pH probe positioning for 24-hour pH-metry by manometry or pH step-up

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Objectives **Before pH measurement, manometry is recommended for precise pH probe positioning. We investigated whether the pH probe could be positioned accurately by the pH difference between the oesophagus and the stomach (pH step-up).**

Methods **Dual-channel 24-h pH-metry with probes positioned 5 cm above either the manometrically determined upper lower oesophageal sphincter margin or the pH step-up was performed in healthy volunteers and reflux patients. To determine the pH step-up, the pH probe was pulled back from the stomach until a sudden rise to pH greater than four occurred. Probe position, reflux episodes and the fraction of the time pH was less than four were compared using the Wilcoxon test for difference and the Hodges–Lehman estimate inclusive confidence interval for equivalence. The pH step-up method was evaluated further during proton pump inhibitor therapy and after drug discontinuation.**

Results **The pH probe was positioned 2 cm and 1 cm closer to the stomach by the pH step-up method in the volunteers and reflux patients, respectively. A small increase in upright reflux episodes but not in supine reflux episodes was registered by the probe positioned by pH step-up. No significant differences in the fraction of the time pH was less than four were obtained between the two probes. The Hodges–Lehman calculation proved equivalence for both methods of probe positioning for 24-h pH-metry. During proton pump inhibitor therapy, no pH step-up was detectable in three volunteers and in one patient. On the first day after discontinuing therapy, the pH step-up method yielded clear-cut results again.**

Conclusion **The pH probe for diagnostic 24-h pH-metry and, with some limitations, also for 24-h pH-metry for therapy control, can be positioned accurately by the pH step-up method.** ***Eur J Gastroenterol Hepatol*** **16:375–382**

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Introduction

Before oesophageal pH measurement is undertaken, manometry is recommended for precise positioning of the pH probe 5 cm above the upper margin of the lower oesophageal sphincter [1,2]. However, the manometric equipment is expensive, seems not to influence the therapeutic decisions in patients with reflux disease [3,4] and is, in the setting of a mere positioning procedure, time-consuming and inconvenient for the patient [5]. An alternative method is to localise the gastro-oesophageal border by measuring the sudden rise in pH (pH step-up) when pulling back the pH probe from the stomach into the oesophagus. Published data are controversial as to whether manometric positioning can be replaced by the pH step-up method. Some authors have reported that the pH probe can be positioned accurately by the pH step-up method [6–8], while others have claimed it to be inaccurate compared with manometry [9,10]. However, from a clinical viewpoint, it is not only the probe position that is relevant but also whether the results of 24-h pH-metry obtained by different methods of probe positioning are equivalent. Comparable sensitivities, specificities and normal values of 24-h pH-metry reported in studies with probe positioning either by manometry [11–13] or by pH step-up [14–16] point to an equivalence of both methods. However, to our knowledge, a direct comparison of the results of 24-h pH-metry obtained simultaneously in the same subjects by two probes – one positioned by manometry and the other by pH step-up – has not been published.

Therefore, the aims of the present study were (i) to re-evaluate the accuracy of the pH step-up method for positioning of the pH probe for 24-h pH-metry, (ii) to compare the results of 24-h pH-metry with probe positioning by manometry and by pH step-up, and (iii) to investigate whether the pH step-up method can be used during or shortly after a powerful antisecretory medication with a proton pump inhibitor (PPI), since

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pH-metry is also recommended [1] for evaluation of persisting reflux symptoms during anti-reflux therapy.

Materials and methods

Subjects

Twenty-five healthy volunteers (13 females, 12 males; median age 36 years, range 25–56 years) and 25 patients with reflux disease (14 females, 11 males; median age 58 years, range 43–77 years) participated in the study. All of the healthy volunteers were non-smokers, took no medication, and had no oesophageal symptoms. Of the reflux patients, 14 showed, endoscopically, reflux oesophagitis (Savary–Miller [17] grade I, $n = 6$; grade II, $n = 5$; grade III, $n = 1$; grade IV, $n = 2$) and 11 had a pathological result in 24-h pH-metry. A hiatal hernia was seen in 16 of the reflux patients. After explanation of the study protocol, which was in accordance with the Declaration of Helsinki and approved by the local ethics committee, all subjects gave their written, informed consent.

Study protocol

Part I

At 1500 h, after a minimum of 4 h fasting, a water-perfused manometric assembly was introduced transnasally into the stomach after local anaesthesia. The probe was pulled back in steps of 1 cm, with the subject in the prone position. The locations of the upper margin of the lower oesophageal sphincter were determined as their distances to the nares. The mean location of the upper margin of the lower oesophageal sphincter was calculated from three radially oriented measuring orifices. These values were depicted in full centimetres, since the location of the lower oesophageal sphincter was determined in steps of 1 cm.

After manometry, an investigator blinded to the results of this procedure introduced two glass pH electrodes transnasally into the stomach, which was confirmed by acidic pH. One of these two pH probes was pulled back in steps of 1 cm until a sudden rise in pH above four occurred. Again, the distance to the nares was noticed, and the mean value of the three manoeuvres was calculated, also depicted in full centimetres. During the pH step-up manoeuvres, the subjects were in a recumbent (prone) position to avoid a false deep pH step-up, which can occur in the upright position when the pH probe passes a fundic air bubble [8].

Subsequently, one of the two electrodes was positioned 5 cm above the upper margin of the lower oesophageal sphincter; the other was positioned 5 cm above the pH step-up. Both probes were connected to a two-channel data-logger (Digitrapper MKII, Medtronic Ltd, Essen, Germany), and an ambulatory 24-h pH-metry was started. The subjects returned after 24 h for removal of the probes and transfer of the data to the computer for analysis by a commercially available software program (EsopHogram, Medtronic Ltd).

Part II

Twenty-four of the 25 volunteers who had participated in Part I took pantoprazole 40 mg (Schwartz Pharma Ltd, Monheim, Germany) in the morning for 7 days. On day 7, the volunteers returned to the laboratory, a pH electrode was introduced into the stomach, and the pH was registered. Thereafter, the probe was pulled back in steps of 1 cm to investigate whether a pH step-up between stomach and oesophagus would still be observed. Again, this manoeuvre was performed three times; in the case of an observable pH step-up, the mean distance to the nares was calculated.

Following cessation of pantoprazole, the volunteers came in every day. Again, the intragastric pH was measured and the mean position of the pH step-up noted. Daily measurements were performed until the antisecretory effect of the PPI ceased, i.e. when the intragastric pH fell to or below a level of 0.2 above the volunteer's intragastric pH before medication.

The pH step-up method was also assessed in six patients with reflux disease during pantoprazole therapy.

Data analysis

Part I

The percentage of subjects with an identifiable pH step-up was determined. The maximal and mean difference of the three pH step-ups in every subject was calculated and compared with the maximal and mean difference of the manometric position of the upper margin of the lower oesophageal sphincter obtained by the three radially oriented measuring orifices. In addition, the manometrically determined mean position of the upper margin of the lower oesophageal sphincter was compared with the mean position of the pH step-up in every subject. The percentage of subjects with a difference of more than 3 cm in the location of the pH probe positioned by manometry and the location of the pH probe positioned by pH step-up was calculated, since such a difference is considered inaccurate [10].

The number of reflux episodes and the fraction time with oesophageal pH below four registered by the two probes during 24-h pH-metry were compared. These comparisons were performed separately for upright (daytime) and supine (night-time) periods.

Part II

The percentage of subjects with an identifiable pH step-up between stomach and oesophagus was calculated. In the case of an identifiable pH step-up, the positions of the pH step-up determined during and after PPI therapy were compared in volunteers. Furthermore, the cumulative percentage of volunteers whose intragastric pH had returned to or below a level of 0.2 above the volunteer's intragastric pH before medication was calculated for each day after discontinuing medication.

Statistical analysis

Part I

The Wilcoxon test for paired samples was used to compare the location of the upper margin of the lower oesophageal sphincter and of the pH step-up, to compare the probe positions, and to compare the number of reflux episodes and the fraction times with pH less than four as measured by the two probes. Since a zero difference (the ideal difference when comparing two different methods with respect to equivalence) will not be considered by the usual Wilcoxon calculation, the calculation was done in the following way: every zero difference was replaced by a difference of 0.1 and then either a minus sign (favouring the manometric method of probe placement) or a plus sign (favouring the pH step-up method of probe placement).

The Hodges–Lehman estimate of the median difference, including the 90% confidence interval, was used to test for equivalence between the manometric and pH step-up method of probe placement for 24-h pH-metry [18]. The Hodges–Lehman procedure is used to estimate the shift between the two distributions generating paired data. Both a point estimate and a confidence interval were computed for the shift parameter using StatXact software (version 4.01, Cytel Software Corporation, Cambridge, MA, USA). Due to the sample size, exact rather than asymptotic calculations were performed. Equivalence is proven when the confidence interval lies completely within the equivalence range. The equivalence range was set prospectively to ± 3 cm for the difference in probe position, since a maximal difference of 3 cm between the location of two probes positioned by different methods is accepted as accurate [10]. The equivalence ranges for the number of reflux episodes and the fraction time with pH less than four were derived from two studies comparing the results of 24-h pH-metry obtained by two probes that were secured together and placed at the same oesophageal position (5 cm above the upper margin of the lower oesophageal sphincter) [19,20]. The equivalence ranges for the number of reflux episodes were ± 17 (volunteers) and ± 57 (patients) for the upright period and ± 2 (volunteers) and ± 27 (patients) for the supine period. The equivalence ranges for the fraction time with pH less than four were ± 1% for the upright and ± 1% for the supine periods in the volunteers and ± 4%, respectively, ± 10% in the reflux patients.

Part II

The modified Wilcoxon test for paired samples was used to compare the location of the pH step-up before, during and after PPI therapy. Again, the Hodges–Lehman estimates of the median difference, including the 90% confidence intervals, were used to test for equivalence between these locations. An equivalence range of ± 2 cm was defined for these calculations, since we observed a maximal difference of 2 cm between the three pH step-ups performed in every volunteer before medication in the first part of the study.

Results

Part I

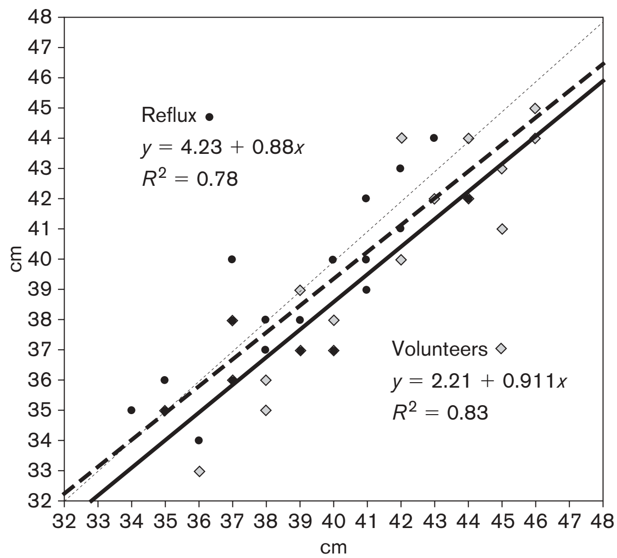
An easily identifiable pH step-up was observed in every volunteer and every reflux patient. The maximal difference in the location of the pH step-up between the three manoeuvres was 2 cm, identical to the maximal radial difference in the location of the upper margin of the lower oesophageal sphincter. Also, the mean differences were identical with 1 cm. On average, the pH step-up was located 2 cm (volunteers) and 1 cm (reflux patients) more distally than the upper margin of the lower oesophageal sphincter (Table 1, Fig. 1). The

Table 1 Comparison of the location of the manometrically determined upper margin of the lower oesophageal sphincter with the location of the pH step-up in healthy volunteers and in patients with reflux disease

		Wilcoxon		Hodges–Lehman calculation	
	Location (cm)	*P*	Median difference (cm)	90% CI	Equivalence range (cm)
Healthy volunteers					
Manometry	38 (33–45)	< 0.001	2.0	1.5–2.0	±3
pH step-up	40 (35–46)				
Patients					
Manometry	38 (34–44)	NS	0.5	0–1.0	±3
pH step-up	39 (34–44)				

CI, confidence interval; NS, not significant.
Data depicted as median distance (range) from the nares.

Fig. 1



Manometric location of the upper border of the lower oesophageal sphincter (*y* axis) versus the location of the pH step-up (*x* axis) (difference from the nares to the tip of the probes) in healthy volunteers (–) and reflux patients. ●, reflux patients; ◇, healthy volunteers; ◆, overlying data points of reflux patients and healthy volunteers; – – –, line of regression for reflux patients; –, line of regression for healthy volunteers; · · ·, line of equivalence.

difference between the probe positions was significant in volunteers ($P < 0.001$) but did not obtain significance in reflux patients. All but one pH probe (i.e. 96%) in the healthy volunteers and all pH probes in the reflux patients positioned by pH step-up were localised within a difference of 3 cm to the manometrically positioned pH probe. The 90% confidence interval of the median difference in the probe positions in healthy volunteers as well as in reflux patients was completely within the equivalence range, demonstrating an accurate probe placement by the pH step-up method (Table 1).

The presence of a hiatal hernia in reflux patients did not result in problems with positioning of the pH probe by pH step-up. The median difference in probe position in patients with and without hiatal hernia was 1 cm. The maximal difference was 3 cm in patients with hiatal hernia and 2 cm in patients without hiatal hernia. Thus, the pH probe positioned by pH step-up was localised in all patients, irrespective of the presence or absence of hiatal hernia, within ± 3 cm of the manometrically positioned pH probe, a difference that is considered accurate [10]. The separate comparison of probe position positioned by manometry or by pH step-up in patients with and without hiatal hernia did not change the result of the Wilcoxon analysis or the Hodges–Lehman calculation of the whole group of reflux patients.

During the 24-h study period, a small increase in the number of reflux episodes, which attained significance in healthy volunteers ($P < 0.05$) but not in reflux patients, was measured during the daytime (upright position) by the pH probes positioned by pH step-up as compared with the manometrically positioned probes (Table 2, Fig. 2). Despite the small increase in reflux frequency, a significant difference in fraction time of pH less than four was calculated neither in healthy volunteers nor in reflux patients (Table 2, Fig. 3). Also, no difference was observed in the numbers of reflux episodes and in the fraction times in the supine period. Despite the differences during the upright period, the confidence intervals of the median differences of the number of reflux episodes and of the fraction time with pH less than four were, in both groups, completely within the equivalence range, i.e. within the maximal difference that can be registered by two probes at an identical oesophageal position (Table 2).

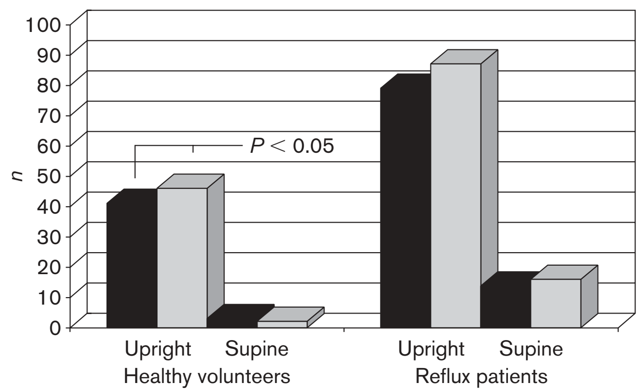
Again, the results of 24-h pH-metry with probes positioned by manometry or pH step-up were analysed separately for reflux patients with and without hiatal hernias (analysis for difference by Wilcoxon test for paired data; analysis for equivalence by Hodges–Lehman estimate). The analysis in both subgroups yielded results that were identical to the analysis of the whole group: no significant differences in the number of reflux episodes and in percentage of time with

Table 2 Comparison of results of dual-channel 24-h pH-metry in healthy volunteers and reflux patients obtained by one pH probe positioned by manometry and the other positioned by the pH step-up method

			Hodges–Lehman calculation		
Volunteers		Wilcoxon *P*-value	Median difference	90% CI	Equivalence range
RE: *n*/period					
Mano-up	41 (8–124)	<0.05	11.0	4.5;17.0	±17
pH-up	46 (14–96)				
Mano-sup	3 (0–17)	NS	1.0	−0.5;2.0	±2
pH-sup	2 (0–22)				
FT: %					
Mano-up	2.5 (0.2–9.9)	NS	0.3	0;0.6	±1.0
pH-up	2.8 (0.3–9.9)				
Mano-sup	0.6 (0–9.0)	NS	0	−0.3;0.8	±1.0
pH-sup	0.5 (0–11.6)				
Reflux patients					
RE: *n*/period					
Mano-up	79 (9–259)	NS	4.0	−1.5;10.6	±57
pH-up	87 (3–359)				
Mano-sup	14 (0–64)	NS	2.0	−0.5;5.5	±27
pH-sup	16 (0–113)				
FT: %					
Mano-up	9.6 (1.2–29)	NS	−0.1	−1.2;0.5	±4.0
pH-up	10.2 (2–24.5)				
Mano-sup	3.5 (0–45.7)	NS	0.2	0;0.8	±10.0
pH-sup	2.8 (0–51.2)				

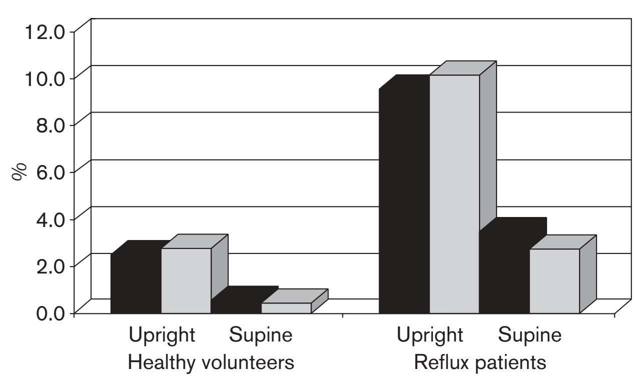
RE = number of reflux episodes; FT = fraction of time oesophageal pH < 4; up = upright/daytime period; sup = supine/night-time period; CI = confidence interval; data depicted as median (range).

Fig. 2



Median number of reflux episodes during dual-channel 24-h pH-metry with probes positioned manometrically (black bars) 5 cm above the upper margin of the lower oesophageal sphincter and 5 cm above the pH step-up (grey bars) in healthy volunteers and reflux patients.

Fig. 3



Median fraction time with pH less than four during dual-channel 24-h pH-metry with probes positioned manometrically (black bars) 5 cm above the upper margin of the lower oesophageal sphincter and 5 cm above the pH step-up (grey bars) in healthy volunteers and reflux patients.

oesophageal pH less than four in the upright and supine periods, and equivalence of the results of 24-h pH-metry obtained by the probes positioned either by manometry or by pH step-up.

Part II

A 'classical' pH step-up (from pH less than four to pH above four) could not be determined in three (13%) volunteers due to a non-acidic intragastric pH on day 7 of pantoprazole therapy. Nevertheless, no pH step-up at all (i.e. no pH difference between stomach and oesophagus) was observed in only one volunteer. In the volunteers with identifiable pH step-up ($n = 21$), an identical location of the pH step-up before and during PPI therapy was observed in 13 volunteers, a difference of −1 cm was seen in seven volunteers, and a difference of −2 cm was seen in one volunteer (Table 3). Thus, all differences were within the maximal difference of 2 cm obtained by determining the pH step-up three times in volunteers without antisecretory therapy. Accordingly, the confidence interval of the median difference between the location of the pH step-up with and without PPI therapy was completely within the equivalence range when testing with the Hodges–Lehman equivalence calculation, despite a significant difference in the Wilcoxon test (Table 3).

Only one (4%) volunteer had a pH above four on the first and second days after stopping PPI therapy. Nevertheless, a small pH difference between stomach and oesophagus was observable in this volunteer. The median location of the pH step-up was identical before and after PPI therapy, and the Hodges–Lehman method demonstrated equivalence (Table 3). The cumulative percentage of volunteers with 'normalized' intragastric pH (intragastric pH returned to or below a level of 0.2 above the volunteer's intragastric pH before medication) was calculated as 67% on the first day, 96% on days 2–6, and 100% on day 7 after discontinuing PPI medication.

In the six reflux patients investigated during PPI therapy, a pH step-up could be identified in all subjects. However, a difference of up to 5 cm between the repeated attempts was observed in one (17%) patient, which would have made the probe positioning by pH step-up unreliable in this patient.

Discussion

Oesophageal manometry is recommended for precise positioning of the pH probe for 24-h pH-metry [1,2]. However, if 24-h pH-metry could be performed without prior manometry, then 24-h pH-metry would be facilitated for routine clinical examination. An alternative method of probe positioning is the pH step-up

Table 3 Comparison of location of the pH step-up before, during and after proton pump inhibitor therapy in healthy volunteers

		Wilcoxon		Hodges–Lehman calculation	
	Location (cm)	*P*	Median difference (cm)	90% CI	Equivalence range (cm)
Before	40 (35–46)				
		< 0.05	1.0	1 to 1.5	± 2
During	42 (36–46)				
After	41 (36–45)				
		NS	0	−1 to 0	± 2
Before	40 (35–46)				

CI, confidence interval; NS, not significant.
Data depicted as median distance (range) from the nares.

method [6–10,14–16]. This uses the sudden rise in pH from an acidic intragastric pH to a neutral intra-oesophageal pH for localisation of the gastro-oesophageal junction when pulling back a pH electrode. In our study in healthy volunteers and in patients with gastro-oesophageal reflux disease, we compared this method with the conventional manometric method of probe placement. Our main findings were: (i) the intraindividual variance of the pH step-up was identical to the radial variance of the manometrically determined upper margin of the lower oesophageal sphincter; (ii) in all but one volunteer (i.e. 96%), and in all reflux patients, the probe positioned by pH step-up was localised within $\pm$ 3 cm of the manometrically positioned pH probe, a difference that is considered accurate [10]; (iii) the pH step-up occurred on average 2 cm (volunteers) and 1 cm (patients) below the upper margin of the lower oesophageal sphincter; (iv) the presence of hiatal hernia in reflux patients did not interfere with probe positioning by pH step-up; (v) compared with manometric positioning, the probe positioned by pH step-up registered slightly more reflux episodes in the upright (daytime) but not in the supine (night-time) position; (vi) the fraction time of pH less than four is not influenced significantly by the method of probe positioning; (vii) the pH step-up method demonstrated some limitations when 24-h pH-metry was performed during PPI therapy; (viii) the pH step-up method could be used without limitations 1 day after discontinuing PPIs; and (ix) the effects of PPI therapy on intragastric pH were detectable up to 6 days after drug withdrawal, which might influence the results of 24-h pH-metry.

Despite being recommended as the gold standard for precise pH probe positioning, the manometrically determined position of the upper margin of the lower oesophageal sphincter is not at a fixed position. Kaye and Showalter reported a difference of up to 2 cm (mean 0.7 cm) in the radially determined location of the upper lower oesophageal sphincter margin [21]. This is in accordance with our data, of a mean radial difference of 1 cm and a maximal radial difference of 2 cm. The manometric positioning might be influenced further by the variable lower oesophageal sphincter length and position during the breath cycle (shorter length and nearer mouth during expiration) and by the variable lower oesophageal sphincter length due to different recording methodologies (rapid pull-through > station pull-through; side-hole recording > end-hole recording) [21–26]. Due to the potential variance in the manometrically determined position of the upper margin of the lower oesophageal sphincter, a difference of maximally 3 cm between two probes positioned by different methods is accepted as accurate [10].

The position of the pH step-up between stomach and oesophagus can also vary like the manometrically determined position of the lower oesophageal sphincter. A pH step-up in the oesophagus more proximal to the mouth is seen by rapid compared with stepwise withdrawal of the pH probe [26]. To our knowledge, no data exist as to whether the location of the pH step-up changes during the breath cycle like the position of the lower oesophageal sphincter. For repeated determinations of the pH step-up, Rokkas and colleagues observed good reproducibility with a difference of only 1–2 cm [7]. In line with these data, we observed, in healthy volunteers as well as in reflux patients, a mean difference of 1 cm and a maximal difference of 2 cm between the three manoeuvres performed in every subject for positioning of the pH probe by the pH step-up method. In contrast, Marples and colleagues reported a difference of up to 11 cm for repeated determinations of the pH step-up [9]. However, a methodological bias may have occurred in their study, since they observed the pH step-up from 16 cm below to 10 cm above the lower oesophageal sphincter. Nevertheless, these data and the reported data of oesophageal manometry demonstrate that neither the manometrically determined position of the pH probe nor the position achieved by pH step-up is a fixed position but can vary within a certain range.

Controversial data are reported in the literature on the accuracy of the pH step-up method as an alternative method for placement of the pH probe for 24-h pH-metry. Walther and DeMeester compared the manometric location of the upper margin of the lower oesophageal sphincter with the location of the pH step-up [6]. They observed a significant correlation between both methods, despite applying an antegrade method of pH step-up localisation, which results in a deeper position of the pH step-up (compared with the pull-back method) due to curling of the probe [26,27]. A difference of maximally 3 cm between the probe positions, which is considered accurate [10], was seen in 80% of the 20 reflux patients investigated. Accurate positioning was also reported in 100% of 14 healthy volunteers [8], in 98% of 46 reflux patients [7] and in 100% of 25 reflux patients [8]. Our findings of a difference within the accepted range of $\pm$ 3 cm in 96% of 25 healthy volunteers and in 100% of 25 reflux patients are in accordance with the above results. In contrast, Mattox and colleagues found the pH step-up outside the range of accuracy in 29% of 14 healthy volunteers and in 58% of 71 reflux patients [10]. Marples and colleagues failed to find any correlation between the two methods [9]. However, the latter authors determined the location of the pH step-up as the mean of three manoeuvres in the upright position and three in the supine position of their volunteers and patients. The large intraindividual variance in the location of the pH step-up and the finding of a pH step-up 16 cm below the lower oesophageal sphincter suggest that their results may be biased by incorrect deep locations of the pH step-up when the pH probe passes a fundic air bubble in the upright position.

Compared with the upper margin of the lower oesophageal sphincter as the manometric fixed point for probe positioning, the pH step-up on average occurs more distally. However, the reported differences between these two locations are mostly small, with −0.2 cm [7], −1.3 cm [8] and, in the present study, −1 cm (reflux patients) and −2 cm (healthy volunteers). The only study with a greater difference of −3.3 cm is that of Mattox and colleagues, who observed, unusually, many pH step-ups distal to the lower oesophageal sphincter [10].

The critical question is whether the pH probe positioned closer to the stomach by the pH step-up method yields different results during 24-h pH-metry when compared with conventional manometric positioning. Lehman and colleagues demonstrated that one does not need to be afraid of sliding of the probe into the stomach when it is positioned more deeply in the oesophagus than at its usual position 5 cm above the lower oesophageal sphincter [28]. However, probes positioned manometrically at or 1 cm above the upper margin of the lower oesophageal sphincter measured a greater fraction time with pH less than four in the upright period compared with a probe positioned 5 cm or 6 cm above the lower oesophageal sphincter [29–31]. No significant differences were observed between probes at the lower oesophageal sphincter rim and 1 cm above [29]. It can be assumed from these results that probes differing more than 3 cm, the range of accuracy, in their position also differ in their results in fraction time pH less than four, while they have comparable fraction times when the difference in probe position is within the range of accuracy. The results of our present study are in line with these data. The pH probes of the pH step-up method, which were positioned in its median position slightly more distally in the oesophagus but were localised within 3 cm to the manometrically positioned pH probes in all but one subject, registered a slightly increased number of (short-lasting) upright reflux episodes but no significant differences in fraction time pH less than four, which is decisive for determination of 24-h pH-metry as pathological or normal [1,11–15]. In accordance with Lehman and colleagues, no increase in the reflux frequency was detectable in the supine position (night-time) during 24-h pH-metry [29]. Additionally, the observed differences in daytime reflux frequency between the pH probes positioned by pH step-up or by manometry are within the physiological variability, as determined by two pH probes secured together and placed at an identical oesophageal position [19,20]. These differences are due to food or mucus sticking to one probe or to sticking of the tip of one probe against the oesophageal wall [20,32,33]. Furthermore, the magnitude of difference in reflux frequency between the pH probes positioned by pH step-up and manometry is much smaller than the day-to-day variability of gastro-oesophageal reflux [34–36]. Therefore, the small difference in daytime reflux measured by the pH probe positioned by the pH step-up method seems to be without clinical importance. This suggestion is supported by the results of the Hodges–Lehman calculation demonstrating equivalence for the results of 24-h pH-metry obtained by the pH probe positioned by the pH step-up method and by the pH probe positioned by manometry.

Oesophageal pH measurement is also recommended to evaluate patients with normal endoscopic findings and reflux symptoms that are refractory to PPI therapy [1]. In this case, pH-metry is done to document a symptom–reflux correlation or to exclude a reflux genesis of the patient's symptoms by documenting the adequacy of therapy. To test whether the pH probe can be positioned accurately in this setting also by pH step-up, we re-evaluated the pH step-up method in our healthy volunteers during and after PPI therapy. A non-acidic intragastric pH (> 4) was found in three (13%) of 24 healthy volunteers during PPI therapy. However, no pH difference between stomach and oesophagus was observed in only one of them. In addition, in one (17%) of six reflux patients measured during PPI therapy, the location of the pH step-up could not be determined reliably. Another argument that may be raised against the use of the pH step-up method during PPI therapy is the observation that the pH step-up occurred in 38% of the volunteers 1–2 cm closer to the stomach with versus without PPI therapy. This might increase the number of registered reflux episodes, as discussed above. However, adequate reflux suppression should also be effective in the most distal oesophagus to heal lesions and to prevent symptoms. Conversely, a more distal position of the pH probe in the oesophagus seems to favour the documentation of a symptom–reflux correlation [31], demonstrating that the patient's symptoms are still the consequence of gastro-oesophageal reflux despite PPI therapy.

In contrast to the potential flaws of the method during PPI therapy, the pH step-up method can be used again for pH probe positioning on the first day after stopping PPI therapy. Nevertheless, a diagnostic 24-h pH-metry should not be performed in the first week after stopping PPI therapy, since in single subjects we and others [37] have observed some effects of PPI therapy on acid secretion and intragastric pH up to 6 or 7 days after drug discontinuation.

In conclusion, the pH probe for 24-h pH-metry is positioned in the distal oesophagus, on average, a little bit closer to the stomach by the pH step-up method than by manometry. Yet, this small difference in probe position does not influence the percentage of time oesophageal pH is less than four, demonstrating that both methods are equivalent for probe positioning for diagnostic 24-h pH-metry. Thus, manometry can be abandoned as a mere positioning procedure before diagnostic 24-h pH-metry in routine clinical use and replaced by the pH step-up method, which possesses the advantage of being faster, easier to perform, less expensive, and less inconvenient for the patient. However, the pH step-up method has limitations when 24-h pH-metry has to be done for therapy control, since no pH step-up can be seen in at least 15–20% of subjects during PPI therapy.

Conflict of interest

None declared.

Authors' contributions

C. Pehl and W. Schepp planned and organised the study; C. Pehl and I. Boccali did all the measurements; M. Hennig performed all statistical calculations.

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