Original Article

Supraesophageal Reflux: Correlation of Position and Occurrence of Acid Reflux; Effect of Head-of-Bed Elevation on Supine Reflux

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What is already known about this topic? Supraesophageal reflux disease (SERD) is associated with a variety of respiratory symptoms. Historically, SERD is thought to occur predominantly while upright and existing treatment regimens have been poorly defined and often ineffective.

What does this article add to our knowledge? This study suggests that supraesophageal reflux often occurs exclusively in the supine position. Our findings also show that elevation of the head of bed results in improvement or resolution of supine SERD in most patients.

How does this study impact current management guidelines? When suspected, SERD is often treated with empiric antisecretory agents. However, these are frequently ineffective. Our findings suggest that incorporation of head-of-bed elevation is important in SERD treatment programs.

BACKGROUND: Supraesophageal reflux of gastric contents can contribute to perennial nasopharyngitis, cough, and asthma. However, effective treatment strategies for supraesophageal reflux disease (SERD) remain inadequately defined.

OBJECTIVE: The purpose of this study is to assess the prevalence and timing of SERD and to investigate the efficacy of head-of-bed elevation in its treatment.

METHODS: A retrospective chart review of patients seen at Scripps Clinic Division of Allergy, Asthma and Immunology was performed who had undergone overnight nasopharyngeal pH monitoring with a commercially available nasopharyngeal pH-monitoring device, Dx-pH Measurement System from Restech, San Diego, Calif. Subjects with reflux were classified based on the position of reflux as either supine only, upright only, or both supine and upright. In a subset of subjects with supine-only reflux, pH monitoring was compared before and after elevating the head of bed 6 inches.

RESULTS: Adequate nasopharyngeal pH-monitoring data were obtained for 235 patients. Reflux was detected in 113 (48%) patients. The pattern of reflux observed was 62 (55%) supine only, 4 (4%) upright only, and 47 (42%) upright and supine. Sequential overnight nasopharyngeal pH monitoring before and after head-of-bed elevation was obtained in 13 individuals with supine-only reflux. Ten subjects demonstrated significant improvement, 8 of whom demonstrated complete resolution of supine reflux with 6 inches of head-of-bed elevation.

CONCLUSION: This study provides new evidence that SERD frequently occurs in the supine position and that 6 inches of head-of-bed elevation is effective in reducing supine SERD.   © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;■:■-■)

BACKGROUND

Supraesophageal reflux disease (SERD) is defined as the retrograde flow of gastric contents proximal to the upper esophageal sphincter (UES) and into the laryngopharynx and upper aerodigestive tract.[1] There exists a clear association between SERD and respiratory symptoms, including throat clearing, cough, asthma, postnasal drainage (PND), sinusitis, laryngopharyngitis, and sleep disturbance.[2-5] Many of these are frequent complaints among patients who seek consultation from an allergist. In one study, over half of patients presenting with throat clearing, PND, or excessive throat mucus and normal sinus imaging were found to have SERD by 24-hour pH monitoring.[6] Comparatively, SERD has been documented in 10% of asymptomatic healthy controls.[7,8]

The diagnosis of SERD is made based on clinical suspicion and confirmed with either documentation of acidic reflux with an overnight nasopharyngeal or laryngeal pH monitor or response to empiric treatment with a proton-pump inhibitor (PPI). Most patients with SERD are unaware of their reflux and seldom report classic gastroesophageal reflux disease (GERD)

Abbreviations used
GERD- Gastroesophageal reflux disease
PND- Postnasal drainage
PPI- Proton-pump inhibitor
RSI- Reflux symptom index
SER- Supraesophageal reflux
SERD- Supraesophageal reflux disease
UES- Upper esophageal sphincter

TABLE I. Patterns and prevalence of supraesophageal reflux disease among an allergy clinic population as measured by overnight nasopharyngeal pH monitoring (N = 235)

No acidic reflux measured	122 (52%)
Acidic reflux measured	113 (48%)
Supine reflux only	62 (55%)
Upright reflux only	4 (4%)
Upright and supine reflux	47 (42%)

symptoms.[9] Therefore, SERD is considered a form of "silent reflux" and may be difficult to diagnose clinically.[10]

Supraesophageal reflux (SER) has been described primarily among an ENT patient population, where studies have shown it to be characterized by a different pattern of occurrence than that of classic GERD. In particular, SERD in that population has been described as occurring primarily during brief intervals in the upright position, as opposed to GERD, which is classically associated with prolonged acid exposure in the supine position.[11,12]

When SERD is suspected, patients are often treated with empiric antisecretory agents.[2] Although there is some evidence that prolonged twice-daily PPIs decrease the severity of throat-based symptoms in patients with SERD, the efficacy of this approach has not been consistently demonstrated between studies.[6,13,14] The observed lack of efficacy of PPI for SERD is thought to be due to the fact that acid-suppressing medications do not prevent inflammatory, nonacidic reflux from reaching the supraesophageal mucosa.[1,15-19] For patients with symptomatic refractory SERD, antireflux surgery may be performed, but is associated with increased risk.[20]

It has been postulated that lifestyle modification may be a preferable approach to the treatment of SERD.[21] Although lifestyle interventions have been well studied in GERD, no clinical trials exist that assess this approach in the treatment of SERD. Among the most efficacious lifestyle interventions in GERD is head-of-bed elevation.[22] This is an intuitively attractive treatment modality for SERD given the role of difficult-to-treat nonacidic reflux, which could potentially be prevented by head-of-bed elevation. The purpose of this retrospective chart review is to assess the prevalence and timing of SERD among an allergy clinic referral population and to investigate the efficacy of head-of-bed elevation in preventing SERD as measured by an overnight nasopharyngeal pH monitor.

METHODS
Study design

After obtaining permission from the Scripps institutional review board, the authors performed a chart review of all patients seen at Scripps Clinic Division of Allergy, Asthma and Immunology, San Diego, between January 2010 and November 2012 who had undergone nasopharyngeal pH monitoring as part of their routine clinical evaluation. Patients were not included if they took acid-suppressing medication during the study period. Any incomplete pH studies and the first and last 5 minutes of all studies were also excluded, as data recorded at the time of probe placement and removal appeared prone to inaccuracy.

The decision of whether to perform overnight pH monitoring was based on individual practitioner judgment and patient preference as guided by the presence or absence of typical signs and symptoms of SERD, including evidence of SERD on nasopharyngoscopy, perceived PND, throat-clearing cough, hoarseness, or rhinitis or sinusitis without another explanation. Most referred patients either had no prior suspicion for SERD (ie, had "silent reflux") or had a history of more typical reflux symptoms that had previously been refractory to PPI. Patients with silent reflux were often too skeptical of an SERD diagnosis to agree to empiric PPI treatment before demonstrating reflux by pH monitoring. For patients with more typical reflux symptoms who previously failed PPI, pH monitoring was essential to differentiate nonacidic SERD versus an unrelated etiology for their symptoms. Specifically, in these patients, the detection of acidic reflux off of antacid served as a surrogate marker to predict nonacidic reflux while taking antacid. Therefore, although all patients were able to choose whether to pursue empiric treatment or pH monitoring, most patients in our study population opted for monitoring. Other common approaches to suspected SERD in our clinic include empiric acid-suppressing medication, lifestyle modification, and referral to ENT or gastroenterology. Patients in whom pH monitoring was not performed were not included in our analysis.

Subjects with reflux were classified based on the timing of the reflux pattern as either supine only, upright only, or both supine and upright. Although initially the goal of the study was limited to assessing the prevalence and pattern of nasopharyngeal reflux, we began to notice that most patients exhibited reflux only in the supine position. This led us to question whether elevating the head of bed might benefit those with supine-only reflux. We therefore began inviting subjects with documented solely supine SERD to return for sequential pH monitoring before and after elevating the head of bed by 6 inches. In this group, the authors performed a descriptive analysis of observed pH data to assess the effectiveness of head-of-bed elevation as a treatment for SERD.

Head-of-bed elevation was defined as sleeping in a conventional bed with either one end raised approximately 6 inches or with a 6-inch wedge pillow. Suggested tools for elevating the head of bed included 4 two-by-fours (1.5″ height each), 2 bricks (2.25″ height each), or a cinder block turned on its side (6″ height). Alternatively, 1-inch stackable bed risers can be purchased in department stores or online that can be stacked to 6 inches. Subjects were specifically asked not to use standard pillows to prop up their head due to the unreliable nature of this technique once asleep. Also using standard pillows can lead to kinking of the thorax and abdomen and thereby potentially worsen reflux. Patients were also specifically asked not to make any other lifestyle change on the night of the repeat study.

Subject inclusion

Included were all patients 18 years of age or older who underwent pH monitoring during the specified time interval. Subjects were asked to hold all antisecretory medications (PPIs and histamine-2
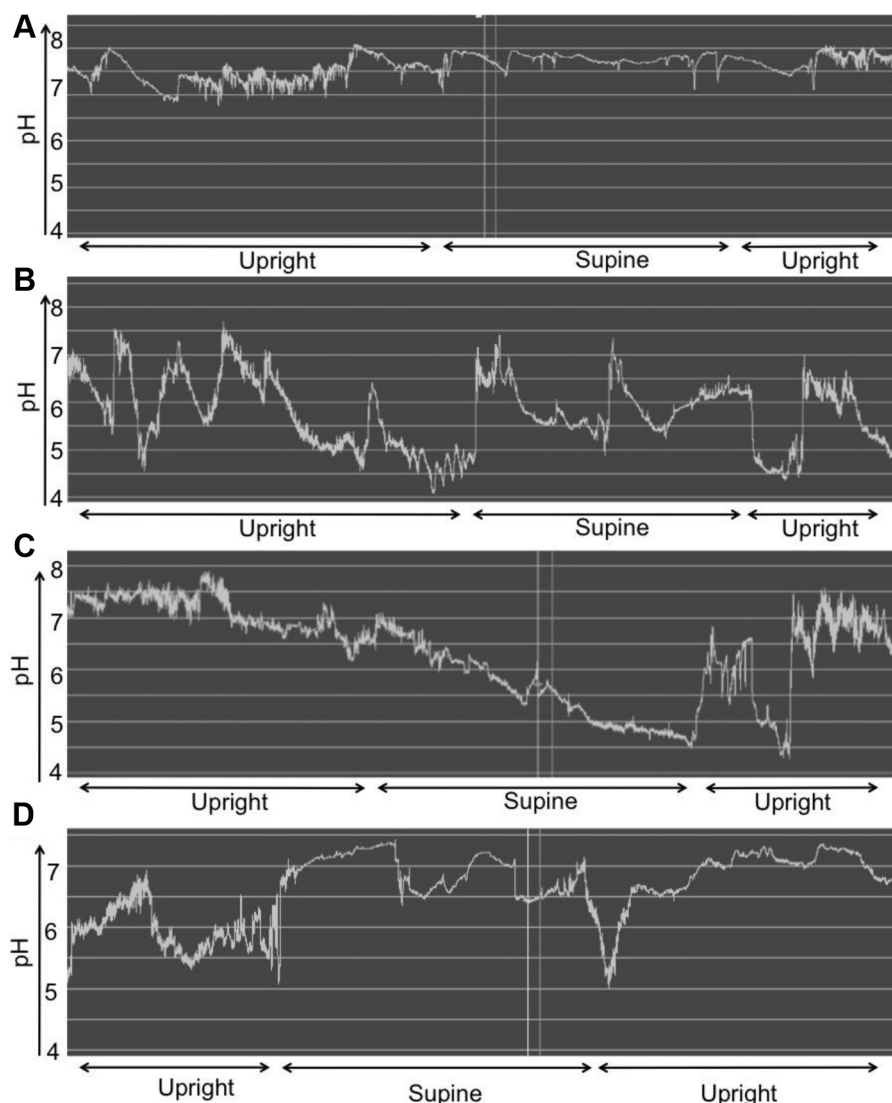
FIGURE 1. Representative patterns of supraesophageal reflux recorded by overnight nasopharyngeal pH monitoring: no reflux (A), reflux in supine and upright positions (B), reflux limited to only the supine position (C), and reflux limited to the upright position (D).

receptor antagonists) 72 hours before all pH monitoring and to withhold buffering agents during the time of data collection.

Data measurement

For all pH measurements, the authors used a commercially available nasopharyngeal pH-monitoring device, Dx-pH Measurement System from Restech, San Diego, Calif.

Criteria for a positive study

For our study, we defined a positive study as one or more drops in pH below a threshold of less than 5, or 2 pH units below baseline, lasting at least 30 minutes. Following head-of-bed elevation, partial resolution was defined as a decrease in time below the established threshold pH to less than a 30-minute total duration. Complete resolution was defined as no drops in pH below the established threshold.

Statistical analysis

The effect of head-of-bed elevation on reflux was assessed by comparing proportions of subjects with and without reflux via χ^2. We used an online statistical package from Social Science Statistics (http://www.socscistatistics.com/). A P value of less than $<.05$ was considered to be statistically significant.

RESULTS
Nasopharyngeal pH monitoring

Nasopharyngeal pH monitoring was performed in 247 patients, 235 of whom generated sufficient data to accurately characterize the pattern of reflux. All patients studied presented with a chief complaint of either throat-clearing cough, postnasal drip, or globus sensation. Significant nasopharyngeal reflux was present in 113 (48%) of these patients (Table I). Of the patients with evidence of reflux, 62 (55%) exhibited reflux while only in the supine position, 47 (42%) in both the upright and supine

TABLE II. The number of reflux events and mean reflux duration among subjects with supine-only reflux and a subset of supine-only reflux subjects who returned for the repeat study with head-of-bed elevation were not significantly different

	n	Mean no. of events	Mean reflux duration (min)
All supine-only reflux patients	162	1.3	157
Subpopulation undergoing the repeat study	13	1.6	144

TABLE III. Effect of head-of-bed elevation on supraesophageal reflux disease among patients with supine-only reflux (n = 13)

No improvement	3 (23%)
Partial resolution	10 (77%)
Complete resolution	8 (62%)

position, and 4 (4%) in the upright position only. Representative overnight nasopharyngeal pH plots for each pattern of reflux are displayed in Figure 1.

Head-of-bed elevation

Among the 62 patients with supine-only nasopharyngeal reflux, 13 returned for comparative overnight nasopharyngeal pH monitoring after head-of-bed elevation. Of the 13 patients, 12 used blocks to elevate the head of the bed and 1 used a wedge pillow. These 13 subjects demonstrated a similar total duration of reflux and number of reflux episodes to the other 49 subjects with supine-only reflux (Table II). Following 6 inches of head-of-bed elevation, 10 of 13 subjects (77%) demonstrated some improvement (P value <.05) and 8 of 13 (62%) demonstrated complete resolution (P value <.05) of supine reflux (Table III). Representative overnight nasopharyngeal pH plots before and after head-of-bed elevation are displayed in Figure 2.

DISCUSSION

This study suggests that when suspected by a clinician, SERD is common among an allergy referral population. We observed that most patients with measurable SERD demonstrated a supine-only pattern of reflux. This is an unexpected finding, given that the most existing literature describes SERD as typically occurring in the upright position.[11,12]

There are several possible reasons for the discrepancy in the observed pattern of SER between our study and previous studies. Initial studies investigating the pattern of SER were performed among ENT patients, the majority of whom suffered from more advanced laryngeal disease such as in situ carcinoma, subglottic stenosis, or granulation.[11] More importantly, recent advances in pH-monitoring techniques have enabled detection of aerosolized acid, which appears to allow for more accurate pH measurements in the nasopharynx.[23] Utilizing this newer technology, Beaver et al also described similar findings among 95 subjects with documented SER, 60% occurring primarily in the supine position.[24]

This study also reveals that SERD, as measured by a pharyngeal pH monitor, can be corrected in the majority of patients by elevating the head of bed by 6 inches. This finding has important clinical implications due to the limited utility of acid-suppressing medications in treating SERD as well as recent increased concern regarding the safety of long-term PPI use.[19,25] For instance, Patterson et al investigated treatment of 82 patients with pH-confirmed diagnosis of SERD who underwent an 8-week trial of twice-daily omeprazole 20 mg that revealed failure to respond in over half of subjects (55.1%).[25] In a randomized placebo-controlled trial of PPI for suspected SERD, Vaezi et al found no significant improvement with PPI treatment.[26] When

effective, treatment with head-of-bed elevation would have the additional advantage of eliminating both acidic and nonacidic reflux, which potentially makes it superior to treatment with PPI. This is in contrast to the treatment of GERD, for which nonacidic reflux is not as prominent a concern due to more robust defense mechanisms of the esophageal mucosa.[27]

The pathophysiology of upper airway symptoms secondary to SERD is not well defined. Likely contributing mechanisms include local inflammatory effects from direct contact with acidic gastric contents, proteolytic damage from pepsin, as well as neural-mediated mucus production from reflux at the level of the esophagus.[17,28] It has been demonstrated that the mucosa of the upper airway is more sensitive to an acidic environment than is the esophagus, and so small amounts of mildly acidic refluxate may be enough to result in inflammation.[1,15] It has also been shown that nonacidic reflux is a contributor to reflux symptoms, which has implications for the use of acid-suppressing medications as treatment for SERD.[16,19] In particular, even among patients with pH documented SERD, response to aggressive acid suppression is around 50% at 2 months.[29]

Nonacidic reflux contains several potentially harmful constituents, including bile, pancreatic enzymes, and pepsin.[18] Pepsin, in particular, likely plays a central role in SERD pathophysiology by binding the upper airway mucosa where it may induce mucosal injury.[15] Although optimally active at the stomach's native pH of 1.6-2.0, pepsin maintains proteolytic capacity at pH levels up to 6.5-6.9.[1,18] Once deposited in the oropharynx, reflux events that decrease local pH to less than 6 may reactivate pepsin's intrinsic proteolytic activity.[18] Pepsin also appears to contribute to tooth decay seen in SERD by degrading protective dental pellicle.[17] The effects of these gastric constituents explain the observation that nonacidic reflux may cause SERD-related symptoms.[16,20] Although pH measurements are unable to detect nonacidic reflux directly, the presence of acidic reflux off of acid-suppressing medication is suggestive of an incompetent UES and likely predictive of nonacidic reflux while taking an antacid. This would explain the often seen failure of acid suppression alone in the treatment of this condition.

The defining pH threshold for diagnosing SERD is not well established. For our study, the threshold for reflux at the level of the nasopharynx was defined as a pH below 5, or 2 pH units below baseline, lasting at least 30 minutes. This criterion is within the generally accepted range for defining SERD, but less stringent than the traditional cutoff used in defining esophageal reflux. The pH cutoff classically used for measuring reflux in the esophagus for the diagnosis of GERD is 4. There is growing evidence that even minimal pH drops in the nasopharynx are likely pathologic. Johnston et al demonstrated that pH well above the cutoff of 4 used in GERD induces cellular injury to the laryngeal mucosa.[15] Wiener et al demonstrated that a pH gradient exists between the distal esophagus and the oropharynx in patients with SERD.[30] They found that a median pH of 4 in the distal esophagus correlates with a median oropharyngeal pH of 5.6. Other authors have also suggested a threshold at the level
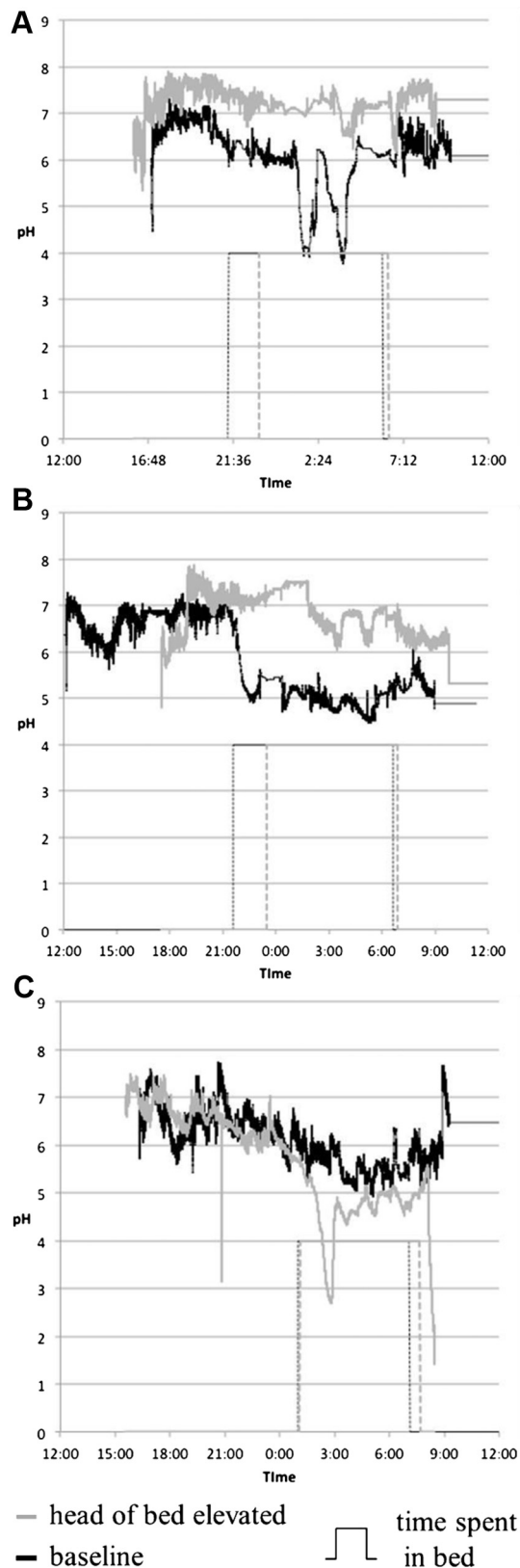
FIGURE 2. Representative nasopharyngeal pH plots before and after head-of-bed elevation in subjects with supine-only supra-esophageal reflux demonstrating resolution (**A**), improvement (**B**), and no change (**C**) in reflux with elevation of the head of bed.

of the pharynx in the range of 5-5.5[23,31] or a 10% drop from baseline.[30] In a recent study using the same pH probe as this study, a nasopharyngeal pH cutoff of 6 correlated with symptoms of SERD.[32]

Most clinicians do not have a means of directly measuring overnight pharyngeal pH and so, in practice, must decide whether to treat empirically with antacids, suggest head-of-bed elevation, or do both. On the basis of our findings that 48% of patients with suspected SERD had confirmatory pharyngeal pH monitoring and 55% of those with positive studies had supine-only reflux, one can predict that approximately 26% of patients referred to an allergy clinic with suspected SERD will have supine-only reflux. Among this population, we found that patients experienced improvement or total resolution of reflux in 77% and 62% of cases, respectively. This translates to a number needed to treat for improvement and resolution of reflux among all patients with suspected SERD of 5.0 and 6.1, respectively. If supine-only reflux can be established with an overnight naso-pharyngeal pH monitor, then the number needed to treat for improvement and resolution of SERD decreases to 1.3 and 1.6, respectively. Knowing these parameters, the decision of whether to recommend empiric head-of-bed elevation can be made based on patient preference and accessibility of pharyngeal pH monitoring. Other factors, including adherence to head-of-bed elevation and other lifestyle changes pertinent to supine reflux and potential changes in patient sleep latency and positioning as a result of head-of-bed elevation, may impact the actual number needed to treat in practice. A prospective clinical trial is needed to assess the potential role of these factors.

Questionnaires have been used as an alternative to direct pH measurements in the diagnosis of SERD. Of these, the reflux symptom index (RSI) is the most commonly referenced in the literature.[33] The RSI was developed and validated by Belafsky et al in 2002 and includes 9 components (hoarseness, throat clearing, PND, swallowing difficulty, coughing when supine, choking, chronic cough, globus, and heartburn). Unfortunately, the RSI has demonstrated suboptimal performance in clinical practice and does not discriminate supine from upright reflux. In particular, Pawar investigated 47 patients and found no correlation between the RSI and SER by pH monitoring or any correlation between response to PPI and the baseline RSI.[6]

We observed greater effectiveness of head-of-bed elevation for the treatment of SERD than has been described for patients with GERD. Studies assessing head-of-bed elevation in GERD have consistently demonstrated a decreased overall latency of esophageal acid exposure, but have not consistently demonstrated a decrease in the number of reflux events.[22,34-36] The observed decrease in esophageal acid exposure in these studies appears to be largely due to improved acid clearance attributed to the effect of gravity.[35] On the basis of our findings, we postulate that the established decrease in latency of acid exposure in the distal esophagus with head-of-bed elevation hinders the ability of acidic liquid and vapor to reach the UES, which translates to fewer SER episodes.

This retrospective study has limitations, including lack of randomization, small group size, and lack of longitudinal follow-up. Challenges in interpreting the results of our study include the absence of a preexisting definition of a positive nasopharyngeal pH study, lack of a control group, and no established gold standard for diagnosing SERD. The precise cutoff for defining a positive nasopharyngeal pH study is unknown, and there is little data regarding nasopharyngeal pH measurements among healthy

individuals. On the basis of increasing evidence that nasopharyngeal pH levels in the range of 5-6 are pathologic, we believe that the cutoff of 5 we used is sufficiently conservative to predict pathologic reflux.

Additional limitations include that there was likely selection bias in favor of patients with nonacid reflux, as patients with symptomatic reflux and SERD responsive to PPI were likely treated by their primary care physicians. Therefore, most referred patients either had "silent reflux" or had a history of more typical reflux symptoms that had been previously treated with PPIs but the SERD symptoms persisted. Also, the primary endpoint considered in assessing the efficacy of head-of-bed elevation in our study was pharyngeal pH. It will be important to correlate these measurements with clinical symptoms in future studies, especially over the long term.

CONCLUSION

In our study, SER was frequently seen among an allergy referral population and, when present, it often occurred exclusively in the supine position. These findings are counter to previously published studies that characterized the timing of SERD as occurring more frequently in the upright position. Our findings also show that in cases of supine-only SERD, elevation of the head of bed resulted in improvement or resolution of SERD in most patients. This is the first study to assess the impact of behavioral modification on SERD, and these positive findings are highly relevant to its treatment. However, further research is needed to predict which patients are likely to suffer from supine-only SERD and who may benefit clinically from head-of-bed elevation.

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