Towards better understanding of symptoms associated with disordered esophageal function
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EFFECT OF RUNNING ON GASTROESOPHAGEAL REFLUX AND REFLUX MECHANISMS

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ABSTRACT

Background
Reflux symptoms are common among athletes and can have a negative impact on athletic performance. Currently, the mechanisms underlying excess reflux during exercise are still poorly understood. The aim of this study was to investigate the effect of exercise on reflux severity and to examine the underlying reflux mechanisms.

Methods
Healthy sporty volunteers were studied using both high-resolution manometry and pH-impedance monitoring. After a meal and a rest period, subjects ran on a treadmill for 30 min at 60% of maximum heart rate, followed by a short rest period and another 20 min period of running at 85% of maximum heart rate.

Results
Ten healthy volunteers were included. Exercise led to a significantly higher percentage of time with an esophageal pH<4 and a higher frequency and duration of reflux episodes. Moreover, exercise resulted in a decrease in contractility and duration of peristaltic contractions. The minimal lower esophageal sphincter resting pressure decreased during exercise while the average and maximum abdominal pressure both increased. Importantly, the percentage of transient lower esophageal sphincter relaxations (TLESRs) which resulted in reflux significantly increased during exercise and all but one reflux episode occurred during TLESRs. In 6 subjects a hiatus hernia was detected during the exercise period but not during rest.

Conclusions
Running induces gastroesophageal reflux almost exclusively through TLESRs. These are not more frequent during exercise, but are more often associated with a reflux episode, possibly due to an increased abdominal pressure, body movement, a change in esophagogastric junction morphology and a decreased esophageal clearance during exercise.
Gastroesophageal reflux disease (GERD) is caused by reflux of gastric contents into the esophagus. It is one of the most prevalent chronic diseases, affecting up to 20% of the population in Western countries with typical symptoms such as heartburn or regurgitation\(^1\). GERD symptoms tend to be common among athletes\(^2,3\), with epidemiological data indicating that upper gastrointestinal symptoms occur in up to 58% of surveyed athletes\(^4,5\). Previous studies have shown that strenuous exercise can induce excessive reflux, both in patients with GERD and in asymptomatic healthy subjects\(^2,6-12\), and that this mainly occurs during vigorous exercise\(^2,10,13\), suggesting that strenuous physical activity can be a risk factor for GERD.

Currently, the mechanisms underlying excess reflux during exercise are still poorly understood. Some studies suggest that an altered esophageal motility could play part\(^14,15\), such as a decreased duration, amplitude and frequency of esophageal contractions during exercise\(^14\). However, this could not be confirmed by another study\(^16\). Factors such as the anatomical compromise of the esophagogastric junction (EGJ)\(^7\), failure of the lower esophageal sphincter (LES) to act as an effective barrier\(^17\), increased intra-abdominal pressure\(^6\), decreased gastrointestinal blood flow and body position during exercise have all been suggested to influence reflux during exercise\(^2\). Even the use of a sports drink has been linked to an increase in reflux during exercise\(^17,18\). Yet again, these results could not be reproduced in a study in which a sports drink was used during cycling\(^19\).

Reflux can have a negative impact on athletic performance due to symptoms such as heartburn or regurgitation, but also because of an increased airway resistance caused by acid reflux\(^20,21\). The current therapeutic approach to exercise-induced reflux symptoms is to use acid suppressive therapy to decrease the acidity of the refluxate. This however, does not always relieve symptoms. Recognizing which factors result in an increase in reflux during exercise allows for a further understanding of the mechanisms revolved around GERD, and these insights could result in future treatment options for this prevalent problem among athletes.

The aim of our study was to investigate the effect of exercise on reflux severity and to examine the underlying reflux mechanisms. This will be achieved by using a combination of pH-impedance monitoring and prolonged high-resolution manometry (HRM), which has not been used in prior studies on this topic. The primary hypothesis was that reflux occurs more frequently with increasing exercise intensity and that this is most likely caused by multiple mechanisms including the failure of the LES as an effective barrier to withstand reflux due to increased intra-abdominal pressure during exercise, a decreased esophageal clearance due to a decrease in amplitude of peristaltic contraction, and an increase in the frequency of transient lower esophageal relaxations (TLESRs).
METHODS

Patients
Ten healthy volunteers were recruited via advertisement in our center. All subjects were required to have frequent physical activity of at least 10 km of running a week, and an age between 18 and 50 years. Participants did not have an existing history of GERD, previous gastrointestinal tract surgery, a history of peptic ulcer disease, known Barrett’s esophagus, or a history of gastrointestinal cancer. Moreover, patients were not pregnant, did not use drugs which affect gastrointestinal function and had no other organic gastrointestinal diseases or functional disorders such as irritable bowel syndrome or functional dyspepsia. The study proposal was approved by the local institutional review board of the Academic Medical Center in Amsterdam, the Netherlands, and was conducted according to the latest version of the Helsinki Declaration.

Esophageal pH-impedance monitoring and high-resolution manometry
Catheters for pH-impedance and HRM were inserted transnasally. The HRM catheter was placed prior to the pH-impedance catheter to allow localization of the LES. HRM was carried out using a solid-state catheter with 36 solid-state unidirectional sensors spaced at 1-cm intervals (Unisensor AG, Attikon, Switzerland). Before the placement of the HRM catheter, the pressure tracings were zeroed to the atmospheric pressure. The HRM catheter was positioned to allow recording from the hypopharynx to the stomach, and the signals were recorded using a sampling frequency of 20 Hz. The subjects received ten standardized wet swallows using 5 ml of water in the last 2 minutes of the rest period and both exercise periods. Using the Medical Measurement System (Enschede, the Netherlands) software, these swallows were analyzed according to the Chicago criteria.

Following the placement of the HRM catheter, the combined pH-impedance catheter was inserted transnasally. The combined pH-impedance catheter contained one ion-sensitive field-effect transistor pH electrode and six impedance recording segments (Unisensor AG, Attikon, Switzerland). The pH electrode was placed at 5 cm from the upper border of the manometrically localized LES while the impedance recording segments were located at 2-4, 4-6, 6-8, 8-10, 14-16 and 16-18 cm above the upper border of the LES. pH and impedance signals were stored on a digital datalogger (Ohmega, Medical Measurement Systems, Enschede, The Netherlands), using a sampling frequency of 1 Hz and 50 Hz respectively. Both the HRM and the pH-impedance catheter were fixed in place by taping them to the nose. The heart rate was measured using a heart rate monitor with a chest strap, and patients ran on a treadmill.
Study protocol

For each test subject the maximum heart rate (HRmax) was calculated using the formula: 208 - 0.7 x age\textsuperscript{24}. In addition, the body mass index (BMI) was calculated. Subjects were instructed to refrain from strenuous exercise during the 24 hours preceding the test and were additionally instructed to avoid drinking alcohol or caffeine, or to smoke during that period as this can influence the LES pressure. Moreover, subjects were required to fast during 4 hours before the experiment but were permitted to drink water.

Subjects had to fill out the reflux disease questionnaire (RDQ)\textsuperscript{25} prior to the experiment, which analyses the frequency and severity of reflux symptoms in the preceding 7 days. Subjects were encouraged to empty their bladder prior to placement of the catheters. The study protocol is shown in Figure 1. After the equipment had been set up, a pH-impedance catheter and a solid-state HRM catheter were inserted transnasally as described. After this, a meal was given to the subject (120 grams of banana consisting of approximately 114 kcal\textsuperscript{26}. Ten minutes after ingestion, baseline pH, impedance and pressure signals were recorded for 30 minutes while the subject was standing. Thereafter ten 5-ml water swallows took place to obtain the esophageal motility values before the start of the exercise. Following this, there were two periods of exercise separated by a rest period of 10 minutes. In the first exercise period, subjects had to run on a treadmill at a work rate eliciting 60\% of HRmax for 30 minutes and in the second exercise period an exertion at 85\% of HRmax was maintained for 20 minutes. If subjects were unable to maintain the workload at 85\% HRmax for the required duration, then the speed was reduced until they were able to complete the exercise. Changes in speed of the treadmill were applied to keep the runners’ heart rate at the predetermined level. In the last 2 minutes of each exercise period, the subject received ten 5-ml water swallows to quantify esophageal motility. All of these standardized swallows were marked on the data recorder. Subjects were allowed to ingest water during the exercise periods. After all exercises had finished, subjects were extubated and dismissed. If heartburn or regurgitation occurred, this was recorded during the exercise.

![Figure 1](image_url)

*Figure 1.* Study protocol after placement of the pH-impedance and solid-state HRM catheter. In the last 2 minutes of the rest period and both exercise periods, ten standardized 5ml water swallows (WS) are given. The meal consists of 120 grams of banana.
**Data analysis**

Esophageal motility was analyzed using the standardized wet swallows in the last 2 minutes of each period (rest period, period of running at 60% of HRmax, and period of running at 85% of HRmax). The maximum amplitude during successful wet swallows was measured in the part of the esophagus ranging from the upper border of the LES up to 5 cm above the LES. The EGJ and intra-gastric pressure were measured at intervals of 4 min throughout the entire measurement after which these were averaged for each period. The EGJ pressure was measured relative to the intragastric pressure using the MMS software. The spatial limits of the EGJ constituted the zone with a proximal border defined by a pressure increase ≥ 2 mmHg relative to the intraesophageal pressure, while the distal border was defined by a pressure increase ≥ 2 mmHg relative to the intragastric pressure. The mean and minimum EGJ pressure were calculated by the MMS software and were defined as the mean and minimum value of the resting pressure period on the LES sleeve channel. The entire HRM measurement was analyzed for TLESRs by two independent observers, according to previously described criteria\textsuperscript{27}; At least four out of six criteria needed to be met: (i) absence of a swallow for 4 seconds before, until 2 seconds after the onset of the TLESR, (ii) LES relaxation rate of ≥1 mmHg per second, (iii) time from onset to complete relaxation of ≤10 seconds, (iv) a nadir pressure of <2 mmHg, (v) inhibition of the crural diaphragm, and (vi) a prominent after-contraction. In case of a disagreement between the two observers, a consensus was made. The frequency of dry swallows, and the proportion which led to successful contractions were measured. The average duration of peristaltic contractions was measured for all non-failed swallows. All HRM recordings were also evaluated for the presence of a hiatus hernia by looking for a double high-pressure zone and assessing the pressure inversion point. If a double high-pressure zone was present, then the axial separation between the LES and crural diaphragm was measured by measuring the axial distance between the two pressure peaks. The entire pH-impedance tracing was analyzed for the occurrence of reflux episodes according to previously published criteria\textsuperscript{28}. The acid exposure time (percentage of time with distal esophageal pH < 4) was calculated for every patient for each period.

Statistical analyses were performed using SPSS version 22 (SPSS, Inc, Chicago, IL, USA). Data were expressed as median value and range. The Wilcoxon signed rank test was used to make statistic comparisons between the various periods. The Mann-Whitney U test was used to compare differences between the subjects with the 50% highest esophageal acid exposure during exercise and the subjects with the 50% lowest esophageal acid exposure. The Chi-Square test was used to determine whether high esophageal acid exposure was related to the presence of a hiatus hernia during exercise. We considered p < 0.05 to be statistically significant.
RESULTS

Ten healthy volunteers (4 females, age 21-41, BMI 16.5-30.7) were included in the study. Reflux Disease Questionnaire score on the day of the experiment ranged from 1-1.75. None of the subjects experienced gastrointestinal symptoms during the experiment.

*pH-impedance monitoring*

Table 1 gives an overview of the effect of graded running on reflux and on esophageal motility. As shown in Figure 2, exercise led to a significantly higher percentage of time with a pH < 4. This increase was already noted during the moderately intense exercise period yet was more prominent as exercise intensity increased. One patient had a substantially higher acid exposure time in the 65% HRmax period, which consisted of six reflux episodes of which three were prolonged. There was no indication of catheter migration. Exercise also led to a significantly higher frequency of reflux episodes and a significantly longer duration of these reflux episodes. The patients with the 50% highest esophageal acid exposure had a significantly longer duration of reflux episodes than the patients with the 50% lowest esophageal acid exposure (p=0.016).

*Esophageal contractility*

An increase in exercise intensity resulted in a lower distal contractile integral (DCI) during wet swallows, with a significantly lower DCI during the 85% HRmax period (rest; 407 mmHg·s·cm, 60% HRmax; 144 mmHg·s·cm, 85% HRMax; 32 mmHg·s·cm (p=0.047)). The amplitude of the successful peristaltic contractions during wet swallows in the distal part of the esophagus was also lower in the 85% HRmax period compared to the rest period. In only one of the 10 patients an increase was seen in both the DCI and the amplitude. On average, the frequency of swallows throughout the measurement decreased as exercise intensity increased. There was no significant difference in the percentage of swallows resulting in a contraction with a DCI > 100 mmHg·s·cm but a trend towards a decrease in frequency of contractions with a DCI > 100 mmHg·s·cm was observed when comparing the 85% HRmax period to the rest period (p=0.093). As exercise intensity increased, there was a decrease during wet swallows in both the average duration of peristaltic contractions and the distal latency, with a significant difference between the 85% HRmax period and the rest period. The average duration of peristaltic contractions and distal latency also decreased significantly when comparing the 85% HRmax with the 60% HRmax data (p=0.017 and p=0.012 respectively). A significantly higher contractile front velocity (CFV) was found during wet swallows when comparing the 60% HRmax period to the rest period, yet this was not the case for the 85% HRmax group. The frequency of failed wet swallows also increased significantly as exercise intensity increased.
### Table 1. Effect of graded running on reflux and esophageal motility

<table>
<thead>
<tr>
<th></th>
<th>Rest Period</th>
<th>60% Max HR</th>
<th>P value</th>
<th>85% Max HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH-impedance</strong></td>
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<tr>
<td>Percentage time pH &lt; 4 (%)</td>
<td>0 (0-0.5)</td>
<td>0.69 (0-13.67)</td>
<td>0.018*</td>
<td>0.87 (0-4.92)</td>
<td>0.018*</td>
</tr>
<tr>
<td>Frequency of reflux episodes (n/min)</td>
<td>0 (0-0.04)</td>
<td>0.059 (0-0.22)</td>
<td>0.012*</td>
<td>0.06 (0-0.12)</td>
<td>0.018*</td>
</tr>
<tr>
<td>Average time pH &lt; 4 per reflux episode (s)</td>
<td>0 (0-9)</td>
<td>6.2 (0-57.8)</td>
<td>0.028*</td>
<td>10.5 (0-59)</td>
<td>0.018*</td>
</tr>
<tr>
<td>Reflux duration (based on impedance) (s)</td>
<td>0 (0-7)</td>
<td>13.5 (0-86)</td>
<td>0.012*</td>
<td>10 (0-40)</td>
<td>0.026*</td>
</tr>
<tr>
<td><strong>High-resolution manometry wet swallows</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Distal contractile integral (mmHg·s·cm)</td>
<td>407 (30-977)</td>
<td>144 (17-1286)</td>
<td>0.594</td>
<td>32 (0-1376)</td>
<td>0.047*</td>
</tr>
<tr>
<td>Amplitude peristaltic contractions (mmHg)</td>
<td>86.4 (34-139.2)</td>
<td>103.4 (48.2-164.8)</td>
<td>0.260</td>
<td>57 (39-148.2)</td>
<td>0.051</td>
</tr>
<tr>
<td>Number of failed swallows (n)</td>
<td>2.5 (0-8)</td>
<td>7 (0-10)</td>
<td>0.102</td>
<td>8.5 (0-10)</td>
<td>0.011*</td>
</tr>
<tr>
<td>Distal latency (s)</td>
<td>6.5 (4.7-8.3)</td>
<td>6.3 (4.6-11.6)</td>
<td>0.314</td>
<td>4.7 (4.4-5.9)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Contractile front velocity (cm/s)</td>
<td>4.8 (2.7-7.6)</td>
<td>6 (4.9-2)</td>
<td>0.008*</td>
<td>4.7 (4.4-5.9)</td>
<td>0.767</td>
</tr>
<tr>
<td>Average duration peristaltic contractions (s)</td>
<td>8.7 (7.5-10.7)</td>
<td>8 (7.3-11)</td>
<td>0.066</td>
<td>6.3 (5.4-8.1)</td>
<td>0.008*</td>
</tr>
<tr>
<td><strong>High-resolution manometry dry swallows</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of swallows (n/min)</td>
<td>2.42 (1.34-4.13)</td>
<td>1.7 (0.67-3.42)</td>
<td>0.093</td>
<td>1 (0.42-2.22)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Percentage of swallows with DCI &gt; 100 mmHg·s·cm (%)</td>
<td>30.3 (9-95.2)</td>
<td>30.4 (10.3-100)</td>
<td>0.333</td>
<td>43.2 (0-100)</td>
<td>0.203</td>
</tr>
<tr>
<td>Frequency of contractions with DCI &gt; 100 mmHg·s·cm (n/min)</td>
<td>0.69 (0.33-2.34)</td>
<td>0.83 (0.19-1.72)</td>
<td>0.333</td>
<td>0.48 (0-1.36)</td>
<td>0.093</td>
</tr>
<tr>
<td>Mean EGJ pressure (mmHg)</td>
<td>34.6 (8.3-51.5)</td>
<td>31.5 (8.8-52.5)</td>
<td>0.445</td>
<td>40.9 (12.5-52.2)</td>
<td>0.285</td>
</tr>
<tr>
<td>Min EGJ pressure (mmHg)</td>
<td>17.5 (4.5-28.3)</td>
<td>6.6 (-1.5-20.6)</td>
<td>0.017*</td>
<td>6.3 (-2.0-20.0)</td>
<td>0.013*</td>
</tr>
<tr>
<td>Average abdominal pressure (mmHg)</td>
<td>6.2 (1.8-11.2)</td>
<td>7.3 (2.8-13.2)</td>
<td>0.022*</td>
<td>6.6 (4.2-18.2)</td>
<td>0.047*</td>
</tr>
<tr>
<td>Max abdominal pressure (mmHg)</td>
<td>8.5 (5.8-17.5)</td>
<td>15.6 (9.5-24.1)</td>
<td>0.005*</td>
<td>20.9 (13.0-30.2)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Min abdominal pressure (mmHg)</td>
<td>2.58 (-1.8-5.7)</td>
<td>1.9 (-2.7-5.6)</td>
<td>0.139</td>
<td>-1.78 (-7-9.83)</td>
<td>0.139</td>
</tr>
<tr>
<td>Frequency of TLESRs (n/min)</td>
<td>0.09 (0.04-0.15)</td>
<td>0.15 (0.11-0.26)</td>
<td>0.005*</td>
<td>0.09 (0-0.18)</td>
<td>0.575</td>
</tr>
<tr>
<td>Proportion TLESRs resulting in reflux (%)</td>
<td>0 (0-50)</td>
<td>41.7 (0-100)</td>
<td>0.012*</td>
<td>50 (0-100)</td>
<td>0.026*</td>
</tr>
<tr>
<td>Maximum Axial Separation (mm)</td>
<td>0 (0-0)</td>
<td>23.5 (0-30)</td>
<td>0.024*</td>
<td>30.5 (0-41)</td>
<td>0.027*</td>
</tr>
</tbody>
</table>

*Statistical significance achieved. The P value shown is compared to rest period. All values are shown as median (range). For each individual and per period, the mean value during the wet swallows was first calculated. For the DCI all wet swallows were included while for the amplitude peristaltic contraction, DL, CFV, and average duration of peristaltic contractions, only successful wet swallows were included.
Esophagogastric junction and gastric pressure

Increased exercise intensity resulted in a significant decrease in minimum EGJ resting pressure (rest; 17.5 mmHg, 60% HRmax; 6.6 mmHg (p=0.017), 85% HRmax; 6.3 (p=0.013)) (Figure 3). This decrease was not found for the mean EGJ pressure. No difference was found concerning the minimum EGJ pressure when comparing the group with the 50% highest esophageal acid exposure to the group with the 50% lowest esophageal acid exposure. The average and maximum abdominal pressure (Figure 4) both increased significantly during the exercise periods. No significant difference was found for the minimum abdominal pressure.

There were significantly more TLESRs during the 60% HRmax period compared to the rest period, but this was not the case for the 85% HRmax period. The percentage of TLESRs which resulted in reflux significantly increased in both the 60% HRmax period (41.7%) and the 85% HRmax period (50%) compared to the rest period (0%). A trend was found towards a higher association between TLESRs and reflux when comparing the five patients with the 50% highest esophageal acid exposure to the other patients (p=0.095). All but one reflux episode occurred during TLESRs. The one reflux episode which was not TLESR-related occurred during a relaxation that was followed by a swallow 1 second after its onset.

In 6 patients (60%) a hiatus hernia was detected during the exercise period but not during the resting state (Figure 5). As a result, a significant increase in the degree of maximum axial separation was found as exercise intensity increased (rest; 0 mm, 60% HRmax; 23.5 mm (p=0.024), 85% HRmax; 30.5 (p=0.027)) (Figure 6). This increase
was also found when comparing the 85% HRmax period with the 60% HRmax period (p=0.027). Four out of the five patients with the 50% highest esophageal acid exposure had a hiatal hernia during intense exercise (p=0.197).

**Figure 3.** Minimum esophagogastric junction (EGJ) pressure shown in mmHg. Data presents the individual variation of the averaged minimum EGJ pressure for all three periods (rest period (rest), 60% HRmax period (60%), and 85% HRmax period (85%)). A significant difference was found for the 60% HRmax period (p=0.017) and the 85% HRmax period (p=0.013) when compared to the rest period. In addition, the presence or absence of a hiatus hernia during exercise is also indicated per individual.

**Figure 4.** Maximum abdominal pressure shown in mmHg. Data presents the individual variation of the averaged maximum abdominal pressure for all three periods (rest period (rest), 60% HRmax period (60%), and 85% HRmax period (85%)). A significant difference was found for the 60% HRmax period (p=0.005) and the 85% HRmax period (p=0.005) when compared to the rest period.
As far as we know, we are the first group to study the effects of exercise on gastroesophageal reflux using high-resolution manometry in combination with pH-impedance measurement. We show that exercise, in our case running, leads to

**Figure 5.** Example of the formation of a hiatus hernia during exercise in a single subject shown with solid-state HRM. a) The esophageal contraction shown is a swallow which took place during the rest period. No hiatus hernia is visible. b) The esophageal contraction illustrated is a swallow which occurred during the 85% HRmax period. This shows the presence of a hiatus hernia. The top arrow indicates the location of the lower esophageal sphincter, and the bottom arrow the location of the crura diaphragmatica.

**Figure 6.** Degree of maximum axial separation between the LES and the crura of the diaphragm shown in mm. Data presents the individual variation of the maximum axial separation for all three periods (rest period (rest), 60% HRmax period (60%), and 85% HRmax period (85%)). A significant difference was found for the 60% HRmax period (p=0.024) and the 85% HRmax period (p=0.027) when compared to the rest period.

**DISCUSSION**
a statistically significant increase in esophageal acid exposure in healthy volunteers. We demonstrate that this increase in percentage of time with pH < 4 is caused by both an increase in the frequency of reflux episodes as well as an increase in the duration of individual reflux episodes.

Our results show that running did not cause a significant change in the mean EGJ pressure. However, a significant decrease in minimum EGJ pressure was seen as exercise intensity increased. As subjects ran, small artifacts were seen in the HRM recording, which led to oscillating zones of higher pressure. Measuring the minimum EGJ pressure compensates for these artifacts, and helps to limit the effect of variations in rate and depth of inspiration as this measures the EGJ pressure during expiration, reducing the impact of the crural diaphragm. However, diaphragmatic breathing has recently been shown to increase the pressure difference between inspiration and expiration, and result in a decrease in the end-expiratory EGJ zone pressure\(^29\). Thus, the decrease in minimum EGJ pressure found during exercise could be caused by an increase in respiratory vigor. Furthermore, we conclude that both the average abdominal pressure, but mainly the maximum abdominal pressure, increases as exercise intensity is increased. As a result of both these factors, one could assume, as has been done previously\(^17\), that the increase in total reflux time during exercise could be the result of more frequent episodes in which the abdominal pressure exceeds the EGJ pressure. However, our analysis showed that all but one episode occurred during TLESRs. Even though there was an increase in frequency of TLESRs during the 60% HRmax episode, this was not the case during the 85% HRmax period, in which the TLESRs were even less frequent than during the rest period. This decrease in TLESRs during the last period could be due to the fact that this period was furthest away from the meal, as previous studies have shown that consumption of a meal leads to an increase in the incidence of TLESRs, and also to an increased chance that TLESRs result in reflux\(^30\). We chose to include a banana as sports meal as this is frequently used by athletes and it is easy to standardize. GERD patients do not have more frequent TLESRs than controls, but instead have a higher proportion of TLESRs associated with acid reflux\(^31,32\). Our results show that this is also the case during exercise as the frequency of TLESRs did not change, yet the association between TLESRs and reflux increased with increased exercise intensity. The measured increased mean and maximum abdominal pressure could play an important role in this increase of TLESR-associated reflux episodes as the barrier function is decreased during TLESRs. Furthermore, the up and down movements while running could result in stomach content sloshing up through the weak barrier during moments of TLESRs.

It has previously been suggested that the anatomical compromise of the EGJ is an important factor in exercise-induced reflux\(^7\). We found that, in 60% of the subjects, a hiatus hernia was present during exercise which was not seen during the resting state. Moreover, we found that the maximum axial separation between the diaphragm and the LES increased as exercise intensity increased. It is therefore likely that exercise
results in a change of EGJ morphology resulting in an increase in reflux during TLESRs. This is an important finding as it is possible that this change in EGJ morphology induced by exercise is the factor which results in TLESRs being more frequently associated with reflux. As discussed previously, GERD patients also have the same frequency of TLESRs as controls but a higher proportion of TLESRs is associated with acid reflux\textsuperscript{31,32}. It seems therefore that exercise induces changes in healthy subjects that resemble abnormalities encountered in patients with GERD.

Another important factor is that the duration of reflux episodes seems to increase during exercise. No statistical difference was found when comparing the 85\% HRmax period with the 60\% HRmax period, however the change compared to the rest period was more pronounced during the 85\% HRmax period. As previous studies have suggested\textsuperscript{14,15}, an altered esophageal motility could play part in the increase in reflux during exercise. In our study we show that the average contractility of wet swallows (measured using DCI and amplitude) was decreased when comparing the 85\% HRmax period with the rest period. As a result of this decrease in contractility, a higher proportion of the standardized wet swallows were considered to be failed (DCI < 100 mmHg·s·cm). Furthermore, a significantly decreased distal latency and average duration of peristaltic contractions were found during heavy exercise when compared to the rest period. This was even statistically different when comparing the 85\% HRmax period to the 60\% HRmax period. As a result, the clearance of acid from the esophagus by esophageal peristalsis could be limited during exercise and thus result in an increased reflux time. Furthermore, a reduced swallow frequency was noted as exercise intensity increased. This could also play an important role in the prolonged acid exposure time during exercise. In order to limit the effect of xerostomia as a cause of the change in swallow frequency, subjects were allowed to ingest water during the exercise periods. Currently, the cause of the altered esophageal motility is unknown. Decreased gastrointestinal blood flow during exercise could play a role.

In conclusion, we found that running results in an increased total reflux time. Furthermore, it seems that exercise induces changes in healthy subjects which resemble abnormalities encountered in patients with GERD. Reflux episodes during exercise occur almost exclusively during episodes of TLESRs. These are not more frequent, but are more often associated with a reflux episode, possibly due to an increased abdominal pressure and due to body movement during exercise. Moreover, we conclude that exercise induces a transient hiatus hernia in many healthy volunteers and thus a change in EGJ morphology induced by exercise could play a pivotal role. Furthermore, running results in an altered esophageal motility with a decreased contractility and duration which could lead to a decreased esophageal clearance.
REFERENCES


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