

Endoscopic pH monitoring for patients with suspected or refractory gastroesophageal reflux disease

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BACKGROUND: Wireless pH studies can offer prolonged pH monitoring, which may potentially facilitate the diagnosis and management of patients with gastroesophageal reflux disease (GERD). The aim of the present study was to evaluate the detection rate of abnormal esophageal acid exposure using prolonged pH monitoring in patients with suspected or refractory GERD symptoms.

METHODS: Patients undergoing prolonged ambulatory pH studies for the evaluation of GERD-related symptoms were assessed. Patients with a known diagnosis of GERD were tested on medical therapy, while patients with suspected GERD were tested off therapy. The wireless pH capsules were placed during upper endoscopy 6 cm above the squamocolumnar junction.

RESULTS: One hundred ninety-one patients underwent a total of 198 pH studies. Fifty ambulatory pH studies (25%) were excluded from the analysis: 27 patients (14%) had insufficient data capture (less than 18 h on at least one day of monitoring), 15 patients had premature capsule release (7%), seven were repeat studies (3.5%) and one had intolerable pain requiring capsule removal (0.5%). There were 115 patients undergoing pH studies who were off medication, and 33 patients were on therapy. For the two groups of patients, results were as follows: 32 (28%) and 22 (67%) patients with normal studies on both days; 58 (50%) and five (15%) patients with abnormal studies on both days; 18 (16%) and three (9%) patients with abnormal studies on day 1 only; and seven (6%) and three (9%) patients with abnormal studies on day 2 only, respectively.

CONCLUSIONS: Prolonged 48 h pH monitoring can detect more abnormal esophageal acid exposure but is associated with a significant rate of incomplete studies.

Key Words: Ambulatory pH monitoring; Endoscopy; Gastroesophageal reflux disease; Treatment

The diagnosis of gastroesophageal reflux disease (GERD) can be challenging due to the wide spectrum of clinical presentations, particularly extraesophageal manifestations (1,2). Conventional esophageal pH monitoring is performed using a transnasal catheter that is placed at 5 cm above the manometrically determined lower esophageal sphincter (3).

Surveillance endoscopique du pH chez des patients souffrant de reflux gastro-oesophagien présumé ou réfractaire

CONTEXTE : La pHmétrie sans fil permet une surveillance prolongée du pH et peut ainsi faciliter le diagnostic et le traitement du reflux gastro-oesophagien (RGO). La présente étude avait pour but d'évaluer le taux de détection de l'exposition anormale à l'acidité oesophagienne par une surveillance prolongée du pH chez des patients présentant des symptômes de RGO présumé ou de RGO réfractaire.

MÉTHODE : Des patients ont été soumis à une mesure prolongée et ambulatoire du pH pour une évaluation de symptômes liés au RGO. Ceux chez qui un diagnostic de RGO avait déjà été posé ont fait l'objet d'évaluation en cours de traitement, tandis que ceux chez qui il y avait présomption de RGO ont fait l'objet d'évaluation avant l'instauration du traitement. Les capsules de mesure du pH sans fil ont été mises en place au cours d'une endoscopie digestive haute, à une hauteur de 6 cm au-dessus de la jonction squamo-columnaire.

RÉSULTATS : Un total de 198 mesures du pH a été effectué chez 191 patients. Cinquante mesures ambulatoires (25 %) ont été écartées de l'analyse : 27 (14 %) pour insuffisance de données (moins de 18 h sur au moins une journée de surveillance); 15 (7 %) pour libération prématurée de la capsule; 7 (3,5 %) pour reprise de l'exploration; 1 (0,5 %) pour douleur intolérable nécessitant le retrait de la capsule. Cent quinze sujets ne prenaient pas de médicaments alors que 33 étaient soumis à un traitement. Voici les résultats enregistrés respectivement dans les deux groupes de patients : 32 (28 %) et 22 (67 %) sujets ont obtenu des résultats normaux au cours des deux journées; 58 (50 %) et 5 (15 %) sujets, des résultats anormaux au cours des deux journées; 18 (16 %) et 3 (9 %) sujets, des résultats anormaux au cours de la première journée seulement; 7 (6 %) et 3 (9 %) sujets, des résultats anormaux au cours de la deuxième journée seulement.

CONCLUSION : La surveillance prolongée du pH sur 48 heures a permis de détecter un plus grand nombre de cas d'exposition anormale à l'acidité oesophagienne, mais elle a été associée à un taux relativement élevé d'exploration incomplète.

The esophageal pH is recorded for 24 h. Ambulatory esophageal acid exposure is the gold standard for the diagnosis of GERD, with good sensitivity and specificity (4-6).

A wireless pH monitoring system, introduced in 2000, allows for prolonged 48 h monitoring (7). One advantage of the wireless system is the avoidance of the transnasal catheter,

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which results in less interference of patient's daily activities of living and improved patient satisfaction (8). Moreover, the wireless pH capsule system permits longer, less intrusive esophageal pH monitoring (9) and thus, may have the potential to improve the diagnostic yield of abnormal esophageal acid exposure in patients with symptoms related to GERD. The aim of the present study was to evaluate the detection rate of abnormal esophageal acid exposure using the wireless, prolonged pH monitoring system. We hypothesized that a 48 h pH monitoring study would increase the number of subjects having evidence of GERD with abnormal amounts of acid exposure when compared with a 24 h pH monitoring period.

METHODS

Study design

All patients undergoing prolonged ambulatory pH studies to evaluate GERD-related symptoms between June 2003 and December 2005 in the Brigham and Women's Hospital (Boston, Massachusetts, USA) were enrolled in the study. The hospital is a tertiary referral centre for patients with GERD-related symptoms in the area. The study was approved by the Partners Human Research Committee. Patients' symptoms included typical and atypical symptoms of GERD, or persistent GERD-related symptoms despite medical therapy. Patients with planned antireflux procedures were also evaluated. Patients with suspected GERD-related symptoms were tested off medical therapy, while patients with persistent GERD symptoms despite medical therapy and those with planned antireflux procedures, were tested on medical therapy. Before testing, patients were instructed to take nothing by mouth for at least 6 h before the procedure. No dietary or activity restrictions were imposed during the monitoring period. Results for patients who were off medications are presented separately from those on therapy.

Placement of the Bravo pH capsule (Medtronic Inc, USA)

All wireless Bravo pH capsules were placed during upper endoscopy. Patients were sedated with midazolam and fentanyl for the upper endoscopy. After direct visualization of the squamocolumnar junction, the endoscope was removed and the capsule was placed 6 cm above the endoscopically determined squamocolumnar junction. In patients with known Barrett's esophagus, the location of the diaphragmatic hiatus was used as the squamocolumnar junction. Immediately after placement, capsule location and function was confirmed by obtaining a pH value of more than 4 on the pH monitor and/or visual reinspection.

Data collection for the pH study

Patients were instructed to resume daily activities of living and a regular diet. The patients were instructed to keep the monitoring unit within 1 m of their body at all times to ensure optimal data transmission and recording for the 48 h period. Reflux-related symptoms were recorded with the pH monitoring unit by pressing buttons corresponding to chest pain, heartburn and regurgitation symptoms. Patients were also asked to keep a diary that recorded food intake, medications, body position and symptoms. The monitor was returned after 48 h. The pH data were then downloaded to the computer unit and analyzed with PolygramNet software (Medtronic Inc, USA).

Definition of abnormal pH study

An abnormal pH study was defined as the total percentage of time that an esophageal pH of less than 4.0 was greater than 4%; an abnormal supine reflux was defined as an esophageal pH of less than 4.0 in the supine position of 1.2% or greater over any 24 h monitoring period; and abnormal upright reflux was defined as an esophageal pH of less than 4.0 in the upright position for 6.3% or greater over any 24 h monitoring period. The Johnson and DeMeester score (10) was calculated using six criteria: per cent of total time that the pH was less than 4.0; per cent of upright time that pH was less than 4.0; per cent of supine time that pH was less than 4.0; total number of reflux events; number of reflux episodes longer than 5 min; and the longest episode of reflux (in minutes). A total composite score of more than 14.72, using these criteria, was considered to be a pathological reflux.

Analysis of the pH results

All pH tracings were reviewed and studies where esophageal pH was consistently less than 4.0 for over 30 min, followed by a persistent rise in pH to above 4.0, were excluded due to presumed premature capsule release. The assumption was that the released Bravo capsule had dislodged into the stomach and subsequently passed into the small bowel. A study with fewer than 18 h of data collection over any of two consecutive 24 h periods was also excluded for insufficient data capture. The overall number of patients with disease and the day-to-day variability of pH measurements were assessed in the two consecutive 24 h periods. A patient was considered to have day-to-day variability when pathological pH, as defined above, was present on day 1 of monitoring and absent on day 2, or vice versa. We also investigated abnormal acid exposure in the upright and supine positions with regard to symptoms and esophageal pH.

Statistical analysis

SAS version 8.02 (SAS Institute Inc, USA) was used to perform data analysis. A McNemar test was performed to evaluate the discordance between day 1 and day 2 esophageal acid exposure by testing the null hypothesis of marginal homogeneity. $P < 0.05$ was considered to be significant.

RESULTS

There were 191 patients who had 198 wireless pH capsules placed during the study period of June 2003 to December 2005. Fifty ambulatory pH studies (25%) were excluded from the analysis due to the following reasons: 27 patients (14%) had insufficient data capture (less than 18 h on at least one day of monitoring), 15 patients (7%) had premature capsule release, seven were repeat studies (3.5%) and one had intolerable pain requiring capsule removal (0.5%).

There were 150 studies performed in patients with suspected GERD symptoms who were off medical therapy. Thirty-five studies were excluded from analysis due to the following reasons: 20 patients (14%) had insufficient data capture, 10 patients (7%) had premature capsule release and five patients had repeat studies. A total of 115 patients with a mean (\pm SD) age of 50 ± 13 years had adequate studies for evaluation and were included in the analysis. There were 76 women (66%) and 39 men (34%).

There were 48 studies performed on patients with refractory GERD symptoms who were on medical therapy.

Fifteen patients were excluded from analysis due to the following reasons: seven patients (15%) had insufficient data capture, five patients (10%) had premature capsule release, two had a repeat pH study (4%) and one had early removal of the capsule due to severe pain (2%). A total of 33 patients with a mean age of 52 ± 14 years had adequate studies for evaluation and were included in the analysis. There were 26 women (79%) and seven men (21%). Of those 33 patients, 13 patients (39%) were on once-daily proton pump inhibitor therapy, with two of 13 also using nocturnal H_2 blockers, 17 patients (52%) were on twice-daily proton pump inhibitor therapy (one was also on a nocturnal H_2 blocker), and two patients (6%) were on three times per day proton pump inhibitor therapy. One patient was on a twice-daily H_2 blocker (3%) due to intolerance of proton pump inhibitors.

Day-to-day variability in esophageal acid exposure

The day-to-day variability in esophageal acid exposure was evaluated by examining the total percentage of time that pH was less than 4.0. In the 115 patients who were off medications and undergoing pH studies to establish the diagnosis of GERD, 58 had abnormal studies on both days, 32 had normal studies on both days, 18 had an abnormal study on day 1 and a normal study on day 2, while seven had a normal study on day 1 but an abnormal study on day 2 (Table 1). There were 25 patients (22%) with abnormal acid exposure on only one of the two days monitored. Seventy-six patients (66%) had abnormal acid exposure on day 1 and 65 had abnormal acid exposure (57%) on day 2 (Table 1). There was a 22% discordance between day 1 and day 2 total esophageal acid exposure ($P=0.03$).

To determine the source of variability in esophageal acid exposure, we examined abnormal esophageal acid exposure in the supine position for patients who were off medications. There were 41 patients with abnormal esophageal acid exposure in the supine position on both days, 49 patients with normal supine acid exposure on both days, 13 patients with an abnormal supine acid exposure on day 1 but a normal supine acid exposure on day 2, and 12 patients with a normal supine acid exposure on day 1 but an abnormal supine acid exposure on day 2. There were 54 patients (47%) with abnormal supine acid exposure on day 1 and 53 patients (46%) with abnormal supine acid exposure on day 2 (Table 1). There was a 22% discordance between day 1 and day 2 supine acid exposure ($P=0.84$). Therefore, the total day-to-day variability in esophageal acid exposure did not appear to be due to changes in supine esophageal acid exposure.

Abnormal esophageal acid exposure in the upright position was evaluated for the 115 patients who were off medical therapy. There were 47 patients with abnormal esophageal acid exposure in the upright position on both days, 44 patients with normal upright acid exposure on both days, 20 patients with an abnormal upright acid exposure on day 1 but a normal upright acid exposure on day 2, and four patients with a normal upright acid exposure on day 1 but an abnormal upright acid exposure on day 2. Overall, there were 67 patients (58%) with an abnormal upright acid exposure on day 1 and 51 patients (44%) with an abnormal upright acid exposure on day 2. On day 1, the mean per cent time upright pH was less than 4.0 was $9.6 \pm 8.3\%$, and on day 2 it was $7.6 \pm 7.5\%$. There was a discordance of 21% between day 1 and day 2 upright esophageal acid exposures

TABLE 1
Esophageal acid exposure variability for diagnosis of gastroesophageal reflux disease: Number of patients with positive (abnormal) versus negative (normal) Bravo* studies

		Total esophageal acid exposure (n=115) [†]		
		pH day 2, n		Total
pH day 1, n		Negative	Positive	
	Negative	32	7	39
	Positive	18	58	76
	Total	50	65	115
		Supine esophageal acid exposure (n=115)		
		pH day 2, n		Total
pH day 1, n		Negative	Positive	
	Negative	49	12	61
	Positive	13	41	54
	Total	62	53	115
		Upright esophageal acid exposure (n=115) [‡]		
		pH day 2, n		Total
pH day 1, n		Negative	Positive	
	Negative	44	4	48
	Positive	20	47	67
	Total	64	51	115

*Bravo pH capsule (Medtronic Inc, USA); [†] $P=0.03$, McNemar test; [‡] $P=0.001$, McNemar test

($P=0.001$) and thus, differences in upright esophageal acid exposures accounted for the total day-to-day variability seen in those patients.

For the 33 patients undergoing pH monitoring performed with refractory GERD symptoms on therapy, five patients had abnormal studies on both days, 22 patients had normal studies on both days, three had an abnormal study on day 1 and a normal study on day 2, while three had a normal study on day 1 and an abnormal study on day 2 (Table 2). There were six patients (18%) with abnormal acid exposure on only one of the two days monitored. Eight patients (24%) had abnormal acid exposure on day 1 and eight patients (24%) had abnormal acid exposure on day 2. The 18% discordance between day 1 and day 2 total esophageal acid exposures was not significant ($P=1.0$).

DISCUSSION

The purpose of our study was to evaluate the detection rate of abnormal esophageal acid exposure using the wireless, prolonged pH monitoring system and compare it to a 24 h pH monitoring study. Our data showed that prolonged 48 h pH monitoring was able to detect more abnormal esophageal acid exposure for patients with suspected GERD-related symptoms with a significant discordance (22%) between day 1 and day 2 monitoring. In patients with refractory GERD symptoms, the discordance between day 1 and day 2 esophageal acid exposure was 18%. Therefore, prolonged 48 h pH monitoring may have clinical advantages over a 24 h pH study.

In patients with suspected GERD symptoms, prolonged pH monitoring clearly improves the diagnostic yield of the test. However, in patients with refractory symptoms, the difference in the esophageal acid exposure was not significant. This may be due to the small sample size of our refractory symptom

TABLE 2
Esophageal acid exposure variability for refractory gastroesophageal reflux disease symptoms: Number of patients with positive (abnormal) versus negative (normal) Bravo* studies

Total esophageal acid exposure (n=33)				
		pH day 2, n		
		Negative	Positive	Total
pH day 1, n	Negative	22	3	25
	Positive	3	5	8
	Total	25	8	33
Supine esophageal acid exposure (n=33)				
		pH day 2, n		
		Negative	Positive	Total
pH day 1, n	Negative	25	3	28
	Positive	3	2	5
	Total	28	5	33
Upright esophageal acid exposure (n=33)				
		pH day 2, n		
		Negative	Positive	Total
pH day 1, n	Negative	23	2	25
	Positive	5	3	8
	Total	28	5	33

*Bravo pH capsule, Medtronic Inc, USA

patient population rather than a true lack of improvement in the diagnostic yield for these patients.

We observed more abnormal acid exposures on day 1 (66%) than day 2 (57%). This could be due to stress related to the placement of the device, as well as anesthetics and anxiolytics required for capsule placement, all of which could reduce the lower esophageal sphincter pressure. Thus, some of the abnormalities noted on day 1 may, in fact, not be due to pathological GERD. This difference was noted in a previous report by Bhat et al (11). It further suggests that prolonged data collection may be helpful in establishing the diagnosis of GERD.

For patients with refractory GERD symptoms, 11 of 33 patients (33%) had abnormal esophageal acid exposure despite taking acid-reducing medications, suggesting inadequate acid suppression for those patients. This information is

particularly helpful for the management of these patients' symptoms. Therefore, prolonged pH monitoring may aid in the treatment of refractory GERD symptoms by detecting patients with inadequate acid suppression.

In a recent study (12) examining day-to-day variability of esophageal acid exposure with the Bravo pH capsule, day-to-day variability was seen in 27% of 190 patients in three tertiary care centres on and off acid suppressive therapy. Differences in capsule placement techniques among the study centres, ie, manometrically or endoscopically placed capsules, could have accounted for the higher variability in the report.

A review of the literature did not reveal conventional transnasal catheter detachment as a major limitation to pH measurement. In one study (8) involving 50 patients, one-half of the patients underwent wireless capsule placement and one-half underwent traditional pH probe placement; in the conventional group, one patient (4%) removed the catheter. One author (13), having performed over 5000 transnasal catheter pH studies, suggests that the inability to obtain adequate pH data occurs in approximately 5% to 10% of patients, although it is unclear what percentage is due to insufficient data capture or catheter removal.

The failure rate reported in the literature is 2% to 11% to wireless pH monitoring (9,11,12,14,15). However, in our study, the failure rate was 21%, due to a combination of insufficient data capture (14% [27 of 198]) and premature capsule release (7% [15 of 198]). The rate of premature capsule release was 9% for the first 100 studies and 6% for the remaining 98 studies. All patients were instructed to keep the monitoring unit within 1 m of their body, although many patients had prolonged periods where the pH data were not recorded. Therefore, future improvements in the technology are needed to reduce the rate of premature capsule release and improve the rate of data capture.

CONCLUSION

Prolonged 48 h wireless esophageal pH monitoring may improve the diagnostic yield for detecting GERD-related symptoms. It may improve the management of patients with day-to-day variability in their esophageal acid exposure by detecting more episodes. However, there is a significant rate of incomplete studies due to capsule detachment, and insufficient data capture and recording.

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