The purpose of this study was to determine the relation between posturally increased intra-abdominal pressure and lower/upper esophageal sphincter pressure changes in patients with gastroesophageal reflux disease. We used high resolution manometry to measure pressure changes in lower and upper esophageal sphincter during bilateral leg rise. We also examined whether the rate of lower and upper esophageal sphincter pressure would increase during leg raise differentially in individuals with versus without normal resting pressure. Fifty eight patients with gastroesophageal reflux disease participated in the study. High resolution manometry was performed in relaxed supine position, then lower and upper esophageal sphincter pressure was measured. Finally, the subjects were instructed to keep their legs lifted while performing 90-degree flexion at the hips and knees and the pressure was measured again. Paired t-test and independent samples t-test were used. There was a significant increase in both lower (P < 0.001) and upper esophageal sphincter pressure (P = 0.034) during leg raise.
Introduction

Gastroesophageal reflux disease (GERD) is a common and serious problem. Anti-reflux barrier mechanisms have been discussed extensively in the literature. An increased thoraco-abdominal pressure gradient (Ayazi et al., 2011), length of lower esophageal sphincter (LES), flap valve at the gastroesophageal (GE) junction or the angle of His have been considered (Mittal and Liu, 2005); transient LES relaxation, hiatal hernia, impaired esophageal clearance and reduced lower esophageal sphincter pressure (LESP) have also been assessed (Rohof et al., 2009). Evidence for the influence of intra-abdominal pressure on LESP has been shown repeatedly (Ayazi et al., 2011; Dodds et al., 1975; Kahrilas, 1999). Mittal and Liu (2005) suggest that two structures contribute to the GE junction pressure – intrinsic or smooth LES muscle and extrinsic or skeletal muscle crural diaphragm. Diaphragm performs complex postural, respiratory and sphincter function. Dual postural and respiratory diaphragmatic function has been shown by Hodges and Gandevia (2000). Abnormal diaphragmatic function plays an important role in the gastroesophageal reflux disease (GERD) (Kahrilas, 1999; Shafik et al., 2006). However, exact correlation between diaphragmatic postural and sphincter function has not yet been illustrated, especially in patients with GERD. Also, it is not clear whether posture-related intra-abdominal pressure changes affect upper esophageal sphincter (UES). Using high resolution manometry (HRM), we examined pressure changes in LES and UES in the relaxed supine posture relative to the supine posture with legs raised and actively held against gravity in patients with GERD (Fig. 1). The aim of this study was to assess the influence of increased intra-abdominal pressure both on LESP and upper esophageal sphincter pressure (UESP) and to explore whether this activation differs in patients with normal vs. abnormal resting LESP and UESP.

Material and methods

Subjects

A convenience sample of 58 volunteers, aged 20–66, 32 males and 26 females, were clinically ascertained to have typical GERD symptoms, i.e. acid regurgitation and heartburn with or without other frequent symptoms such as chronic dry cough, halitosis, epigastric pain, dyspepsia or nausea. Descriptive statistics of the patient sample are shown in Table 1. Exclusion criteria were: previous gastroesophageal surgery, concomitant other chronic disease that would affect esophageal motility (neuromuscular disease, achalasia, diffuse esophageal spasm, scleroderma) or

Table 1 Descriptive statistics of the sample.

<table>
<thead>
<tr>
<th>Description</th>
<th>Mean</th>
<th>SD</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
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<tr>
<td>Age</td>
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<td>20</td>
<td>66</td>
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<tr>
<td>Height (cm)</td>
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<td>196</td>
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<td>Weight (kg)</td>
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<td>110</td>
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<tr>
<td>Body mass index</td>
<td>26</td>
<td>5</td>
<td>19</td>
<td>39</td>
</tr>
<tr>
<td>LESP rest (mmHg)</td>
<td>14</td>
<td>10</td>
<td>4</td>
<td>41</td>
</tr>
<tr>
<td>UESP rest (mmHg)</td>
<td>90</td>
<td>68</td>
<td>9</td>
<td>388</td>
</tr>
<tr>
<td>LESP leg raise (mmHg)</td>
<td>31</td>
<td>18</td>
<td>3</td>
<td>79</td>
</tr>
<tr>
<td>UESP leg raise (mmHg)</td>
<td>104</td>
<td>78</td>
<td>10</td>
<td>330</td>
</tr>
</tbody>
</table>

Notes. SD = standard deviation; LESP = lower esophageal sphincter pressure; UESP = upper esophageal sphincter pressure.
Leg raise effect on esophageal sphincter pressure

structural pathology (pharyngeal pouch, diverticulum), and massive hiatus hernia.

Methods

This study was approved by the institutional ethical committee. All subjects were questioned to ensure that they met the inclusion criteria of the study. All testing procedures were thoroughly explained to the participants with a detailed description of the HRM assessments. All subjects reported that they understood the test procedures and gave informed consent.

Routine HRM procedure was performed. Water-perfused HRM catheter was applied transnasally with the patient in a sitting position. UES and LES were identified, and the catheter was fixed. Then the subject was instructed to lie supine and perform a series of 10 swallows of 5 ml of water. First, pressure was recorded in UES and LES at rest. Then the patient’s lower extremities were passively raised by a clinician and positioned to 90 degrees of flexion at the hips and knees and the subject was instructed to maintain this position actively (Fig. 1). Again, pressure was recorded in UES and LES. After putting the legs down, the patient performed one more swallow of 5 ml of water, and the catheter was pulled out after the patient was seated. All patients tolerated the measurement procedure well.

The member of our team with the most clinical experience (J.S.) performed all measurements; we paid careful attention to assuring that the conditions under which testing was conducted were uniform and we used the same catheter for all assessments. Clinical diagnosis of GERD was found to agree highly with HRM software-generated diagnosis (reliability $\kappa = 0.79$) previously (Singendonk et al., 2015).

The manometric data were analyzed using a MMS Solar GI HRM software.

Statistical analysis

The statistical analysis was performed using the software Statgraphics Centurion XV, version 15.2.06. Paired sample t-test were used to examine whether esophageal pressure (lower and upper) would change with lower extremity activation. Independent samples t-test were performed to compare whether the change in lower or upper esophageal pressure was different for those with initially low vs. high esophageal pressure. Note that the groups with initially low vs. high esophageal pressure did not differ significantly in terms of potentially relevant variables age, sex, or body mass index ($p > 0.10$). Therefore, we proceeded without controlling for these variables, which allowed us to reduce bias towards Type II error due to a relatively small sample size. The significance level was set at two-tailed 0.05.

Results

Aim 1: examine whether LESP and UESP would change as a result of lower extremities activation in patients with GERD

The paired sample t-test indicated that the mean LESP was significantly higher with legs raised compared to the resting supine position ($\text{Mean} = 30.5$, $SD = 18.3$ mm Hg vs. $\text{Mean} = 13.6$, $SD = 9.5$ mm Hg; $p < 0.001$). Fig. 2 illustrates this result. Similarly, the mean UESP was significantly higher with legs raised compared to the resting supine position ($\text{Mean} = 103.7$, $SD = 78.4$ mm Hg vs. $\text{Mean} = 89.6$, $SD = 67.7$ mm Hg; $p = 0.034$). Fig. 3 illustrates this result. Of note in relation to Fig. 3 is the outlier with very high resting UES. We speculate that this value is the result of the individual’s extreme lumbar hyperlordosis in the supine position. When the participant lifted his legs, the lumbar hyperlordosis reduced greatly. The idea is that the posture with legs lifted may have actually been more relaxing than the supine position, resulting in lower readings with legs raised.

Aim 2: examine whether the change in LESP or UESP with postural leg activation would be different in individuals with normal versus abnormal resting LESP and UESP

Results of the independent samples t-test indicated that the individuals with higher resting LESP ($> 10$ mmHg) experienced a significantly greater increase in LESP during leg raise than those with lower resting LESP ($\text{Mean} = 36.6$, $SD = 18.7$ mm Hg vs. $\text{Mean} = 23.0$, $SD = 14.9$ mm Hg; $p = 0.002$). Fig. 4 illustrates this result. In terms of UESP, those with higher resting UESP ($> 44$ mmHg) experienced a significantly greater increase in UESP during the leg raise than those with lower resting pressure ($\leq 44$ mmHg).

Fig. 2 Statistical comparison of lower esophageal sphincter pressure data (mmHg) measured at rest in supine position and with leg raise.
Mean Z₁₃₃.₁, SD Z₇₉.₀ mmHg vs. Mean Z₄₈.₀, SD Z₃₆.₀ mmHg; P < 0.001). Fig. 5 illustrates this result.

**Discussion**

The aim of this study was to assess the influence of increased intra-abdominal pressure on LESP and UESP and to determine if this effect differs in individuals with normal vs. abnormal resting LESP and UESP. In support of our hypotheses, we found a significant increase both in LESP and UESP with legs raised compared to the initial resting position. Patients with initially higher LESP (>10 mmHg) exhibited a greater increase in LESP during the leg raise than those with initially lower pressure. Similarly, patients with higher resting UESP (>44 mmHg) showed a greater increase in UESP during the leg raise than those with lower resting pressure.

The overarching goal of this study was to explore the relationship between intra-abdominal pressure changes and LESP (UESP) dynamics. The LESP significantly increased with the leg raise in the whole group of 58 subjects. Following the ASGE Technology Committee (2012) criteria, we compared an increase in LESP with legs raised between...
individuals with abnormally low resting LESP, i.e. \( <10 \text{ mmHg} \) (26 subjects) versus those with normal resting LESP, i.e. \( >10 \text{ mmHg} \) (32 individuals). LESP increased significantly more with a leg raise for those who had normal LESP at rest (more than 10 mmHg) than for those who had abnormally low resting LESP (at or lower than 10 mmHg). These results provide evidence for the influence of intra-abdominal pressure changes on LESP.

In the context posturally related LESP changes, it is likely that the observed results point to the critical role of the diaphragm as an important respiratory, postural and sphincter muscle. The crural diaphragm plays an important role in the gastroesophageal competence mechanism (Shafik et al., 2006), serving as a "second sphincter" during abrupt increases in intra-abdominal pressure (Kahrilas, 1999). Mittal et al. illustrated an increase of LESP during straight leg raising in healthy individuals and by means of EMG confirmed that tonic contraction of the crural diaphragm is a mechanism for LESP increase (Mittal et al., 1999). Future research should examine directly whether results reported here truly are driven by the diaphragm function.

During postural locomotion activities such as hip flexion, postural activity of the diaphragm increases (Kolar et al., 2012, 2010). This mechanism plays an important role in reflux prevention during increases of intra-abdominal pressure (Kahrilas, 1999) that is related to any physical strain, locomotion or even an active static position. In a study by Dodds et al., the LESP increases associated with leg raising were unrelated to the initial sphincter pressure (Dodds et al., 1975). The results of our study using patients with GERD are not in line with the study by Dodds et al. (1975). One possibility is that measurement differences contributed to the differences in outcomes. Dodds et al. used a relatively rough method (although the best method available at the time) that may not have been able to capture this phenomenon to the same extent as the new HRM assessment used in this study. Also, our results support the findings by Cohen and Harris (1970) and Mittal et al. (1999), both of whom pointed to the increased pressure during a leg raise on which we build to suggest a potential greater increase in those with initially higher pressure.

Our results may indicate a decreased LESP response to the increase in intra-abdominal pressure, causing reflux or even regurgitation especially during forward bending or other postural challenges (e.g. weight lifting). Perhaps both the resting LESP and the amount of LESP increase during postural challenge are critical anti-reflux barrier mechanisms. But we may speculate that also the role of diaphragmatic activation is different in GERD patients comparing to healthy subjects.

The diaphragm is an important respiratory, postural and sphincter muscle that consists of several sections. It can be expected that in patients with GERD mainly its crural part, which plays a role of the second sphincter, is dysfunctional whereas in patients with chronic low back pain its costal and middle sections have been identified as dysfunctional (Kolar et al., 2012). Also, an abnormal position and a steeper slope of the diaphragm was found in individuals with chronic back pain in comparison with a healthy population (Kolar et al., 2012). Perhaps this change in diaphragmatic position and contour can be of some importance in GERD as well. Abnormal diaphragmatic function can be a common denominator in patients suffering from both GERD and chronic back pain. Yamane states that kyphosis is associated with gastric acid reflux, osteoporotic vertebral fractures are associated with the presence of hiatus hernia, aggravating GERD symptoms, and that there is a strong positive correlation between intra-abdominal pressure and the lumbar compression force (Yamane et al., 2011). A longitudinal study published by Smith et al. (2014) presents a relationship between incontinence, breathing disorders, gastrointestinal symptoms, and back pain. All individuals involved in our study reported repetitive chronic back pain for which they were repeatedly treated at the rehabilitation department. Approaching diaphragmatic activation with a rehabilitation treatment can influence LESP and thus also GERD symptoms as confirmed by previous research (Carvalho de Miranda Chaves et al., 2012; da Silva et al., 2013; Eherer et al., 2012; Nobre e Souza et al., 2013).

Probably the most unique part of this study is the confirmation of intra-abdominal pressure influence on UESP. In our study, the UESP significantly increased with the leg raise. While extensive research addresses LES function in patients with GERD, much less attention has been paid to the role of the UESP. Resting UESP norms have been established (Bremner et al., 2001; Jungheim et al., 2015) but postural influence on UESP has not been clearly defined. We followed the norms published by Bremner et al. (2001; Neville et al., 2005) indicating 73 ± 29 mmHg for resting UESP. In the entire sample, 20 had resting UESP bellow the lower limit of normal (44 mmHg) while 38 individuals had resting UESP above the lower limit of normal and 20 had the resting UEP above the upper limit of normal (102 mmHg).

Individuals with higher resting UESP (more than 44 mmHg) exhibited a significantly greater increase in UESP during the leg raise than those with lower resting pressure (Fig. 5). To confirm this statistical inference, we also conducted an analysis with the 73 mmHg threshold (according Bremner the UESP norm is 73 ± 29 mmHg) (Bremner et al., 2001; Neville et al., 2005), and the same relationship between resting UESP and an UESP increase during a leg raise was confirmed. In individuals with resting UESP above 73 mmHg, the increase in resting UESP during a leg raise was significantly more than for those with lower resting pressure (Mean = 147.5, SD = 81.1 mmHg vs. Mean = 60.0, SD = 45.0 mmHg; P < 0.001). In other words, the selected threshold did not seem to play an important role. Our results indicate that the rate of the increase in intra-abdominal pressure is dependent on the level of the initial resting UESP. This finding applied to all by one patient, in whom the opposite was true — the resting UESP was higher than UESP during the leg raise.

The findings have clinical implications. Generally, in patients with very low UESP, we expect an increased risk of gastroesophageal refluxate aspiration (Patti et al., 1992), while the high UESP may cause dysphagia, odynophagia or globus (Peng et al., 2015). But consensus does not exist even on this topic. For example, according to Choi et al., a HRM analysis suggests that UESP is not associated with globus (Choi et al., 2013). Kwiatek demonstrated that respiration-related change in resting UESP is significantly

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amplified in globus patients (Kwiatek et al., 2009). Respiration, as well as an intra-abdominal pressure increase due to postural limb activation, are related to changes in diaphragmatic position (Kolar et al., 2010, 2009). The diaphragm constantly fulfills combined respiratory, postural and sphincter function. These diaphragmatic roles are interrelated. Our data support the notion that the postural situation under which HRM LESP and UESP are measured should be considered. Carmo et al. (2015) state that resting UESP is significantly lower in the sitting posture compared to supine, suggesting that obtained data should be interpreted with caution in light of accepted norms. Most studies using HRM are conducted based on measurements in supine, whereas deglutition but also other movements and activities occur mostly in the upright position (do Carmo et al., 2015).

Combined diaphragmatic function (respiratory, postural and sphincter) and its influence on UESP and LESP should be evaluated not just in patients with GERD, but also in patients with back pain where diaphragmatic activation is abnormal (Janssens et al., 2013; Kolar et al., 2012; Vostatek et al., 2013) as well as in patients with respiratory disorders. HRM appears to be an appropriate method to evaluate this combined diaphragmatic function.

There are a few limitations to this study. First, although GERD was carefully clinically ascertained in the sample and the presence of common associated diseases and conditions was ruled out during the assessment, it is still possible that some other physiological process or condition were present. Second, all patients with GERD involved in the study also complained of chronic pain in the musculoskeletal system but a specific relationship between these symptoms and obtained data was not addressed. This will be a topic of a future study. Third, no direct diaphragm measurements were done in this study. However, it has already been demonstrated by Mittal et al. (1990) by means of EMG diaphragmatic recording that increase in LES during periods of increased intra-abdominal pressure is associated with a tonic contraction of the crural diaphragm. Fourth, the sample was relatively small, potentially compromising explanatory power. However, a greater sample would only be likely to provide stronger statistical evidence for our hypotheses.

Finally, with these limitations in mind, and considering that our findings are not in line with some of the previous relevant research studies, our findings need to be interpreted with caution. Future research needs to address the influence of postural situation on UESP and LESP in chronic back pain patients and its relationship to GERD. The effects of treatment (diaphragmatic training) on LESP and UESP and on subjective symptoms in GERD and back pain population should also be explored.

Conclusion

The findings demonstrate the influence of intra-abdominal pressure both on LESP and UESP in patients with GERD. We also found that the amount of LESP and UESP increase during postural activation depended on resting LESP and UESP. The results illustrate the influence of increased intraabdominal pressure on intraesophageal pressure, confirming combined diaphragmatic postural and sphincter function. HRM evaluates not only sphincter, but indirectly also postural diaphragmatic function. This may aid in the design of functional assessment and conservative treatment of individuals with esophageal motility disorders, but also respiratory disorders and back pain where compromised combined diaphragmatic function maybe a common denominator.

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Conflict of interest

None of the authors has any conflict of interest.

References


Leg raise effect on esophageal sphincter pressure


