Objectives: To determine the incidence of gastroesophageal reflux in patients with subglottic stenosis (SGS) and to determine if upper esophageal reflux occurs in addition to lower esophageal reflux in these patients.

Design: Esophageal pH probe studies were reviewed in patients diagnosed as having SGS.

Setting: A tertiary care pediatric medical center.

Patients: All patients diagnosed as having SGS between January 1990 and July 1996 who had undergone monitoring with an overnight esophageal pH probe. Seventy-four patients qualified for the study. All 74 patients underwent lower probe testing, and 55 of the 74 underwent dual (upper and lower) probe testing.

Main Outcome Measures: The percent of time a pH measurement of less than 4.0 was recorded in the upper and lower esophagus. A lower probe pH measurement of less than 4.0 more than 10% of the study time was considered high risk for developing reflux-associated pathologic symptoms. A lower probe pH measurement of less than 4.0 for 5% to 10% of the study time was considered a marginal risk for developing reflux-associated pathologic symptoms. Upper probe criteria for reflux-associated symptoms have not been established. Therefore, patients were grouped as having a pH of less than 4.0 in the upper esophagus for 0%, 0.1% to 0.9%, 1.0% to 1.9%, 2.0% to 3.0%, or more than 3% of the study time.

Results: Thirty-seven of the 74 patients who underwent lower probe testing had a pH of less than 4.0 more than 5% of the study time, and 24 had a pH of less than 4.0 more than 10% of the study time. Twelve of the 55 patients who underwent upper probe testing had no measurable reflux; 27 of the 55 had a pH of less than 4.0 more than 1% of the study time; 14 had a pH of less than 4.0 more than 2% of the study time, and 11 had a pH of less than 4.0 more than 3% of the study time.

Conclusions: Gastroesophageal reflux is frequently present in patients with SGS. Gastric contents frequently reach the upper and lower esophagus in these patients. In addition, the high incidence of gastroesophageal reflux in these patients suggests that it may play a role in the development of SGS. The possible effect of gastroesophageal reflux on the surgical repair of SGS requires further study.

PATIENTS AND METHODS

A list was reviewed of all patients evaluated for SGS at the Children’s Hospital Medical Center in Cincinnati, Ohio, between January 1990 and July 1996. Of the more than 300 patients evaluated, only those who had undergone pH probe testing at our institution were included in the study. Many patients had undergone GER evaluation at other institutions, and as a result, details of their pH studies were unavailable, and they were not included in the study. Seventy-four patients qualified for the study, and a retrospective chart review was performed for each.

The following information was recorded for each patient: sex, age at the time of testing, the presence of a tracheotomy tube at the time of testing, associated medical conditions and birth history, previous reflux surgery, grade of airway stenosis identified on endoscopy, and number of previous airway surgeries. Airway grading was recorded from the endoscopy performed closest to the date of pH probe testing and was based on the Myer/Cotton grading system (Figure)\textsuperscript{10}

All dual-probe monitoring was performed with a portable pH measuring unit (model Mk3 dual-channel Digitrapper, Synectics Medical). Single-probe studies were performed with a Mark II single-channel unit (Synectics Medical). Most dual-probe studies were performed in the latter half of the study (1993-1996). All electrodes were calibrated in buffer solutions with a pH of 7.0 and then in solutions with a pH of 1.0. The pH electrodes were inserted through the patient’s nose into the esophagus and placed such that the tip of the electrode was 2 to 3 cm above the gastroesophageal junction. When present, the upper probe was positioned within 1 to 2 cm of the upper margin of the esophagus. Ideally, the probe was placed below the upper esophageal sphincter in the esophageal inlet. One of 3 different-sized electrodes was used, depending on the age of the child. For patients from birth to 1 year of age, the proximal sensor of the probe was placed 5 cm above the distal sensor. For patients 1 to 3 years of age, the proximal sensor was placed 10 cm above the distal sensor. For patients 3 years of age and older, the proximal sensor was placed 15 cm above the distal sensor. All patients underwent fluoroscopy or chest radiography to confirm correct placement of the probe. A reference electrode was placed on the patient’s abdomen when required. Recordings were obtained for at least 18 hours.

All patients were instructed to pursue their normal activities. Patients had no meal restrictions, but the beginning and ending of feeding times were recorded. If patients were taking acid-inhibitory or prokinetic medications, those regimens were discontinued at least 24 hours prior to the study (except in one patient who was taking ranitidine hydrochloride [Zantac] during our study because pH probe testing at another institution had indicated severe reflux).

The pH probe results were recorded and distinguished based on upper and lower probe location and the percent of time with a pH measurement less than 4.0. This was calculated by adding the total time within 60 minutes with a pH of less than 4.0 following a meal to the total time for more than 60 minutes with a pH of less than 4.0 following a meal. This sum was then divided by the total time of the study and multiplied by 100 to derive the percent of time with a pH less than 4.0. This calculation was performed separately for upper and lower probe measurements.

Lower pH probe measurements of less than 4.0 were recorded as occurring more than 10% of the study time, 5% to 10% of the study time, or less than 5% of the study time. Upper pH probe results of less than 4.0 were recorded as occurring 0%, 0.1% to 0.9%, 1.0% to 1.9%, 2.0% to 3.0%, or more than 3% of the study time.

Kendall $\tau$ rank correlation analysis and nonparametric analysis of variance were performed on all variables mentioned.

RESULTS

Of the 74 patients who qualified for the study, 43 (58%) were male and 31 (42%) were female. The average age of the patients at the time of pH probe testing was 5 years (age range, 0.3-14.3 years). Fifty-five patients (74%) underwent dual (upper and lower) probe testing, and 19 (26%) underwent only lower probe testing.

Sixty (81%) of the 74 patients were dependent on a tracheotomy tube at the time of pH probe evaluation. Of the 44 concomitant medical conditions identified, the most common were prematurity and bronchopulmonary dysplasia:

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>48 (64.9)</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia</td>
<td>23 (31.1)</td>
</tr>
<tr>
<td>Gastrostomy tube</td>
<td>13 (17.6)</td>
</tr>
<tr>
<td>Tracheomalacia</td>
<td>11 (14.9)</td>
</tr>
<tr>
<td>History of Nissen fundoplication</td>
<td>11 (14.9)</td>
</tr>
<tr>
<td>Reactive airway disease</td>
<td>10 (13.5)</td>
</tr>
<tr>
<td>Patent ductus arteriosus ligation</td>
<td>10 (13.5)</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>7 (9.5)</td>
</tr>
<tr>
<td>Congenital SGS</td>
<td>6 (8.1)</td>
</tr>
<tr>
<td>Brain injury</td>
<td>6 (8.1)</td>
</tr>
</tbody>
</table>

Eleven patients (14.9%) had undergone Nissen fundoplication prior to our study, and 13 (17.6%) were dependent on a gastrostomy tube. Of the patients who had undergone endoscopy of the airway, 65 (88%) had been diagnosed as having grade II or III stenosis (Figure). Twenty-nine (39%) of the 74 patients had under-
gone previous airway reconstructive surgery, and 6 (21%) of those 29 had undergone previous airway reconstructive surgeries. The high number of previous airway surgeries reflects the referral pattern of our institution.

All 74 patients underwent lower pH probe testing. The results were as follows:

<table>
<thead>
<tr>
<th>% of Time pH &lt;4.0</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>37 (50.0)</td>
</tr>
<tr>
<td>5.0-10.0</td>
<td>13 (17.6)</td>
</tr>
<tr>
<td>&gt;10.0</td>
<td>24 (32.4)</td>
</tr>
</tbody>
</table>

Fifty-five patients underwent dual probe testing and thus had upper probe measurements. The results were as follows:

<table>
<thead>
<tr>
<th>% of Time pH &lt;4.0</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12 (21.8)</td>
</tr>
<tr>
<td>0.1-0.9</td>
<td>16 (29.1)</td>
</tr>
<tr>
<td>1.0-1.9</td>
<td>13 (23.6)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>3 (5.5)</td>
</tr>
<tr>
<td>&gt;3.0</td>
<td>11 (20.0)</td>
</tr>
</tbody>
</table>

There was no correlation between grade of airway stenosis and the percent of time with a pH measurement of less than 4.0. A correlation of 0.48 (P<0.01) was identified for percent of time with upper and lower pH probe measurements less than 4.0.

Of the 11 patients who required fundoplication prior to our study, 4 now had lower pH probe measurements of less than 4.0 less than 5% of the time, 1 for 5% to 10% of the time, and 6 for more than 10% of the time. The data indicate that 5 of these patients who required fundoplication had significant reflux in the past. However, pH probe testing at our institution indicated no further reflux.

The presence of a tracheotomy tube did not increase the risk of reflux in our study population.

Gastroesophageal reflux is increasingly being recognized as a contributing factor in the pathogenesis of pediatric airway disorders. Such disorders include apparent life-threatening events, recurrent pneumonia, and reactive airway disease.11-13 The percentage of children with respiratory problems thought to be induced by GER is estimated at 30% in some reports.14

Koufman17 found abnormal lower pH probe results in 23 (72%) of the 32 patients (11 pediatric and 21 adult) he studied with laryngeal and tracheal stenosis. He defined an abnormal lower probe measurement as a pH of less than 4.0 more than 4.39% of the total study time (when the patient was either upright or supine). He found abnormal pharyngeal reflux, defined as any single episode of a pH less than 4.0, in 67% (10/15) of these patients. In another study, Koufman17 induced subglottic mucosal injury in 20 dogs and painted the injured areas with saline solution, acid, or acid with pepsin. Findings included nonhealing and inflammation in the acid with pepsin group.

Based on the aforementioned information, many physicians consider SGS to be a complication of GER.18 With respect to laryngotracheal reconstruction (LTR), Gray et al19 report that patients with uncontrolled GER have a higher rate of failure following surgical reconstruction than those without GER. Based on 20 years of experience, Cotton and O’Connor20 state that a “reflux workup” is now considered essential to the success of LTR. Empirical treatment of GER has been recommended for patients undergoing LTR.21

The importance of GER in LTR has been refuted by Zalzal et al,22 who state that neither the presence of GER nor its treatment are major factors in determining the outcome of LTR. They studied 4 groups of patients who underwent LTR: those who had no preoperative GER evaluation, those whose preoperative GER evaluation findings were abnormal, those whose preoperative GER evaluation findings were normal, who failed to receive appropriate treatment, and those whose preoperative GER evaluation findings were abnormal who received appropriate therapy consisting of a prokinetic agent and/or a histamine2 blocker in most cases. Limitations of that study include the fact that it was not double blind, a staging system for airway stenosis was not used, and the sample size of patients with GER was small; as a result, the conclusions of that study are questionable. Although not addressed in that article, 73% of the patients studied had evidence of reflux.

Intraesophageal pH monitoring remains the criterion standard for the diagnosis of GER.6,23,24 Gastroesophageal reflux is best defined by distal esophageal acid exposure, which is identified by a pH of less than 4.0. A confounding factor in the diagnosis of GER is that coughing and wheezing can promote episodes of reflux, such that a child with a tracheotomy tube may have more re-
frequently to determine if GER is present, it must be re-
evaluated. A pH of less than 4.0 means that the study time is
considered a borderline risk for GER, while GER for less than 5% of the time is
considered normal.25

Very few data are available on proximal pH probe
results. Ideally, the probe is placed below the upper esoph-
agal sphincter in the esophageal inlet. In a study by Dob-
hans and Castell,26 minimal acid exposure occurred in the
proximal esophagus (<1% of the total time) in patients with
normal distal pH probe results. Shaker et al.28 evaluated
patients with reflux laryngitis using pH monitoring
at the distal esophagus, proximal esophagus, and phy-
ryn. Findings included a significantly higher percentage
of reflux episodes in the pharynx of patients with
laryngitis compared with control patients. The criteria
were the number of episodes with pH less than 4.0 in the
specified anatomical location. Contencin and Narcy27
monitored pharyngeal pH in infants and children with
and without laryngotracheitis. For the pharyngeal chan-
nel, acid reflux was defined as a decrease in pH below
6.0. A pathologic condition was diagnosed if a pH of lower
than 6.0 was recorded more than 1% of the total time.
Another study28 found that patients without distal GER
had a proximal esophageal pH of less than 4.0 for 0.76% of
the time, while patients with distal GER had a prox-
imal esophageal pH of less than 4.0 for 6.5% of the time.
It is currently unclear what pH value should be used as
a cutoff to identify pathologic pharyngeal or upper esoph-
agal reflux.

Our lower pH probe data found that more than
30% of the patients with SGS were considered to be at
high risk for GER, and that more than 50% were at
marginal or high risk for GER. When we included the
patients who had previously undergone fundoplication
(4 patients) or had severe reflux that had been treated
medically (1 patient), the percentage of patients in our
study who were at marginal or high risk for GER was
57%. This high incidence of GER in patients with SGS
does not provide evidence that GER contributes to SGS;
rather, further investigation is needed to determine its
significance.

Our study found that 48% of the patients who
underwent upper pH probe testing had a pH of less than
4.0 more than 1% of the time. The significance of this
data is unclear because upper probe reference data are
not available. Our analysis did reveal that most patients
with upper reflux more than 1% of the time had lower
probe measurements that indicated they were at mar-
ginal or high risk for GER. Furthermore, of the 16 pa-
tients who underwent dual-probe testing and were con-
sidered at high risk for GER based on lower probe testing,
13 had upper reflux more than 1% of the time. This sug-
gests that lower probe data are somewhat predictive of
upper probe data.

Although pH probe monitoring is the test used most
frequently to determine if GER is present, it must be re-
membered that pH probe results do not identify basic
and neutral GER. If basic or neutral GER is suspected, a gas-
cic-emptying scan should be performed. It is generally ac-
cepted that pH probe monitoring is more sensitive and
specific in diagnosing GER than a gastric-emptying scan.29
It remains to be seen if laryngeal disorders or biopsy, which
theoretically would indicate conclusively whether in-
flammatory changes are present, will play a role in diag-
osing GER in the future. We are currently investigat-
ing this question.

A large number of patients in our study were born
prematurely and many had other notable associated
medical conditions. It is impossible to draw conclusions
about the relationship between GER and SGS from this
type of retrospective review. In addition, this study does
not examine what effect the presence of GER had on
these patients after airway reconstruction. What can be
learned from these data is that the incidence of GER in
patients with SGS seen at our institution was at least 3
times greater than the incidence of GER reported in the
general pediatric population. Well-controlled studies
are necessary to further our understanding of the role of
GER in the pathogenesis of SGS and to determine its
impact on the success of reconstructive surgery.

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Corresponding author: David L. Walner, MD, Depart-
ment of Otolaryngology and Bronchoesophagology, Rush-
Presbyterian-St Luke’s Medical Center, 1633 W Congress
Pkwy, Chicago, IL 60612.

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