).** Proportion of recording time where there was liquid presence determined by the impedance sensors and the pH <4.

**Non-acid time (%).** Proportion of recording time where there was liquid presence determined by the impedance sensors and the pH >4.

**Number of reflux events.** Number of acid and non-acid events in the distal (5 cm above the LES) and proximal (>15 cm above the LES).

**Esophageal Motility Testing**

Motility studies were conducted using a solid state high resolution manometry impedance catheter (O.D 4.0 mm) (Sandhill Scientific InSIGHT, Highlands Ranch, CO, USA). The catheter was composed of 6 impedance sensors for detection of bolus movement and 32 solid state pressure sensors (spaced 1 cm apart) to allow measurement of pressure from the pharynx to the stomach. The catheter was calibrated between 0-100 mm Hg outside of the patient prior to each study. Thermal compensation was applied to the recording at the conclusion of the study.

An electronic sleeve was applied on the LES to measure pressure within this zone, enabling accurate monitoring of the high pressure within the LES while accounting for sphincter movement during respiration and swallowing. Using the electronic sleeve, the software displays the highest instantaneous pressure reading from any of the pressure sensors located in the defined zone (comprised of 5 individual sensors spaced at 1-cm intervals) on a single channel.²

The mucosa of the nasal passage and throat were anesthetized using 4% lidocaine spray and the catheter inserted transnasally. The catheter was positioned so that initially all pressure sensors
were located in the stomach. Once a gastric baseline had been recorded, the catheter was withdrawn so that the pressure was recorded along the entire esophagus, stomach and pharynx.

Patients were placed on their right hand side and given 10 min to acclimatize to the catheter. A 30-s period of stable recording (with no swallowing) was obtained to measure basal LES pressure. Patients were then given a 5-mL bolus of saline (room temperature). In total we recorded 10 of these saline swallows, separated by a 30-s period devoid of swallowing or other artifact. Patients were then given 10 x 5 mL viscous swallows (Viscous solution, Sandhill Scientific InSIGHT, Highlands Ranch, CO, USA) in a similar manner.

Motility parameters were defined as follows:

**Basal LES pressure.** Basal end-expiratory LES pressure was measured over a stable 30-s recording (i.e., no swallowing or other pressure artefact present), prior to the swallow study. LES pressure was referenced to intragastric pressure as is convention. The LES was defined as hypotonic if the baseline LES pressure was <10 mm Hg (13.7 cm H2O).3

**LES length.** Total length of the LES was measured as well as the length of the LES which was intra-abdominal (i.e., below the diaphragm).

**Swallow-induced LES relaxation.** This was characterized by the nadir LES pressure and the duration of LES relaxation. Nadir LES pressure was defined as the minimum pressure recorded during the relaxation referenced to intragastric pressure. The duration of each relaxation was defined as the time the where LES pressure starts to drop below baseline to where it rises to or above the resting pressure.
**Esophageal peristalsis.** Peristaltic wave amplitude (peak pressure referenced to esophageal baseline) was measured in the proximal, mid and distal esophagus using sensors approximately 3, 8, 13, 17 cm above upper border of LES.

Peristaltic wave velocity was determined from pressure sensors approximately 3 and 8 cm above the upper border of the LES from the major upstroke in the pressure wave.

**Bolus transit.** Complete bolus transit was defined as the proportion of boluses that were successfully cleared from the esophagus.

**Questionnaires**

The Pittsburgh Sleep Quality Index has been shown to be a valid and reliable index of degree of sleep disturbance.\(^4\) Scores >5 are generally considered to indicate disturbed sleep.

The Carlsson Gastroesophageal Reflux Disease (GERD) questionnaire is a 7-item measure of symptoms consistent with GERD.\(^5\)

The Epworth Sleepiness Scale is (ESS) is a widely used, reliable and valid measure of daytime sleepiness.\(^6\) A score ≥10 is considered indicative of excessive daytime sleepiness.

The Gastroesophageal Reflux Questionnaire (GERQ)\(^7,8\) was used to assess the frequency and severity of symptoms associated with GER. GER symptoms were classified as follows: heartburn or acid regurgitation experienced at least once in the last 12 months was defined as “any GER” and, if experienced at least once a week, was defined as “frequent GER.” The term “GER symptoms” refers to symptoms experienced at any time during the day or night while “nighttime GER (nGER) symptoms” specifically refers to symptoms which woke the patient from sleep.
RESULTS

Univariate Associations between AHI, BMI, and GER

During the 24-h recording period, significant univariate associations were evident between BMI and reflux time (%) and number of distal reflux events. There were no associations between AHI and any reflux variable (Table S1).

During the wake period, there was a significant association between BMI and number of distal reflux events. There were no associations between AHI and any reflux variable (Table S1).

There were no significant univariate associations between AHI or BMI and any reflux variable during the sleep period (Table S1).

Multivariate Associations between AHI, BMI, and GER

Age, gender, BMI, and AHI were entered into multivariate analyses. During the 24-h recording period, BMI was the only significant predictor of the number of distal events ($r^2=0.16$, $p=0.01$).

Likewise, during the wake period BMI was the only significant predictor of the number of distal events ($r^2=0.14$, $p=0.01$). These variables were not able to significantly predict acid clearance time, longest event, reflux time, or number of proximal reflux events.

Age, gender, BMI, and AHI were not able to predict any reflux variable during the sleep period.
REFERENCES


Table S1. Univariate linear regression analyses between OSA, BMI, and GER

<table>
<thead>
<tr>
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<th>AHI</th>
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<th>BMI</th>
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<tr>
<td></td>
<td>Wake</td>
<td>Sleep</td>
<td>24-h</td>
<td>Wake</td>
<td>Sleep</td>
<td>24-h</td>
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<td>Acid Clearance time (based on pH only)</td>
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<td>0.01</td>
<td>0.01</td>
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<td>0.03</td>
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<td>Longest event</td>
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<td>0</td>
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<td>Reflux time (acid time + non-acid time)</td>
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<td>0.01</td>
<td>0.02</td>
<td>0.06</td>
<td>0.06</td>
<td>0.1*</td>
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<tr>
<td>Number distal events (acid + non-acid)</td>
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<td>0.01</td>
<td>0.03</td>
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<td>0.16*</td>
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<td>Number proximal events (acid + non-acid)</td>
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<td>0</td>
<td>0</td>
<td>0.05</td>
</tr>
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</table>

R² values derived from univariate linear regression analysis between reflux variables and BMI or AHI. Data includes all individuals (n=45). Acid and non-acid reflux combined. Distal: 5 cm above the LES; Proximal: 15 cm above the LES. AHI (apnea hypopnea index); BMI (body mass index). * p < 0.05 for linear regression analysis.