# Implementation of Objective Activity Monitoring to Supplement the Interpretation of Ambulatory Oesophageal PH Investigations

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<td>Date Submitted by the Author:</td>
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| Complete List of Authors: | Kwasnicki, Richard; Imperial College London, Hamlyn Centre  
                            | Ley Greaves, Robert; Imperial College London, Hamlyn Centre  
                            | Ali, Raza; Imperial College London, Hamlyn Centre  
                            | Gummett, Paul; Imperial College Healthcare NHS Trust, Department of Gastroenterology  
                            | Yang, Guang-Zhong; Imperial College London, Hamlyn Centre  
                            | Darzi, Ara; Imperial College London, Hamlyn Centre  
                            | Hoare, Jonathan; Imperial College Healthcare NHS Trust, Department of Gastroenterology |
| Keywords:         | activity, pH, GERD, reflux, esophagus |
Diseases of the Esophagus – Review/Rebuttal

Manuscript DES-06-14-0218 – ‘Implementation of Objective Activity Monitoring to Supplement the Interpretation of Ambulatory Oesophageal PH Investigations’

Main revisions:

1. Improved data analysis comparing pH to activity – implementing an activity associated reflux % metric (new Table 2), in addition to Spearman’s rank correlation coefficient.

2. Consideration of results from oesophago-gastro-duodenoscopy, including the relationship between hiatal hernia and activity associated reflux.

3. Enhancement of Figures 1, 3, and 4 – in line with review comments.

Editor’s Comments:

1. Need specifics on the definition for a "positive" association between acid reflux episodes and activity. What is the association window? 1 min, 2 min? A simple visualization of the tracing was too descriptive and not good enough for a manuscript.

The Spearman’s Rank correlation was used with the aim of quantifying the relationship between activity and pH continuously. The revision includes manual assessment of association between reflux episodes and activity. In this case, the association window is 15 minutes (up to 10 minutes activity preceding reflux or 5 minutes after to account for error margin in alignment of data). A reflux episode was defined as pH < 4, and a bout of activity as in the personalised high intensity range.

2. Please define strong vs weak association using Spearman's rank coefficient? How is that different than symptom index and SAP, the conventional way to correlate symptoms with acid reflux event.

This description of association has been removed. Unfortunately the symptom index was poorly used (and understood) by the study subjects and therefore omitted from analysis. The revision includes manual assessment of association between reflux episodes and activity.

3. What was the % of reflux episodes associated with activity, (= # reflux episodes associated
with activity divide by total # of reflux episodes) of each of the 13 subjects? This would be easier to understand than Spearman's rank coefficient.

This has been completed as requested – please see point 1 for details.

4. From the paper, only 2 of 13 subjects had a significant association between reflux events and activity. That's not very good.

It is possible that reflux was associated with other triggers, including eating or posture, or also possible that some activities were not detected by the sensor (typically carrying shopping or cycling). The indication for pH manometry was not specified in the study inclusion criteria, and therefore patients with hiccups or coughs were recruited (n=5). It would be less likely that these subjects would have exercised induced reflux.

5. Was there a specific software to collection and analysis the pH and activity data together?

No – data outputs from pH manometry software (Polygram Net PH Testing application, Medtronic) and e-AR sensor software (bespoke, Imperial College London) were in the same format (space separated values – easy conversion to spreadsheet etc.) so were easily amalgamated. The sampling frequencies were different by a factor of 16, so the e-AR activity data was down sampled following activity intensity calculations to synchronise datasets for manual analysis. Due to the similarities in data format, in the future it is likely that the devices could be combined, possibly with the accelerometer embedded in the receiver (rather than the probe), allowing dual outputs and streamlined data analysis.

6. Why wasn't pH-impedance catheter use instead of just pH catheter?

A pH-impedance catheter was used. There was no dysmotility reported for any of the subjects. The manuscript has been amended to show this.

7. Figure 2 is a box plot, please define the box borders and lines.

The box plot definitions have been added to the figure legend.
Reviewer(s)' Comments to Author:

Reviewer: 1

This was an interesting and novel way to record activity during pH testing which could be used in the future. However, the paper has several major limitations that make the results difficult to draw conclusions from other than what is already known: decreased activity with pH catheter testing. Small number patients limits power of the study. Only 2/13 patients demonstrated increased reflux episodes with increased activity. Dr. Fass already showed in the past that there was a decreased level of activity and alteration in daily activities during pH testing based on patient reports. He noted significant changes in number meals, coffee intake which could play a role in the results of the pH testing.

Thank you for the comments. You are correct re. Dr Fass’ findings, and we have reported this explicitly (ref 6), however this study aimed to prove the point using an objective measure of physical activity, as there are inherent limitations with activity questionnaires/diaries. Regarding the fact that only 2/13 patients had exercise-induced reflux, this might be explained by the indication for pH manometry not being specified in the study inclusion criteria, and therefore patients with hiccups or coughs were recruited (n=5). It would be less likely that these subjects would have exercised induced reflux. More detail has been added to the results (particularly Table 2) which we hope will improve clarity here.

1. It is important to report patient diaries in the study including their activities, meals, and sleep. These are important confounders noted in prior studies to correlate with reflux episodes.

Data analysis was conducted using only data collecting during wakeful hours. We have reported activity, meals, and supine posture or sleep from the data collected (Fig. 3). Reflux episodes during meals (or up to 30 mins after) and supine posture was omitted from analysis when considering associations with activity.

2. Unclear what level/intensity of activity correlated with each score of restful, low, moderate and high intensity. 1 minute intervals seems too short to classify an activity.
The authors wanted to provide relative, patient-specific levels of activity to compare. As such a method similar to that described by Crouter SE et al (2010) (ref 13) was implemented, where activity intensity is quantified temporally, then classified using intensity boundaries. As the boundaries are individualised, it is not possible to say exactly what activities correspond to each classification. However the authors feel this was the best method to use to answer the primary clinical question of the study. Regarding the second point, the 1-minute intervals provide minute-by-minute activity levels, which are able to characterise one’s physical activity with reasonable temporal resolution. Although it is possible, in this study we were not identifying or classifying specific activities. A higher sensor sampling frequency would be required and this would reduce the battery life, which would add further logistical challenges to data collection. However this may be worth investigating in the future.

3. No symptom index was reported with pH testing.

The authors found that the symptom index was either poorly used, or not used at all by patients in this study. Upon questioning, patients’ understanding of the function was inconsistent. As such, we have not included it in the analysis.

4. Not noted how pH probes were place ie manometry or endoscopically

Manometrically – this has been added to the methods section.

5. No EGD's were documented for patients. Could be useful as those with large hiatal hernias will reflux more with more activity

Data regarding EGD’s has been added to the manuscript, and your prediction seems to be the case – the 2 patients with highest reflux/activity relationship have hiatal hernias.

6. Too strong statement that activity alone should justify recalibration of the Demeester score. Would also need to evaluate normals and changes in activity to see the significance.

The authors acknowledge this comment, and agree that the wording is too strong. It has been amended. We do however believe that should a significant reduction in activity be recorded
during the test, the validity of the investigation is questionable.

7. Not stated that pH testing was done off PPI. I assumed this was the case.

Thank you for this comment. We thought that it would be a common assumption with the readers, but have added it to the methodology to remove any ambiguity.

8. Useful to have baseline demographics table

Demographic details have been included in a new table in the results section.

Reviewer: 2

Comments to the Author
The study by Kwasnicki et al. evaluated objective activity monitoring during standard ambulatory 24 hour esophageal pH testing. Objective activity monitoring was performed using a validated technique (i.e. ear-worn motion sensor) 2 days prior to and the day of 24 hour esophageal pH testing. The main findings were that average patient activity levels decreased by 26.5% during pH monitoring. No prior studies have objectively measured patient activity in adults and I applaud the authors for addressing this problem with their study. However, the data on the relationship between activity and esophageal pH are somewhat thin/sparse especially knowing that this was one of the aims of the study. Including additional data/analysis/metrics on the association between activity and reflux would help to strengthen the manuscript.

Thank you for the comments. As your comments on the activity vs. reflux data are common amongst reviews and the editor, we have worked to add more detail and transparency to the manuscript.

(1) There were several instances throughout the paper of poor grammar and sentence structure (e.g. sentence 1 of the introduction; paragraph 2, sentence 2 of the introduction [use of is rather than are]; sentence 1 of the last paragraph in the introduction [use of who’s rather than whose; last sentence of the conclusion]). These need to be addressed.
I apologise for the errors in grammar. Thank you for providing examples related to this comment. I hope you find the changes satisfactory.

(2) Figure descriptions need not be in the body of the text as separate paragraphs. Please address this formatting issue.

The figure descriptions now only appear in the page specified for figure legends at the end of the manuscript.

(3) Most readers will not be familiar with the ear-worn activity recognition sensor. It would be nice to have a photo of the actual device in addition to seeing how the device is worn (Figure 1).

Figure 1 has been adjusted to include both an image of the device as well as how it is worn.

(4) In the methods section, the authors mention that a sampling frequency of 50 Hz was used within an acceleration range of +/- 3g so that the device did not require charging during the data collection period. Are these standard settings that have been validated in prior studies of gait analysis, activity classification, and energy expenditure?

The acceleration range is fairly standard for such human worn devices, a balance of sensitivity to capture most small movements but not have a ceiling/floor effect for larger movements. The sampling frequency of the e-AR sensor can be modified depending on the application. For detailed gait analysis (i.e. capturing heel contact and toe off), our group usually uses approximately 100Hz (see Jarchi et al. IEEE Trans Biomed Eng. 2014 for interest), yet for energy expenditure or activity levels, the e-AR sensor has been validated at just 4 Hz (Bouarfa et al. IEEE Trans Biomed Eng. 2013) which was the chosen sampling frequency for this study. The 50Hz mentioned in the initial manuscript is incorrect. This has been changed to 4Hz and the appropriate reference has been added.

(5) In the methods section regarding esophageal pH data…how was an esophageal acid reflux event defined? were meal periods excluded in the pH analysis? were pH data analyzed automatically by the pH software or were the data individually analyzed (thus eliminating
false positive and false negative reflux events)?

The revision includes manual assessment of association between reflux episodes and activity. In this case, the association window is 15 minutes (activity up to 10 minutes before reflux or 5 minutes after to account for a small margin of error in the alignment of data). A reflux episode was defined as pH < 4, and a bout of activity as in the personalised high intensity range. Reflux episodes during meals (or up to 30 mins after) and supine posture was omitted from analysis when considering associations with activity. This has been added to the methodology.

(6) I have no problems with how the data was analyzed for the ear-worn activity recognition sensor [calibrated for each participant into quartiles]. However, I would like to see more information/data on activity level (rest, low intensity, moderate intensity, high intensity) with pH related data (# of acid related events during each of the various activity levels along). This would allow one then to compute an activity index or activity associated probabilities (similar to the classic symptom index and symptom associated probability).

Further analysis of reflux episodes and the associations with activity have been reported in the revised manuscript.

(7) The dates in the methods section and the first paragraph of the results are not consistent. Please clarify.

Thank you – this has been clarified in the manuscript.

(8) Figures 3 and 4 should be better labeled (use of arrowheads and/or arrows) in order to clearly/effectively demonstrate relationship between activity and reflux.

The figures have been amended to improve the clarity in relationships between activity and reflux.
IMPLEMENTATION OF OBJECTIVE ACTIVITY MONITORING TO SUPPLEMENT THE INTERPRETATION OF AMBULATORY OESOPHAGEAL PH INVESTIGATIONS

Kwasnicki R M,1 Ley Greaves R,1 Ali R,1 Gummett P A,2 Yang G Z,1 Darzi A,1 Hoare J.2

1 Hamlyn Centre, Institute of Global Health Innovation, Imperial College London
2 Department of Gastroenterology, Imperial College Healthcare NHS Trust

Contact:
Mr. Dr. Richard Mark Kwasnicki
Hamlyn Centre, 3rd Floor Paterson Centre
St Mary’s Hospital, Praed Street
Paddington
London W2 1NY United Kingdom

Telephone: +44 (0)7851759471
Email: Richard.Kwasnicki07@imperial.ac.uk

Running head: Activity during ambulatory pH monitoring

This paper was presented at the British Society of Gastroenterologists annual meeting - Manchester, UK (June 2014)
Abstract

Background

Conventional catheter-based systems used for ambulatory oesophageal pH monitoring have been reported to affect patient behaviour. As physical activity has been associated with gastro-oesophageal reflux disease (GORD), there is a risk that abnormal behaviour will degrade the value of this diagnostic investigation and consequent management strategies.

Purpose

To quantify the effect of conventional pH monitoring on behaviour and to investigate the temporal association between activity and reflux.

Methods

Twenty patients listed for 24h pH monitoring underwent activity monitoring using a lightweight ear-worn accelerometer (e-AR sensor, Imperial College London) 2 days prior to, and during their investigation. pH was measured and recorded using a conventional nasogastric catheter and waist-worn receiver. Daily activity levels, including subject-specific activity intensity quartiles, were calculated and compared. Physical activity was added to standard pH output to supplement interpretation.

Results

Average patient activity levels decreased by 26.5% during pH monitoring (Range -4.5 - 51.0%, \(p=0.036\)). High intensity activity decreased by 24.4% (Range -4.0 - 75.6%, \(p=0.036\)), and restful activity increased on average by 34% although this failed to reach statistical significance.
significance (-24.0 – 289.2%, \( p=0.161 \)). Some patients exhibited consistent associations between bouts of activity and acidic episodes.

**Conclusions**

The results of this study support the previously reported reduction in activity during ambulatory oesophageal pH monitoring, with the added reliability of objective acquired data. In the absence of more pervasive pH monitoring systems (e.g. wireless), quantifying activity changes in the setting of activity-induced reflux might facilitate recalibration, guide the physicians’ interpretation of patient DeMeester scores and therefore resulting in more appropriate management of GORD.

Keywords: activity; pH; GORD; reflux; oesophagus
Introduction

Gastro-intestinal disorders, including gastro-oesophageal reflux disease (GORD) and dyspepsia, feature in up to as much as 10% of general practice consultations in the UK. In addition to the significant costs incurred by the NHS (£760m in 2004), the associated impact on patient quality of life is well documented in both GORD and dyspepsia.

A multitude of exacerbating factors exist, including eating and drinking, particularly spicy foods, coffee and alcohol, body orientation, and physical activity. Due to the sporadic nature of the condition, the diagnosis and characterisation of the disease is often achieved by collecting ambulatory oesophageal pH measurements over 24-hours. Conventionally, pH is measured 5cm proximal to the oesophageal-gastric junction with a naso-gastric catheter. The DeMeester Score is calculated based on the number of reflux episodes and the amount of time an oesophageal pH of less than 4 is recorded, under various conditions such as upright and supine (as recorded by the patient).

Although the catheter is largely unrestrictive, the extracorporeal component is visible, creating the potential for a psychosocial behavioural response. Fass et al. investigated this response using patient diaries, which reported a reduction in activity, number of meals and cups of coffee during pH monitoring. Furthermore, comparisons with implantable pH monitors such as the Bravo system have shown patients coping better and interfering less with daily activities, eating and sleep. However, other work contradicts these findings. In one study of 114 patients, although 65% recalled a reduction in physical activity, no other behavioural changes were noted including eating, alcohol, smoking and sleeping. A similar study with not dissimilar methodology also showed lifestyle alteration being minimal in
patients undergoing pH monitoring, with no association between lifestyle alteration and pH profiles.⁹

Most of the work on this matter has involved ample patient samples, yet weakness lies within data collection strategies. Each study implemented a different survey or questionnaire in which patients were asked to recall behaviours. This approach is inherently flawed due to subjectivity related to interpreting and answering the questions, and is a possible cause for the apparent dispute in the literature.

Numerous devices have been developed to monitor activity and classify behaviour, including pedometers, bi/tri-axial accelerometers, and GPS trackers. An ear-worn motion sensor (e-AR, Imperial College London) has been proven to provide valid predictions of energy expenditure,¹⁰ gait parameters,¹¹ and activity classification.¹² The implementation of such a device in this scenario may provide more reliable, objective information regarding activity behaviour during pH monitoring.

In the setting of a patient whose activity is directly related to their symptoms, pH data collected during a day in which behaviour is abnormal may not provide an accurate representation of their pathophysiology. Therefore the important questions to answer are firstly, is the patient’s pathology associated with activity, and if so, has the patient’s activity changed significantly during the investigation. In this situation, the DeMeester score should be interpreted with caution, and a re-calibration of the score may be necessary.
In light of this, our aim was to implement a wearable activity monitor before and during pH investigations to assess associations between pH and activity, and to objectively assess investigation-related changes in physical activity.
Materials and Methods

Twenty patients scheduled to undergo 24-hour ambulatory oesophageal pH monitoring at St Mary’s Hospital, London, between January–March 2012 and January–February 2013 were recruited. Exclusion criteria included extremes of age (18 > Age > 65), having already undergone pH testing, hospital inpatients or care home residents, patients with mobility disorders, and being unable to wear the sensor (e.g., bilateral hearing aids). As recruitment occurred in the clinic setting, NHS translators often accompanied non-English speaking patients, and as such, we were able to include these patients if the consent procedure was successfully translated.

Two days prior to the investigation, participants were given a lightweight, ear-worn activity recognition sensor (e-AR, Sensixa Ltd and Imperial College London) to wear during wakeful hours. On the day of the investigation, a standard pH-impedance catheter was placed in the distal oesophagus 5 cm above the manometrically identified lower oesophageal sphincter. Patients were asked to stop all antacid medication 7 days prior to the investigation. The e-AR sensor was returned to the investigators upon removal of the naso-gastric catheter (end of day 3). This provided a 3-day dataset for each patient, where the first 2 days were ‘normal’ (Monday, Tuesday) and the third day was the ‘investigation’ day (Wednesday). Although patients were told that the sensor monitored activity, the hypothesis of the study was not revealed. At the end of the study period, patients were asked to complete a short questionnaire to assess sensor compliance and any unforeseen events during data collection that might have affected activity levels.

Figure 1. e-AR sensor and oesophageal pH catheter in situ (subject is co-author, not patient)
The e-AR sensor is a lightweight (7.4g), ear-worn tri-axial accelerometer (ADXL330), which has been validated in gait analysis, activity classification and energy expenditure.\textsuperscript{10-12} A sampling frequency of 450Hz was used, within an acceleration range of +/- 3g. These settings have been validated for estimating energy expenditure.\textsuperscript{10} Furthermore, the low sampling frequency prevented the device from needing charging during data collection. All data were stored on the sensor.

Oesophageal pH and manometry data, recorded at 0.25Hz, were uploaded from the waist-worn processing unit using Polygram Net PH Testing Application (Medtronic, Denmark). Oesophageal dymotility, and a measure of oesophageal acid exposure, the DeMeester Score,\textsuperscript{5} were calculated from the data for each participant.

This clinical trial was registered at clinicaltrials.gov (NCT01507298) and received ethical approval by the Research Ethics Committee of London (11/LO/1981).

**Data Analysis**

E-AR sensor data for each participant were segmented according to experimental day, starting and finishing upon placement or removal of the sensor. A ‘counts-based’ method was used to estimate activity from body (sensor) motion intensity.\textsuperscript{13, 14} Activity levels were grouped at 1-minute intervals into restful, low, moderate or high intensity activity. Activity levels were calibrated for each participant, classifying activity into quartiles, where the most inactivity was labelled ‘Restful’, 2\textsuperscript{nd} quartile ‘low intensity’, 3\textsuperscript{rd} quartile ‘moderate intensity’ and upper
quartile ‘high intensity’. This provided a personalised activity profile with which to compare activity during the investigation.

Activity during the investigation was aligned with oesophageal pH in order to investigate possible association. Correlation of these non-parametric data was assessed statistically using Spearman’s rank coefficient. Also, manual assessment of association between reflux episodes and activity was performed (i.e. episodes of reflux associated with activity / total episodes of reflux, %). The association window was 15 minutes (activity up to 10 minutes before reflux or 5 minutes after, to account for error margin in alignment of data). A reflux episode was defined as a pH < 4, and a bout of activity in the personalised high intensity range. Reflux episodes during meals (or up to 30 minutes after) and during supine posture were omitted from analysis when considering associations with activity to minimise false positives. Non-parametric, paired data were analysed using Wilcoxon signed rank tests to assess whether activity changes during the investigation were statistically significant.

Statistical analysis was performed using Statistical Package for Social Sciences version 21 (SPSS, IBM Corp, NY, USA).
Results

Twenty patients scheduled for ambulatory oesophageal pH monitoring were recruited between March 2012 and February 2013. Six patients were excluded as they couldn’t tolerate the nasogastric catheter insertion, and 1 patient lost the e-AR sensor. Of the participants whose data were analysed (n=13), there were 6 females and 7 males with a mean (SD) age of 53 (11). The main indication for the investigation in the majority of patients was dyspepsia (n=8), with other causes including chronic cough and hiccups. There was no significant difference in the demographics of those who were excluded.

There was no difference in overall activity between day 1 and day 2 (100% vs. 94.7%, $p = 0.674$). There was a statistically significant difference between overall activity during day 1 and 2 (combined) and the test day (97.4% vs. 75.4%, $p = 0.036$). When assessing activity based on subject-specific activity quartiles, high intensity activity decreased by 24.4% (Range -4.0 - 75.6%, $p = 0.036$), and restful activity increased on average by 34% although this failed to reach statistical significance (-24.0 – 289.2%, $p = 0.161$). Low and moderate intensity activity appeared to be relatively unchanged. (Figure 2 and Table 1)

Figure 2—Relative change in physical activity during the ambulatory pH monitoring investigation. A significant reduction in high intensity activity was seen, with a corresponding increase in restful activity (approaching significance).

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<th>Table 1. Investigational changes in physical activity (stratified according to activity intensity)</th>
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Demographic data alongside the results of the clinical investigations and activity measurements are shown in Table 2. These results are displayed for the purpose of proving the concept of measuring reflux associated with activity, not for statistical subgroup analysis.

Table 2

Patients with dyspepsia as the indication for investigation appeared to have a higher proportion of reflux associated with activity (32 vs. 5%). Of the 6 patients who had OGD’s, the 3 patients with hiatal herniae had on average 45% of their reflux episodes associated with bouts of activity. Two of the 3 patients with hiatal herniae also had a statistically significant correlation between longitudinal activity and pH (Spearman’s Rho = 0.208 and 0.326, p < 0.001).

Activity was plotted alongside pH to supplement interpretation of results. (Figure 3) Patient 10 was dyspeptic and had a hiatal hernia diagnosed on OGD. Their level of moderate and high intensity physical activity during the investigation was reduced by 25%, with corresponding increases in restful and low intensity activity. In the setting of high activity-induced reflux (55%) it is plausible that the DeMeester score (6.7) would have been higher if the patient’s activity behaviour during the investigation was more representative of a typical day. (Figure 4)

Figure 3. Synchronised activity and oesophageal pH over 12-hours, including expanded 2-hour segment. It is possible to see both supine posture and activity associated with acidic episodes.

Figure 4. Patient with low DeMeester score but with distinct reflux episodes associated with bouts of
Discussion

This study is the first of its kind in adults to report objectively measured reductions in physical activity during ambulatory oesophageal pH investigations. The main source of activity reduction was from diminished high intensity activity and increased restful activity. Low and moderate intensity activity appeared to remain relatively unchanged. There was however considerable variation in response, with some patients showing minimal activity change or even a small increase during the investigation. Continuous motion data allowed physical activity to be plotted alongside standard clinical outputs, providing additional context to any pH changes noted. In some patients, an association was seen between pH and bouts of activity.

A small body of evidence exists regarding behavioural changes during pH monitoring. This diagnostic test is conducted in the ambulatory setting in order to profile natural fluctuations in oesophageal pH during a standard 24-hours. However, living and behaving normally whilst a naso-gastric catheter is in situ is not without challenges. Evidence suggests that the catheter isn’t physically restrictive, but more so a visual embarrassment, inhibiting normal social behaviours. This coincides with reported reductions in physical activity yet normal eating, drinking, smoking and eating habits, all of which can be done in the home environment. There does exist one study where behavioural changes in children undergoing ambulatory oesophageal pH testing were investigated using a tri-axial accelerometer (similar to e-AR sensor). Similar to the present study, this work reported substantial decreases in physical activity, particularly those of high intensity.
Activity levels did not decrease in all patients, and results appeared to depend somewhat on occupation, though sample size was insufficient to test this theory. Subjects who held a full-time job often planned on taking a day off work and finding seclusion during the investigation to prevent unwanted disclosure of personal information in the workplace or social circles. It is probably unfeasible to prevent sick leave under these circumstances, yet it might be more acceptable to advocate a short protocol of activities which might be experienced during daily life such as some vigorous marching on the spot or some lifting and carrying, particularly if this is when patients tend to experience symptoms.

In some subjects the association between activity and low pH was clear. Activity is a very simple but effective adjunct to standard monitoring outputs, and relatively easy to record. An accelerometer could feasibly be incorporated into the current pH device. The addition of activity and body orientation data may help provide a better insight into patient pathophysiology, and improve the selection of the best course of treatment.

It is unreliable to make any assumptions of altered behaviour based on questionnaire data. However, collecting peri-investigational activity data probably requires an extra appointment, which is not always feasible. A more efficient method might be to collect activity data during the investigation, then should pH correlate with activity, ask for a further (post-investigational) activity sample without the catheter in situ for comparison. A significant change in physical activity may then be taken into account by the physician during the interpretation of the DeMeester score. activity be significantly different, the DeMeester score can be activity-adjusted.
In theory, implantable pH monitoring with systems such as the Bravo may largely remove the psychosocial effects from the test. Minimally invasive methods are likely to negate the disadvantages of the catheter-based approach with regards to physical activity. However, activity data may still prove useful to supplement the interpretation of pH changes.

Interpretation of results must be done so in the context of study limitations. Most limiting was the study design aspect requiring patients to attend an extra appointment to collect the e-AR sensor. Although the investigators were flexible regarding appointment times, the extra appointment was certainly a hindrance to recruitment and may have skewed the sample towards unemployed subjects. In this event, the results would have more likely been under emphasised, as one might postulate unemployed subjects are less likely to change their lifestyle during the test. Furthermore, data from 7 subjects were unusable as 6 patients failed to tolerate the catheter insertion and 1 patient lost the sensor. Though patient demographics of this subgroup were not dissimilar to that of the remaining cohort, there is potential for selection bias. Whilst the method of activity data collection implemented is more reliable and comparable than that in questionnaire studies, it increases the demand on the user, giving rise to a new set of challenges. Improving the coordination of sensor distribution to patients and streamlining data analyses is essential for future research or clinical applications.

Conclusions

This is the first study in adults to show objective reduction in activity during ambulatory oesophageal pH investigations. The results further demonstrate how activity data may be used to supplement the interpretation of pH changes. As the prevalence and healthcare burden of GORD is significant, and the results of the investigation at hand may provide
indications for a major surgical procedure, the practical limitations of ambulatory pH monitoring must be defined, and if not overcome, factored in to the interpretation of results.
Acknowledgements

Thank you to Miss Ella Etienne for her assistance in patient recruitment.

Funding, in part, was provided by the Engineering and Physical Sciences Research Council (EPSRC) as part of the ESPRIT programme grant, and the National Institute for Health Research (NIHR) Biomedical Research Centre based at Imperial College Healthcare NHS Trust and Imperial College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The e-AR sensor was provided by Sensixa Ltd, a spin-off from Imperial College London, for which GZY is the director.

Contributions

RMK and AD provided the concept for the study, RMK, GZY and JH designed the study, RMK, RLG, RA and PAG collected and analysed the data, RMK, GZY and JH interpreted the results, RMK wrote the paper. All authors approved the final version of the manuscript.
References


Figure legends

Figure 1. E-AR sensor (also inset) and oesophageal pH catheter in situ (subject is co-author, not patient)

Figure 2. Relative change in physical activity during the ambulatory pH monitoring investigation. A significant reduction in high intensity activity was seen, with a corresponding increase in restful activity (approaching significance). The values on the box plot from bottom to top represent the minimum, lower quartile, median, upper quartile, and maximum values.

Figure 3. Synchronised activity and oesophageal pH over 12-hours, including expanded 2-hour segment. It is possible to see both supine posture and activity associated with acidic episodes.

Figure 4. Patient (10) with low DeMeester score but with distinct reflux episodes associated with bouts of activity.

Table 1. Investigational changes in physical activity (stratified according to activity intensity)

Table 2. Study cohort demographics and reflux associated with activity activity-related reflux %
Table 1. Investigational changes in physical activity (stratified according to activity intensity)

<table>
<thead>
<tr>
<th>Activity Intensity</th>
<th>Normal activity Mean</th>
<th>Test activity Mean (SD)</th>
<th>Relative change (%)</th>
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<tr>
<td>Rest</td>
<td>25</td>
<td>33.5 (16.7)</td>
<td>+ 34</td>
<td>0.161</td>
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<tr>
<td>Low</td>
<td>25</td>
<td>24.1 (5.6)</td>
<td>- 4</td>
<td>0.484</td>
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<tr>
<td>Moderate</td>
<td>25</td>
<td>23.6 (7.6)</td>
<td>- 6</td>
<td>0.674</td>
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<tr>
<td>High</td>
<td>25</td>
<td>18.9 (7.0)</td>
<td>- 24</td>
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Table 2. Study cohort demographics and activity-related reflux %

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>Indication</th>
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<tr>
<td>2</td>
<td>55 F</td>
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<td>HH</td>
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<td>55</td>
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<tr>
<td>3</td>
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<td>4</td>
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<td>9</td>
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<td>-</td>
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<td>Gastritis</td>
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<td>Hiccups</td>
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<td>(112^*)</td>
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</table>

*Patient removed catheter after 6 h. HH – Hiatal hernia

Subject 9 – no pH data available

Excluding sleep/supine, during meals and 30m post prandial.
Diseases of the Esophagus

Diseases of the Esophagus

Meal
Supine

pH

Oesophageal

pH Activity
