Published in final edited form as:

Dis Esophagus. 2014 January ; 27(1): 5–12. doi:10.1111/dote.12038.

The acoustic cough monitoring and manometric profile of cough and throat clearing

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Abstract

Background—Cough may coexist with throat clearing and it is possible that these two entities may be difficult to differentiate on acoustic monitoring and ambulatory manometry. The aim of this study was to assess the accuracy of acoustic monitoring for detecting cough and throat clearing and to also determine whether these two symptoms present with different manometric profiles on esophageal pressure topography.

Methods—Ten asymptomatic volunteers (7 females, mean age 31.1) were trained to simulate cough and throat clearing in a randomized order every 6 minutes during simultaneous acoustic monitoring and high resolution manometry. The accuracy of automated acoustic analysis and a blinded reviewer were compared against the scripted protocol. The pattern of the events and the duration of the pressure changes were assessed using the 30 mmHg isobaric contour to determine whether distinct patterns could be identified.

Results—In total, there were 50 cough and 50 throat clearing events according to the protocol. The sensitivity and specificity of acoustic cough monitoring was 84% and 50% for cough; while the blinded analysis based on sound alone revealed a sensitivity and specificity of 94% and 90%. The pressure topography manometric profile of both cough and throat clearing began with a decrease in esophageal pressure, followed by a distal excursion of the esophagogastric junction high-pressure zone and an increase in EGJ and UES contractile pressure that was followed immediately by a simultaneous abrupt increase in gastric and esophageal pressure. Cough was associated with a greater number of repetitive pressurizations, a more pronounced EGJ shift and a more vigorous augmentation of the UES pressure compared with throat clearing.

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Conflict of interest: John E. Pandolfino [Given imaging (consulting, educational), Sandhill Scientific Inc. (Consulting)]

No other conflicts for remaining authors (YX, DC, LB, ZL, FN, MC, JM, PJK)

Conclusions—The automated acoustic analysis software has a moderate sensitivity and specificity to detect cough. The profile of cough and throat clearing in pressure topography revealed a similar qualitative pattern of pressurization with more vigorous pressure changes and a greater rate of repetitive pressurizations in cough.

Background

Gastroesophageal reflux is a potential cause of chronic cough [1, 2]. However, accurate assessment of the relationship between cough and reflux requires precise timing of both the reflux and cough events because the time sequence between the two events is extremely close and patients are unable to signal the event marker with enough precision to provide a valid assessment during ambulatory reflux testing [3]. In order to improve the detection of reflux associated cough, two adjuvant techniques have been incorporated into ambulatory reflux monitoring to improve identification of cough: acoustic cough monitoring and manometry. Acoustic cough monitoring was developed to detect the cough event through sound to remove the variability of patient self-reporting [4]. Similarly, ambulatory manometry has been added to reflux testing to detect the pressure changes associated with cough to improve accuracy. However, both techniques are still in the investigative stage and are currently not used widely in clinical practice.

A potential confounder in the utilization of acoustic cough monitoring and ambulatory manometry is difficulty in distinguishing cough from throat clearing. Both are protective mechanisms to propel irritants away from the airway. Throat clearing is a conscious or unconscious attempt to remove an irritant in the throat. The sound of throat clearing is similar to cough potentially making it difficult to distinguish between the two by sound alone. Additionally, throat clearing may also be associated with changes in the intrathoracic and intra-abdominal pressures that may potentially mimic cough on manometry. Hence, more information regarding the acoustics and pressure topography patterns of throat clearing may be helpful in understanding the pathogenesis of cough and differentiating it from throat clearing [5, 6].

The aim of this study was to evaluate the acoustic signal for both cough and throat clearing using a new acoustic cough monitoring system that utilizes a combination of tracheal, chest wall and ambient sound sensors to record acoustic signals that are then analyzed with computer software to identify cough events. We hypothesize that this technique may be able to distinguish cough from throat clearing based on key elements of the cough signal. Given that manometry has also been used to refine reflux testing in terms of cough detection, we also sought to define the manometric signature of throat clearing as this has not been rigorously studied.

Methods

Subjects and study protocols

Ten asymptomatic volunteers (7 females, mean age 31.1) were included. Volunteers were recruited by advertisement or word of mouth and had no history of gastrointestinal symptoms or surgery. All subjects underwent simultaneous acoustic cough monitoring, high

resolution manometry (HRM), and esophageal multichannel intraluminal impedance-pH (MII-pH) monitoring for 80 minutes. The subjects were trained to simulate cough and throat clearing in a randomized order every 6 minutes during the study after an accommodation period. Altogether, 5 episodes of cough and 5 episodes of throat clearing for each subject were required. The study protocol was approved by the Northwestern University Institutional Review Board and informed consent was obtained from each subject.

Esophageal high resolution manometry

HRM studies were performed using a 4.2 mm outer diameter solid-state assembly with 36 circumferential sensors at 1-cm intervals (Sierra Scientific Instruments, Los Angeles, CA). Transducers were calibrated at 0 and 300 mm Hg using externally applied pressure. The manometric assembly was placed transnasally and positioned to record from the hypopharynx to the stomach with about three intragastric sensors. The study was carried out with the patients in the upright position.

Acoustic cough monitoring

Acoustic cough monitoring (Sandhill Scientific Inc., CO, USA) was used to detect the cough through a combination of the following: 1) a vibratory sensor placed above the sternal notch to record the vibration of the trachea (tracheal sensor), 2) a vibratory sensor placed at the 2nd intercostal space in the mid-clavicular line to record the chest wall sounds (thoracic sensor), 3) a microphone on the collar to record the ambient sound, 4) a respiratory belt positioned on the lower thoracic cavity to monitor respiration (Figure 1).

Multichannel intraluminal impedance-pH (MII-pH) monitoring

MII-pH monitoring was performed using a Sleuth™ system - Multichannel Intraluminal Impedance Ambulatory System (Sandhill Scientific Inc., CO, USA), which includes a portable data logger with impedance-pH amplifiers and a catheter containing two pH channels and six impedance channels. The catheter was calibrated at pH 4 and 7 with buffer solutions before intubation. It was placed transnasally alongside of the HRM catheter and positioned to record the pH change 5 cm above the LES and impedance change 3, 5, 7, 9, 15, 17 cm above the LES.

Data analysis

The HRM for each subject was reviewed manually using the Smart Mouse tool in ManoView™ software (Given Imaging). Intra-esophageal pressure, intra-gastric pressure and the gastric-esophageal pressure gradient were analyzed 5 seconds before the event as well as during the cough and throat clearing events. The pattern of the events and the duration of the pressure changes were assessed using the 30 mmHg isobaric contour to determine whether distinct patterns could be identified. Occlusive maximal pressure force along the length of the upper esophageal sphincter (UES) and esophagogastric junction (EGJ) was measured using the e-Sleeve and referenced to gastric pressure (Figure 2).

For acoustic cough monitoring analysis, automated cough detection analysis was performed with PulmoTrack computer software (iSonia, CA, USA) to identify cough events and time of onset. The automated analysis used a two step analysis algorithm in which cough

“candidates” are identified based on sound amplitude patterns. In the second step the “candidates” are verified based on fit to a cough pattern in both the time and frequency domains. A blinded investigator reviewed the audio recordings to verify the timing of the cough and throat clearing. The accuracy of the automated acoustic analysis and the blinded reviewer were compared against the original protocol.

Impedance-pH tracings were analyzed manually, all reflux episodes were characterized as acidic ($\text{pH} < 4$), weakly acidic ($4 \leq \text{pH} < 7$), or weakly alkaline ($\text{pH} \geq 7$) according to a consensus report on the detection and definitions of GER[7]. The contents of refluxate including liquid, gas and mixed were detected as previously described [8].

Statistical analysis

All the parameters were presented as a median value (interquartile range). The sensitivity and specificity for both the acoustic cough monitoring and the blinded investigator to define the cough were calculated to validate the accuracy of the device. Manometric measures of cough and throat clearing were compared using the Mann-Whitney test. All P values were two-tailed with the level of significance defined at 0.05.

Results

The accuracy of acoustic cough monitoring

In total, there were 100 events during the study protocol; 50 cough and 50 throat clearing. Using the protocol as the gold standard, 8 episodes of cough (16%) were missed by the automated acoustic analysis and 25 episodes of throat clearing (50%) were mistakenly detected as cough. Thus, the sensitivity and specificity of automated acoustic analysis was 84% and 50% for cough compared to the protocol (Table 1). There were 31 spontaneous natural sounds outside of the protocol that were recorded and documented by an investigator monitoring the patient. These were noted during the protocol and defined as cough ($n=7$), throat clearing ($n=12$), belching ($n=7$) and laughing ($n=5$). The automated acoustic analysis missed 1 of the 7 spontaneous cough events (14%) and 10 other spontaneous sounds (32%) were misclassified as cough (5 spontaneous throat clearings and 5 laughs).

The manual assessment of listening to the events by the independent blinded reviewer revealed a higher sensitivity and specificity compared to the automated acoustic analysis. Five episodes of cough (10%) were missed and 3 episodes of throat clearing (6%) were mistakenly categorized as cough by the investigator. Using the protocol as the gold standard, the blinded analysis based on sound alone revealed a sensitivity and specificity for cough of 94% and 90% (Table 1).

The manometric profile of cough and throat clearing

Fifty cough and 50 throat clearing events were analyzed manometrically. Typical pressure topography of cough and throat clearing events are illustrated in Figure 3. Both events began with a decrease in esophageal pressure (brief inspiration), followed by a distal excursion of the EGJ high-pressure zone and UES with a concomitant increase in UES and EGJ occlusive pressure relative to intragastric pressure, followed shortly by an abrupt simultaneous

increase in gastric and esophageal pressure (Figure 3). All throat clearing events had a single pressure burst, while the cough events had bursts which varied from 1 to 3 with a median of 2. Thus, the coughs were typically associated with more repetitive pressurizations.

Comparison of the manometric profile between cough and throat clearing (Table 2) revealed a higher gastro-esophageal pressure gradient within 5 seconds before coughing than before throat clearing ($p=0.048$). Additionally, there were greater occlusive UES pressure, intra-gastric ($p<0.001$) and intra-esophageal pressures ($p<0.001$) during cough. The distal gastroesophageal junction shift was also more pronounced during cough ($p<0.001$). Furthermore, the total duration of sustained pressure increase was significantly longer in cough than throat clearing ($p<0.001$). However, when the duration of only a single pressure burst was compared, the first pressure burst of cough and throat clearing had similar duration ($p=0.131$). Cough and throat clearing were equally likely to be followed by swallows (52.9% vs. 43.4%, $p=0.391$), whereas the throat clearing had a shorter latency for swallows following the event (1.5 s vs. 3.5 s, $p=0.036$). Interestingly, the gastroesophageal gradient and the occlusive EGJ pressure were similar during the events. Comparison of the manometric parameters between the protocol cough events detected and those missed by the acoustic cough automated analysis was performed to determine whether cough events that were misclassified were overtly different in terms of the pressures generated during the event and there was no significant difference between the coughs that were detected and those that were missed (Table 3).

In order to validate the manometric pattern we obtained from the protocol cough and throat clearing events, we also analyzed spontaneous random events. We identified 19 cough and throat clearings among 31 spontaneous events outside of the protocol to review. Two throat clearings were too weak to cause any change on the esophageal pressure topography, leaving 10 spontaneous throat clearing events and 7 spontaneous coughs for analysis. The sensitivity and specificity of the manometric patterns defined by the protocol to detect cough were 71.4% and 50%. The spontaneous cough events that were mistakenly categorized as throat clearing were all associated with a single pressurization.

The simultaneous MII-pH tracing were reviewed manually. In total, there were 5 reflux episodes during the procedure and no reflux events occurred during the throat clearing or cough events. One weakly acidic gas reflux occurred 30 seconds after throat clearing, one weakly acidic mixed reflux and one weakly acidic gas reflux occurred 42 seconds after cough. The other two weakly acidic gas reflux episodes occurred during belching.

Discussion

Studies on the cough-reflux relationship have been hampered by difficulty in accurately identifying the time sequence between cough and reflux on ambulatory reflux testing. The acoustic cough monitoring system is a newly developed device to detect cough through an automated sound recognition paradigm that would remove the unreliable nature of patient event marking [4]. However, we hypothesized that the accuracy of acoustic monitoring could be compromised by throat clearing which has similar sound characteristics and is also potentially related to reflux. Our results support that the automated cough detection system

was associated with good sensitivity, but was unable to accurately distinguish cough from throat clearing with 50% of the protocol throat clearing events being scored as a cough. Additionally, we also discovered that the manometric profile of cough and throat clearing are similar in qualitative pattern, but differ in that the former had more vigorous pressure changes and was often associated with repetitive pressurizations. These findings suggest that throat clearing may be difficult to distinguish from cough either manometrically or acoustically.

Acoustic cough analysis uses a combination of chest wall sound, vocal cord sound, ambient sound and respiratory movement to detect cough and distinguish it from potential confounders. Based on our results, this technique appeared to be extremely reliable when the four variables are utilized. However, throat clearing shared a similar sound pattern and thus, the system over-diagnosed cough resulting in poor overall specificity. The difficulty in distinguishing cough from throat clearing may result from the fact that they share similar physiology. Cough is caused by stimuli in the trachea, clearing the material in the airway, while throat clearing is caused by a stimuli in the throat and clears the larynx. Hence they both represent physiological clearing mechanisms. To our knowledge, this was the first study to compare the manometric profile of throat clearing and cough. We observed that cough and throat clearing shared a similar pattern: 1) an initial decrease of esophageal pressure caused by thoracic movement associated and deep inspiration; 2) a distal excursion of the EGJ high pressure zone with downward diaphragmatic movement that was associated with an increase in EGJ and UES pressure; followed by 3) an abrupt increase of intragastric and intraesophageal pressure. Thus, both events utilize a sharp change in intra-abdominal and intra-thoracic pressure in an attempt to expel the irritant from the airway. The pressure changes associated with cough were more vigorous and were often associated with a repetitive pressure change related to multiple bursts of cough. In fact, throat clearing was rarely associated with repetitions of pressurization on manometry and this represented a reliable distinguishing feature on manometry. Thus, one could rationalize that throat clearing is similar to a mild cough and a mild cough can function as an attempt to throat clear.

The finding that the EGJ and UES pressures are augmented to a level above intragastric and intraesophageal pressure during the events in asymptomatic controls suggests that this may be a defense mechanism preventing reflux during periods of increased intragastric pressure (Figure 4). This was supported by the impedance data which did not reveal any episodes of reflux during the actual cough and throat clearing events. Whether compromise of the EGJ or UES is associated with clinically relevant gastroesophageal or laryngopharyngeal reflux during coughing and throat clearing will require further study in well defined patient populations.

Previous studies have tried to use 24-hour ambulatory esophageal manometry as an adjunct tool to define cough [5]. The study by Bogte et al showed that combined 24-h pH and pressure monitoring was useful in the evaluation of patients with chronic unexplained cough [5]. In that study, only a minority (39.2%) of the cough bursts detected manometrically were marked by patients who had undergone both combined 24-h pH and pressure recording. That low detection rate of cough might be due to the fact that the patient did not report throat clearing and this symptom could have mimicked cough manometrically. While one

could make the argument that these two symptoms could be lumped together because they both facilitate airway clearance, it is still useful to distinguish between them in research and clinical practice. Even though the automated system utilized in the study was poor in distinguishing cough from throat clearing, the manual assessment was very accurate and thus, there is still hope that further modifications to the automated acoustic analysis may be helpful.

One limitation of the current study was the nature of the simulation of the cough and throat clearing by the volunteers. The mechanism of cough and throat clearing may be different when one is associated with a stimulated reflex or a involuntary effort to expel an irritant. All protocol events were voluntary simulations, which might be more or less vigorous than spontaneous events, and this could have altered the manometric pattern. However, we were able to identify a small number of spontaneous coughs and throat clearings during the study and the manometric profile of those events were consistent with the simulated events. Certainly, a more vigorous assessment of spontaneous events in a more well-defined patient population will be required to improve acoustic detection and also to validate whether the manometric pattern of cough and throat clearing can be utilized to distinguish these events. Additionally, these findings will also have to consider how the pathophysiology of cough and throat clearing are altered by perception of the stimuli and the potential that these events may be modulated by behavioral and psychological factors.

In conclusion, the automated acoustic method of cough detection was associated with good sensitivity and poor specificity suggesting that investigator verification is requisite until software modifications facilitate distinguishing cough from throat clearing. Our data also suggest that pressure topography may help distinguish cough from throat clearing. However, it also suggests that they share similar pressure patterns and this may hamper our ability to differentiate these two respiratory defense mechanisms. While it is tempting to suggest that cough and throat clearing can be lumped together when assessing an associated reflux etiology, further work is required to better define the associated laryngeal mechanisms and neurologic control. Currently, it appears that manual verification of automated acoustic monitoring is an accurate tool to assess the association of cough and throat clearing with reflux and its utility can expand to other physiologic phenomenon associated with these symptoms in the ambulatory setting.

Acknowledgments

This work was supported by R01 DK079902 (JEP) and R01 DK56033 (PJK) from the Public Health Service.

Equipment was provided by Sandhill Scientific Inc..

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Figure 1.
Sensor placement for acoustic cough monitoring.

Figure 2.

Methodology for measurement of occlusive UES and EGJ pressure using the e-Sleeve. The pressure within the e-Sleeve for the EGJ and UES measurement is referenced to intragastric pressure so the two sphincters can be compared directly.

Figure 3.

The manometric profile of throat clearing and cough. Panel A illustrates a typical throat clearing, Panel B illustrates a one component cough, Panel C illustrates a two-component cough, and Panel D illustrates a three-component cough.

Figure 4.

The spatial pressure variation along the length of the esophagus. The two panels represent an EPT plot of a throat clearing event (A) and a cough (B). The white overlaid lines represent the pressure at a distinct time point (0.2 seconds) to highlight the pressure gradients through the EGJ and UES. The pressure levels at the EGJ are greater than intragastric pressure supporting that reflux is unlikely based on pressure gradients during both event types. Similarly, the UES pressure is much greater than the intraesophageal pressure making belching or laryngopharyngeal reflux unlikely based on the pressure gradients.

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The accuracy of acoustic cough monitoring and the blinded investigator to detect the cough

Table 1

	Event detected by acoustic cough monitoring		Event detected by the investigator through sound		Total
	cough	Throat clearing	cough	Throat clearing	
Protocol cough (n=50)	42	8	45	5	50
Protocol throat clearing (n=50)	25	25	3	47	50

Table 2Manometric profile of cough and throat clearing (median (25th, 75th))

	Cough (n=50)	Throat clearing (n=50)	P-value
Pre-event pressure (mmHg)			
Occlusive UES pressure *	36.7 (24.4, 48.6)	39.6 (21.6, 52.1)	0.508
Intra-esophageal	−9.0 (−12.0, −4.0)	−6.0(−10.0, −3.0)	0.052
Intra-gastric	10.0 (7.8,13.3)	10.0 (7.8,13.3)	1
Gastric-esophageal gradient	20.0 (14.2,26.3)	16.0 (13.0,21.3)	0.048
Occlusive EGJ pressure *	20.6 (8.1, 33.5)	22.7 (11.9, 29.6)	0.484
During the event pressure (mmHg)			
Occlusive UES pressure *	152.5 (106.9, 183.8)	79.1 (24.5, 125.1)	<0.001
Intra-esophageal	54.0 (27.5,72.0)	26.5 (17.0,33.0)	<0.001
Intra-gastric	65.5 (38,76.3)	38.0 (30.0,46.0)	<0.001
Gastric-esophageal gradient	11.5 (7.0,15.0)	12.0 (9.0,16.5)	0.303
Occlusive EGJ pressure *	19.4 (11.1, 29.8)	23.4 (11.6, 29.6)	0.361
Junction shift (cm)	−1.6 (0.9,1.2)	−0.68 (0,1.0)	<0.001
First component duration (s)	0.4(0.16,0.5)	0.3(0,0.6)	0.131
Event duration (s)	0.68 (0,1.0)	0.4 (0.1,0.9)	0.001

* Referenced to gastric pressure, all other values were referenced to atmospheric pressure

Table 3

Comparison of manometric profile between detected and missed cough by the automated acoustic cough analysis (median (25th, 75th))

	Detected Cough (n=42)	Missed Cough (n=8)	P-value
Pre-event pressure (mmHg)			
Occlusive UES pressure *	37.4 (24.4, 50.3)	35.8 (23.9, 40.8)	0.612
Intra-esophageal	-8.6 (-12.5, -4.1)	-8.7(-10.1, -11.1)	0.887
Intra-gastric	10.3 (7.5,14.3)	9.3 (7.2,11.2)	0.490
Gastric-esophageal gradient *	20.2 (13.8,27.4)	18.3 (14.6,22.1)	0.524
Occlusive EGJ pressure	20.6 (6.4, 34.0)	20.2 (14.8, 28.6)	0.746
During the event pressure (mmHg)			
Occlusive UES pressure *	155.9 (113.6, 195.6)	133.1 (105.7, 153.9)	0.458
Intra-esophageal	58.0 (35.3,72.0)	35.0 (17.8,56.2)	0.117
Intra-gastric	68.0 (42.0,79.3)	44.5 (33.5,71.2)	0.176
Gastro-esophageal gradient	11.0 (7.0,15.0)	14.0 (6.0,17.2)	0.397
Occlusive EGJ pressure *	20.2 (10.6, 30.1)	17.9 (13.9, 30.4)	0.990
EGJ shift (cm)	-2.1 (1.6, 2.9)	-1.8 (1.0, 2.7)	0.278
First burst duration(s)	0.4(0.2, 0.5)	0.2(0.2,0.4)	0.105
Event duration (s)	0.8 (0.2 ,1.0)	0.5 (0.2,0.9)	0.290

* Referenced to gastric pressure, all other values were referenced to atmospheric pressure