

## Patterns of laryngopharyngeal and gastroesophageal reflux

K SATO, H UMEMO, S CHITOSE, T NAKASHIMA

### Abstract

**Objectives:** Double-probe, 24-hour pH monitoring remains the ‘gold standard’ for the diagnosis of laryngopharyngeal reflux disease, even though there is no consensus on how to interpret the data collected.

**Methods:** Tetra-probe, 24-hour pH monitoring was performed in 56 patients with suspected laryngopharyngeal reflux, in order to investigate patterns of laryngopharyngeal and gastroesophageal reflux.

**Results:** The number of reflux episodes and the total and percentage time periods spent with pH < 4.0 were correlated with the distance of the probe from the lower oesophageal sphincter. The number of reflux episodes and the total and percentage time periods with pH < 4.0 were greater when patients were upright (i.e. during the daytime). There were few laryngopharyngeal reflux events recorded for pH levels of <4.0; however, there were a significant number of laryngopharyngeal reflux events recorded for pH levels of <5.0, a level capable of causing laryngopharyngeal reflux disease. When a pH level of <5.0 was used, the number, total time and percentage time of laryngopharyngeal reflux episodes was greater during the supine period (i.e. during sleeping) in a quarter of the cases, compared with results when a pH of <4.0 was used.

**Conclusions:** It is valid to use a pH level of 5.0 as indicative of laryngopharyngeal reflux in the hypopharynx.

**Key words:** Laryngopharyngeal Reflux Disease; pH Monitoring; Tetra-probe

### Introduction

There is no clear consensus on the findings or clinical manifestations of laryngopharyngeal reflux (LPR) disease.<sup>1</sup> Furthermore, there are no ideal diagnostic procedures for evaluating LPR disease, and diagnostic outcome criteria are ambiguous.<sup>1</sup> Double-probe, 24-hour pH monitoring remains the ‘gold standard’ for the diagnosis of LPR disease.<sup>1–3</sup> However, there is no consensus on how many pH sensors to use, their precise location or how to interpret the data collected.<sup>3,4</sup>

In this paper, tetra-probe, 24-hour pH monitoring was performed to investigate the pattern of LPR and gastroesophageal reflux and the validity of using a pH level of 5.0 to indicate LPR.

### Materials and methods

Tetra-probe, 24-hour pH monitoring was performed in 56 patients with suspected LPR. Seven out of 56 patients had organic lesions and the remainder had non-organic lesions. Four cases had laryngeal

granuloma, one had epithelial hyperplasia and one had Reinke’s oedema.

### *Tetra-probe, 24-hour pH monitoring*

Twenty-four hour pH monitoring was performed with a tetra-probe, antimony pH catheter (Zinetics 24 ME Multi-use pH catheter, Medtronic Functional Diagnostics, Skovlunde, Denmark). The four pH probes of the catheter were located every 10 cm. The proximal probe sensor (channel one) was placed in the hypopharynx (just above the upper oesophageal sphincter), the second probe (channel two) in the middle oesophagus, the third probe (channel three) above the lower oesophageal sphincter and the distal probe (channel four) in the stomach.

The proximal probe of the catheter was placed under direct vision, using transnasal videolaryngoscopy. A videofluorogram was thereafter performed to ensure accurate placement of the proximal probe (just above the upper oesophageal sphincter) and of the other three probes (positioned in the middle

oesophagus, a few centimetres above the lower oesophageal sphincter, and in the fundus of the stomach).

The pH probes were simultaneously calibrated in buffer solutions at pH 7 and pH 1 before initiation of the study. The pH values were recorded second by second on a pH monitor (Digitrapper pH, Medtronic Functional Diagnostics).

#### Data analysis

Data were analysed using the Polygram Net TM software program (Medtronic, Skovlunde, Denmark). We took a pH level of  $<4.0$  or  $<5.0$  to indicate a significant reflux event at channel one, and a pH level of  $<4.0$  to indicate a significant reflux event at the other channels. The pH values recorded at all four channels were calculated second by second. Recordings were made while subjects were upright and supine, and during preprandial, mealtime and postprandial periods. We evaluated the number of reflux episodes, number of long reflux episodes ( $>5$  minutes), duration of the longest reflux episode, time spent with pH  $<4.0$  or  $<5.0$  (in minutes), percentage of time with pH  $<4.0$  or  $<5.0$ , minimum pH, maximum pH, mean pH and median pH.

## Results

### Reflux at each site

Figure 1 shows reflux data for monitoring sites one, two and three, using a cut-off of pH  $<4.0$ . The

number of reflux episodes and the total time and percentage time of reflux correlated with the distance of the probe from the lower oesophageal sphincter.

The number of gastroesophageal reflux episodes was greater than that of LPR episodes. However, the total time and percentage time for gastroesophageal reflux were less than those for LPR. These results indicated that gastroesophageal reflux occurred with greater frequency (i.e. a greater number of reflux acid exposure events) but lesser duration (i.e. smaller total and percentage time durations of reflux acid exposure events), compared with LPR.

### Gastroesophageal reflux

The number, total time and percentage time of gastroesophageal reflux episodes (i.e. pH  $<4.0$ , measured at channel three) were assessed both while patients were supine (i.e. while sleeping) and upright (i.e. during the daytime) (Figure 2). The number, total time and percentage time of gastroesophageal reflux events were greater when patients were upright compared with supine.

### Laryngopharyngeal reflux

Results for LPR episodes (i.e. the number, total time and percentage time of reflux events, measured just above the upper oesophageal sphincter (channel one)) were compared during supine and upright periods, for pH  $<4.0$  (Figure 3) and pH  $<5.0$

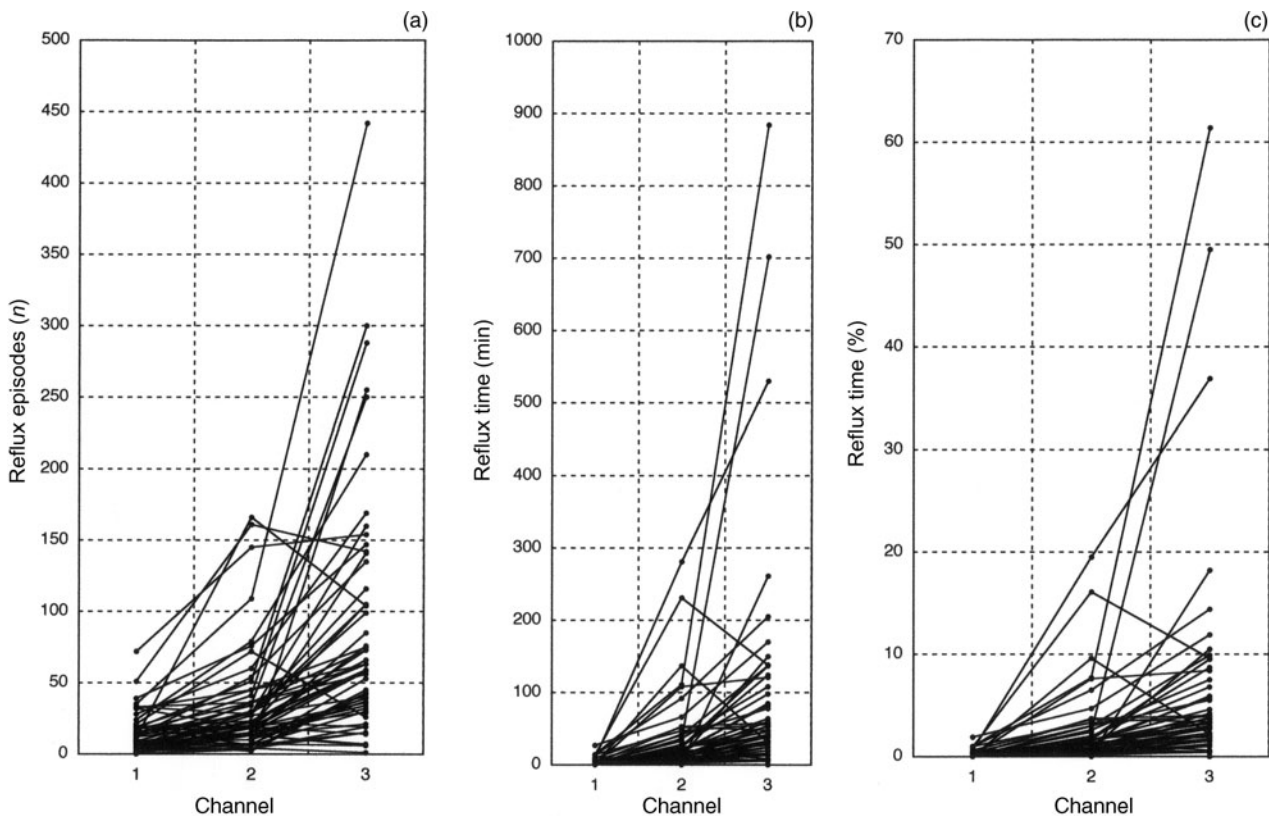


FIG. 1

Results for (a) total number of reflux events, (b) total reflux time and (c) percentage reflux time, for monitoring channels one, two and three, using a cut-off of pH  $<4$ .

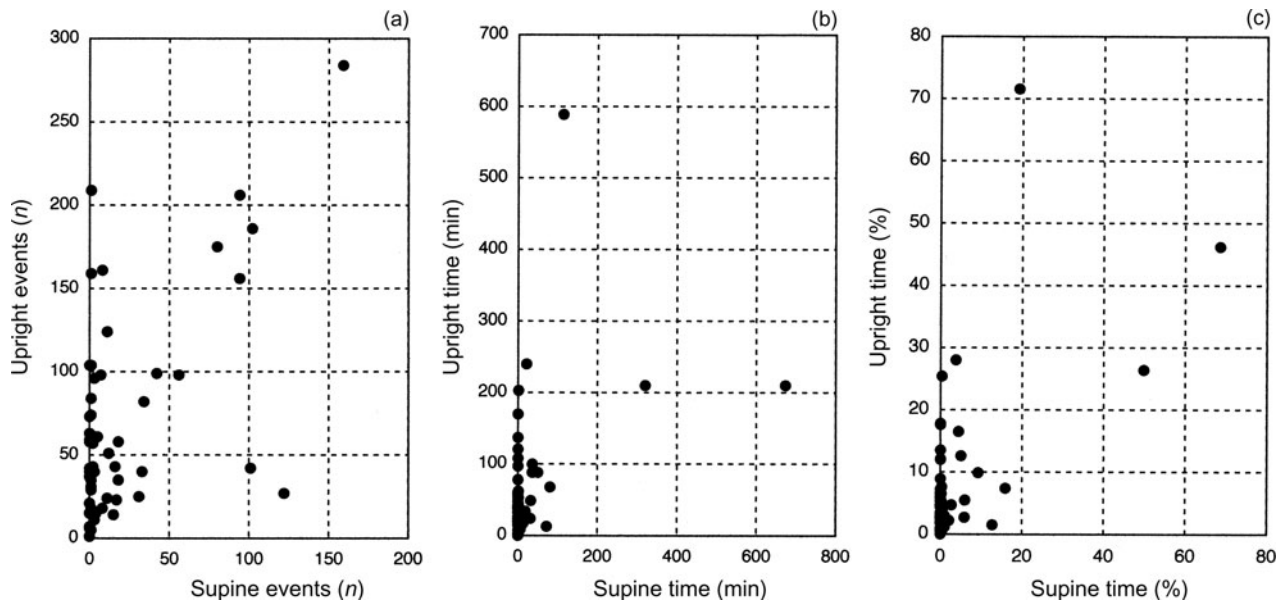


FIG. 2

Comparison of upright and supine results for gastroesophageal reflux (measured at channel 3), assessed at pH < 4: (a) total number of reflux events; (b) total reflux time; and (c) percentage reflux time.

(Figure 4). The number, total time and percentage time of LPR were greater when patient were upright compared with supine. However, when a pH level of <5.0 was used, the number, total time and percentage time of LPR became greater during the supine period in a quarter of patients (27 per cent).

Figure 5 shows the relationship between LPR results (at channel one) for pH levels of <4.0 and <5.0. When a pH level of <4.0 was used to indicate a significant reflux event, three out of 56 patients were assessed as having no episodes of reflux into the pharynx. However, when a pH level of <5.0 was used to indicate

a significant reflux event, all three of these patients were assessed as having significant reflux events. While there were few LPR events at a pH level of <4.0, there were a significant number at a pH level of <5.0, a level capable of causing LPR disease.

Table I shows how many times the events increase when a pH level of <5.0 was used, when compared with a pH level of <4.0 was used as a significant reflux event. When a pH level of <5.0 was used as a significant reflux event, 43% (24/56) of the cases had more than ten times as many events as the total number of reflux events, 55% (31/56) of the cases had more than

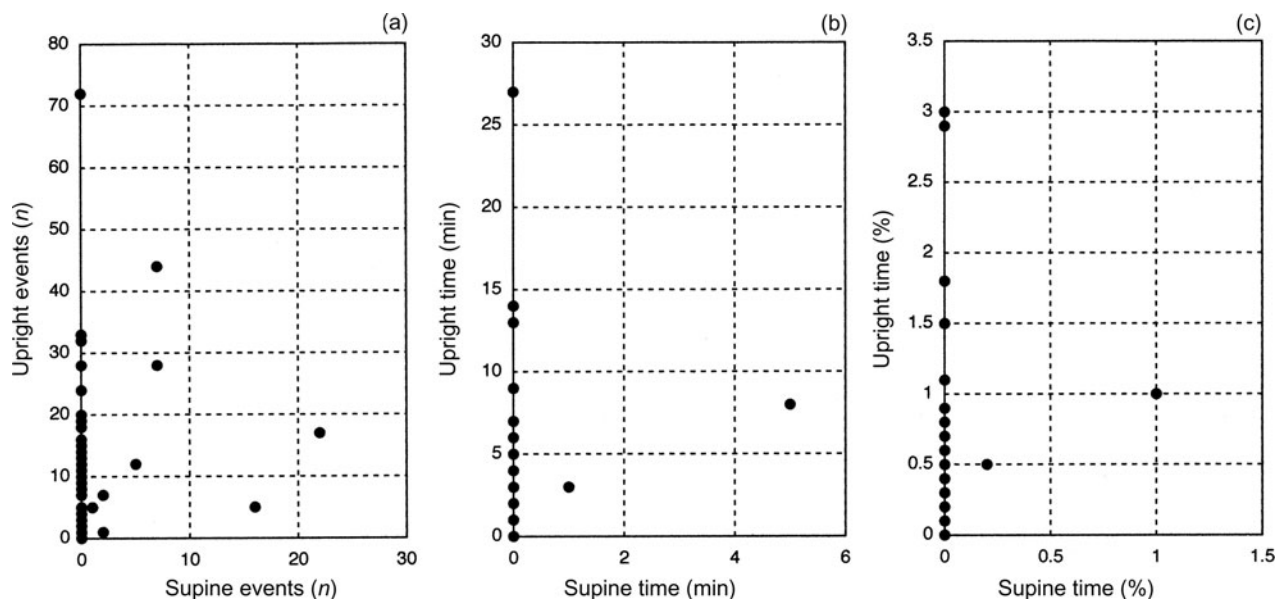


FIG. 3

Comparison of upright and supine results for laryngopharyngeal reflux (measured at channel one), assessed at pH < 4: (a) total number of reflux events; (b) total reflux time; and (c) percentage reflux time.

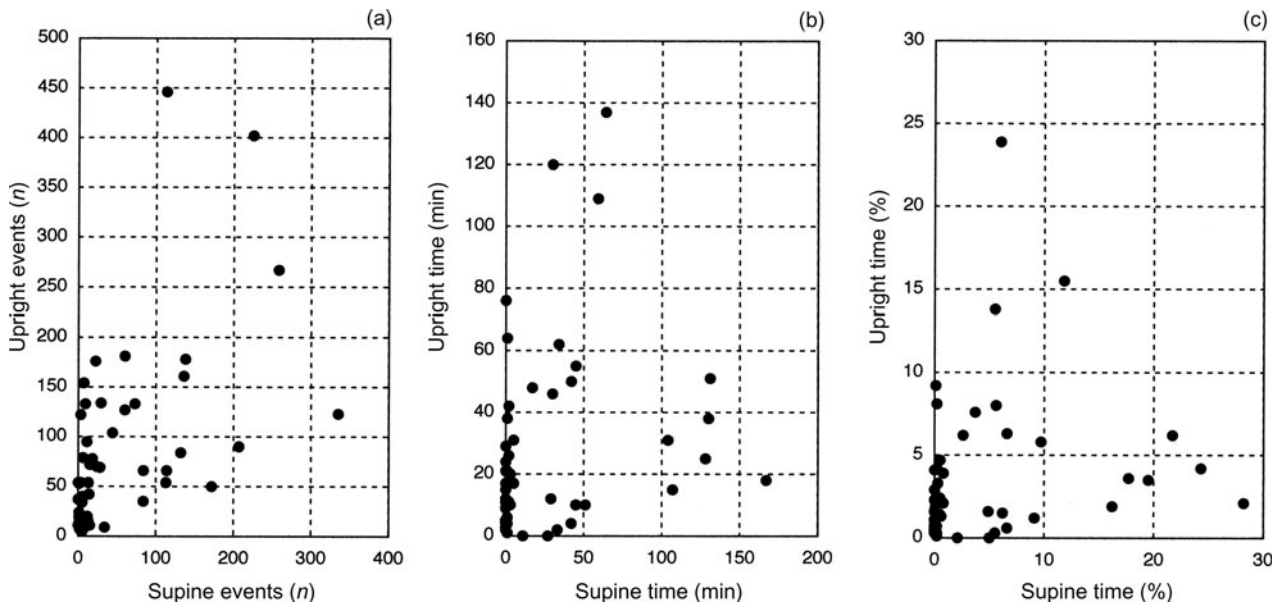


FIG. 4

Comparison of upright and supine results for laryngopharyngeal reflux (measured at channel one), assessed at pH < 5: (a) total number of reflux events; (b) total reflux time; and (c) percentage reflux time.

ten times as many events as the total reflux time, and 32% (18/56) of the cases had more than ten times as many events as the percentage reflux time, when compared with a pH level of <4.0 was used as a significant reflux event. Each of the maximum times was 62.3 times the events in the total number of reflux events, 61.6 times the events in the total reflux time, and 53 times the events in the percentage reflux time.

From these results, it was considered valid to use a pH level of not only <4.0 but also <5.0 as indicative of LPR in the hypopharynx.

**Discussion**

The diagnosis and treatment of LPR disease are still controversial. Ambulatory, double-probe, 24-hour (simultaneous oesophageal and hypopharyngeal) pH monitoring is currently considered the gold standard for LPR disease diagnosis.<sup>1-3</sup> However, this technique is still somewhat controversial, especially regarding interpretation of results.

The advantage of tetra-probe, 24-hour pH monitoring is that the pH can be monitored simultaneously at four sites, enabling gastric acid levels and

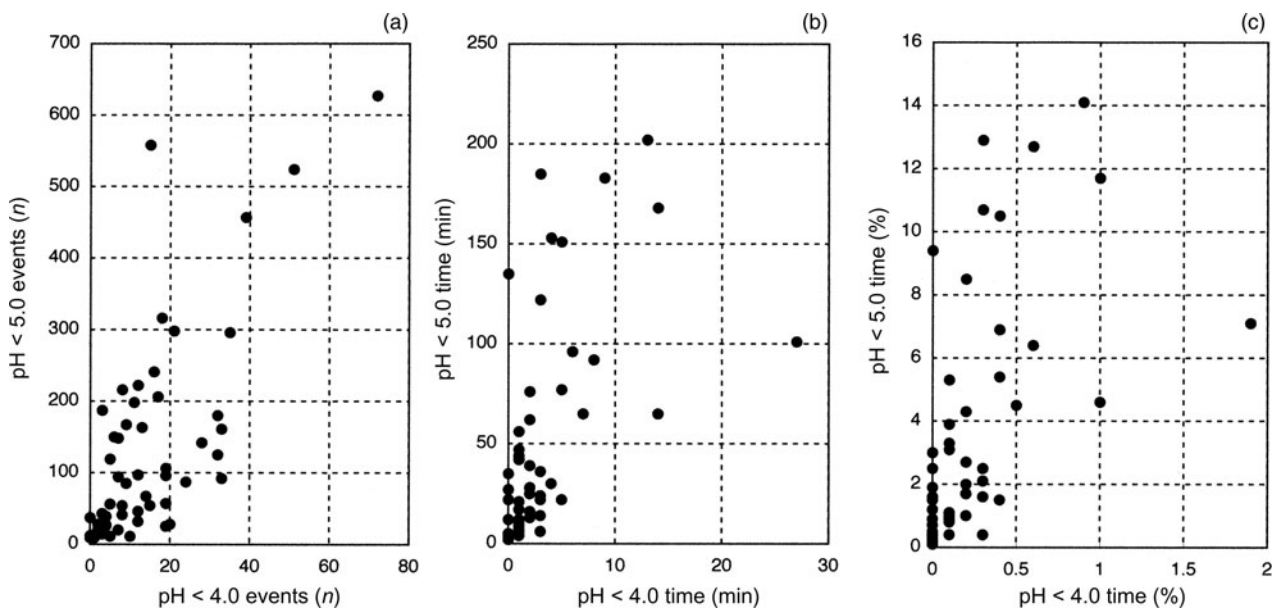


FIG. 5

Comparison of laryngopharyngeal reflux results (measured at channel one) assessed at pH < 4.0 and at pH < 5.0: (a) total number of reflux events; (b) total reflux time; and (c) percentage reflux time.



TABLE I  
RESULTS FOR PH LEVELS OF <4.0 AND <5.0 AT CHANNEL ONE

<pH 5.0/ <pH 4.0	Reflux events (n)	Total reflux time (n)	Percentage reflux time (n)
≤5	15	14	27
5 < x ≤ 10	17	11	11
10 < x ≤ 15	12	10	6
15 < x ≤ 20	5	5	2
>20	7	16	10
Max	62.3	61.6	53

Data represent number of patients. Max = maximum

gastroesophageal and laryngopharyngeal reflux to be thoroughly assessed.<sup>5</sup> This tool reveals gastric acid levels and reflux patterns, and enables the relationship between the four probe locations to be well documented.<sup>5</sup> However, even with such extra precision, data interpretation has still been ambiguous.

It has been stated that patients with LPR appear to have a different pathophysiological mechanism and pattern of reflux, compared with patients with gastroesophageal reflux disease. The relationship between LPR disease and gastroesophageal reflux disease is also controversial.

In this study, patterns of LPR and gastroesophageal reflux were investigated using tetra-probe, 24-hour pH monitoring. The study also investigated the interpretation of pH within LPR, especially the validity of using a pH level of <5.0 as indicative of LPR. Finally, the relationship between LPR disease and gastroesophageal reflux disease was considered.

#### *Interpretation of laryngopharyngeal reflux pH*

The interpretation of pH monitoring for gastroesophageal reflux disease has been studied (for oesophageal acid levels 5 cm above the lower oesophageal sphincter) and normal pH values are well established, as is the percentage time duration for pH < 4.0.<sup>6</sup> In contrast, there are no ideal diagnostic procedures for evaluation of LPR, and diagnostic outcome criteria are ambiguous.<sup>1,2</sup> The use of pH monitoring is considered the gold standard for LPR disease; however, there is no consensus on how many pH sensors to use, where to locate them or how best to interpret the results.

Smit *et al.*<sup>7</sup> assessed the percentage of time during which a pH of <4.0 was detected in cases of LPR. They suggested that the proportion of time required to indicate pathological reflux was more than 0.1 per cent for total recording, 0.2 per cent for upright recordings and 0 per cent for supine recordings. In addition, they considered more than four reflux episodes to be pathological.<sup>7</sup> On the other hand, there is an opinion that a single episode of reflux into the pharynx indicates LPR.<sup>4,8</sup> Postma *et al.*<sup>4</sup> have established four criteria that must be met in order for an event to be defined as pharyngeal reflux: (1) a decrease in pH to <4.0 (or <5.0); (2) a decrease in pharyngeal pH level immediately following distal oesophageal acid exposure; (3) no decrease in pH level during eating or swallowing; and (4) a rapid

and sharp decrease in pH level at the proximal sensor, rather than a gradual decrease.

The mucosal linings of the oesophagus, pharynx and larynx differ in their susceptibility to peptic acid injury. Laryngeal epithelium can sustain peptic acid injury at a pH level of 5.0 or more,<sup>9</sup> and is far more sensitive to reflux-related injury than oesophageal epithelium. Other authors have suggested that the use of a pH level of 5.0 may be valid in indicating LPR,<sup>4</sup> because proximal acid exposure times are short and the dilutional and neutralisation factors present in saliva are greater at this level.<sup>10</sup>

In the current study, a pH level of <4.0 or <5.0 was calculated at the proximal probe (channel one, just above the upper oesophageal sphincter). Three out of 56 cases had no single reflux event into the pharynx when a pH level of <4.0 was assessed as a significant reflux event. However, these cases all had significant reflux events when a pH level of <5.0 was assessed as a significant reflux event. When a pH level of <5.0 was assessed as a significant reflux event, many cases had a greatly increased number of reflux events, compared with assessment using a pH level of <4.0. Thus, while there were few LPR events with a pH level of <4.0, there were a significant number of such events at a pH level of <5.0, a level capable of causing laryngeal lesions.

These results suggest that it is appropriate to use pH levels of not only <4.0 but also <5.0 as indicators of significant LPR events. Thus, we would consider it valid to use a pH level of <5.0 as indicative of LPR in the hypopharynx.

#### *Relationship between laryngopharyngeal and gastroesophageal reflux*

The relationship between laryngopharyngeal and gastroesophageal reflux disease is also controversial. Patients with LPR appear to have different pathophysiological mechanisms and patterns of reflux, as well as different symptoms, signs and responses to treatment, compared with patients with gastroesophageal reflux disease.<sup>2</sup> The majority of patients with LPR do not have oesophagitis or its primary symptom, heartburn.<sup>2</sup> Patients with LPR suffer predominantly upright (daytime) reflux events, whereas patients with gastroesophageal reflux disease suffer predominantly supine (nocturnal) reflux events.<sup>2</sup> Patients with gastroesophageal reflux disease suffer prolonged periods of acid exposure, while those with LPR do not.<sup>2</sup> Patients with gastroesophageal reflux disease have dysmotility and prolonged oesophageal clearance, whereas those with LPR do not.<sup>2</sup> The primary defect in gastroesophageal reflux disease is lower oesophageal dysfunction, whereas the primary defect in LPR is upper oesophageal sphincter dysfunction.<sup>2</sup>

It is obvious that LPR occurs subsequent to gastroesophageal reflux when the upper oesophageal sphincter is dysfunctional. The laryngeal epithelium is far more sensitive to reflux-related injury than the oesophageal epithelium. In the present study, tetra-probe, 24-hour pH monitoring was performed

to investigate patterns of laryngopharyngeal and gastroesophageal reflux. Laryngopharyngeal reflux occurred subsequent to gastroesophageal reflux, and the recorded reflux events correlated with the distance of the monitoring probe from the lower oesophageal sphincter. When a pH level of <5.0 was assessed as a significant reflux event, many patients had many times more reflux events registered, compared with the number registered when a reflux event was defined as pH < 4.0.

It has been postulated that the pH level indicative of LPR, and the differences in susceptibility to peptic acid injury between oesophageal, laryngeal and pharyngeal mucosa, indicate that patients with LPR have a different pathophysiological mechanism and pattern of reflux, compared with patients with gastroesophageal reflux disease.

### Conclusion

There are currently no ideal diagnostic procedures for evaluating LPR disease, and diagnostic outcome criteria are ambiguous. Double-probe, 24-hour pH monitoring remains the gold standard for the diagnosis of LPR disease; however there is no consensus on how best to interpret the data collected.

In the present study, there were few LPR events with a pH level of <4.0, but a significant number of LPR events at a pH level of <5.0, a level capable of causing LPR disease. We therefore consider it appropriate and valid to use a pH level of not only <4.0 but also <5.0 as indicative of a significant LPR event.

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Address for correspondence:

Dr Kiminori Sato,  
Department of Otolaryngology-Head and Neck Surgery,  
Kurume University School of Medicine,  
67 Asahi-machi,  
Kurume 830-0011, Japan.

Fax: 81 942 37 1200

E-mail: kimisato@oct-net.ne.jp

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