Hiatal hernia predisposes to nocturnal gastro-oesophageal reflux

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Abstract

Background: Nocturnal reflux has been associated with severe complications of gastro-oesophageal reflux disease and a poorer quality of life. Hiatal hernia predisposes to increased oesophageal acid exposure, but the effect on night reflux symptoms has never been investigated. The aim of the study was to investigate if hiatal hernia is associated with more frequent and severe night reflux symptoms.

Methods: A total of 215 consecutive patients (110 male, mean age 52.6 ± 14.7 years) answered a detailed questionnaire on frequency and severity of specific day and night reflux symptoms. Subsequently, all patients underwent upper endoscopy and were categorized in two groups based on the endoscopic presence of hiatal hernia.

Results: Patients with hiatal hernia were more likely to have nocturnal symptoms compared to those without hiatal hernia (78.6 vs. 51.8%, $p = 0.0001$); 59.2% of patients with hiatal hernia reported heartburn and 60.2% regurgitation compared to 43.8 and 39.3% of those without hiatal hernia, respectively ($p = 0.033$ and $p = 0.003$). The proportions of patients with day heartburn or regurgitation were not significantly different between the two groups. Night heartburn and regurgitation were graded as significantly more severe by patients with hiatal hernia (4.9 ± 4.2 vs. 3.2 ± 3.7 , $p = 0.002$, and 3.8 ± 4.2 vs. 2.2 ± 3.5 , $p = 0.001$, respectively). Patients with hiatal hernia had more frequent weekly night heartburn and regurgitation compared to those without hiatal hernia ($p = 0.004$ and $p = 0.008$, respectively).

Conclusions: More patients with hiatal hernia reported nocturnal reflux symptoms compared to those without hiatal hernia. Furthermore, nocturnal reflux symptoms were significantly more frequent and graded as significantly more severe in patients with presence of hiatal hernia rather than in those without hiatal hernia.

Keywords

Hiatal hernia, nocturnal GORD

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Introduction

Nocturnal reflux symptoms have been shown to affect one-half to three-quarters of patients with gastro-oesophageal reflux disease (GORD).¹ Patients with nocturnal GORD are more likely to have poor sleep quality, day time fatigue, and impaired work productivity.^{2,3} In addition, nocturnal GORD has been associated with more severe oesophageal mucosal damage such as peptic strictures, Barrett oesophagus, and adenocarcinoma.^{4,5} As a group, GORD patients had more nocturnal reflux events than healthy subjects, the majority of which were weakly acidic and reached the proximal oesophagus.⁶ Moreover, supine reflux events showed

a longer duration and a slower resolve compared to reflux events in the upright position.^{4,7} It is well established that oesophageal reflux exposure is determined by the balance between factors allowing reflux access to the oesophageal mucosa and factors promoting reflux clearance.

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Among the various factors that may contribute to the pathophysiology of GORD, hiatal hernia plays an important role. Although how exactly hiatus hernia causes reflux is only slightly understood, its presence is clearly associated with mechanistic abnormalities. The altered geometry of the cardia imposed by a hiatal hernia made the gastro-oesophageal junction of patients with GORD more distensible and shorter than in patients without hernia.⁸ In addition, presence of hiatal hernia reduced threshold for distension-induced transient lower oesophageal relaxations (TLOSRS) and increased the likelihood of prolonged proximal oesophageal reflux exposure.^{9–11} Studies have confirmed that increasing size of hiatal hernia is strongly correlated with increasing severity of oesophagitis.^{12,13}

Although considerable data exists about the association of hiatal hernia with GORD, studies examining its role in nocturnal GORD are limited. As mechanisms involved in the occurrence of nocturnal reflux are not completely elucidated, presence of hiatal hernia may cause increased reflux in the supine position leading to nocturnal GORD. Thus, the primary aim of our study was to investigate whether presence of hiatal hernia is associated with increased risk for night reflux symptoms. The secondary aim was to examine whether frequency and severity of nocturnal reflux symptoms differ between patients with and without hiatal hernia.

Methods

Patients

Outpatients presenting for evaluation of suspected GORD were eligible to participate in the study. Inclusion criteria were typical GORD symptoms (heartburn and/or regurgitation) occurring at least 2 days/week for a period longer than 1 month. Exclusion criteria were as follows: (i) age <18 years, (ii) evidence of oesophageal or gastric cancer, (iii) history of oesophageal or gastric cancer, (iv) pregnancy, (v) gastric surgery, and (vi) use of acid-suppressive therapy within 1 month of evaluation. The study was approved by the Ethics Committee of our hospital and appropriate informed consent was obtained. Each patient who gave consent to participate in the study subsequently answered a detailed questionnaire on frequency and severity of night and day reflux symptoms. Seven to ten days later, patients underwent upper endoscopy performed by an investigator unaware of the questionnaire's results.

Questionnaire

Investigator-developed questionnaire assessed the frequency and severity of heartburn and regurgitation

during the previous 1 month. Symptom frequency was assessed on the following scale: 1, none of the time; 2, 1 day/night per week; 3, 2–3 days/night per week; 4, 4–6 days/nights per week; and 5, every day/night. Symptom severity was measured on a 10-point Likert scale ranging from 1 (very mild) to 10 (very severe). The frequency and severity of nocturnal and daytime symptoms were assessed separately for each particular GORD symptom separately (heartburn, regurgitation).

So far, there is no consensus definition for nocturnal reflux. Patients were classified as having nocturnal reflux symptoms if heartburn and/or regurgitation occur when lying down to sleep at night.

Endoscopy

All patients underwent upper endoscopy. The gastro-oesophageal junction was identified by the proximal margin of the gastric folds coinciding with the pinch at the end of tubular oesophagus. Hiatal hernia was determined as the distance between the superior aspect of diaphragmatic hiatus and the gastro-oesophageal junction. If there was at least 2 cm between diaphragmatic indentation and the top of the gastric mucosal folds a diagnosis of hiatal hernia was made.¹⁴ Measurement of hiatal hernia size was performed during withdrawal of endoscope after deflation of the stomach. For the study we used a modified endoscope marked at 1 cm-interval. With this modified endoscope, overall accuracies in measuring lengths ≥ 2 cm were 95%.¹⁵ During endoscopy, the presence of oesophagitis was noted and graded according to the Los Angeles classification.¹⁶

Sample size calculation

Based on the crude estimation from the literature that at least 65% of GORD patients overall have nocturnal symptoms and our hypothesis that hiatal hernia adds at least 20% risk of nocturnal symptoms, which is our primary endpoint, we calculated that a sample size of at least 164 patients would be required to test our hypothesis with a power of 0.80. However, in order to pick up statistically significant differences between patients with and without hiatal hernia in specific nocturnal symptoms frequency and severity (secondary endpoints) we opted for a larger patient sample size.

Statistical analysis

Results for qualitative data are presented as absolute and value percent. Results for quantitative data are presented as mean $\pm$ SD or median (range). Mann–Whitney U test, t-test, or chi-squared test were used for appropriate comparisons. For the univariate

analysis, gender, age, body mass index, grade of oesophagitis, and severity and frequency of day and nocturnal heartburn and regurgitation were analysed.

Parameters differing significantly according to the univariate analysis ($p < 0.05$) were included in a multivariate regression analysis. Statistical significance was defined as a p -value of <0.05 . Statistical analysis was done using the statistical package Statgraphics Centurion (StatPoint Technologies, Warrenton, VA, USA).

Results

This study invited 236 consecutive outpatients with GORD symptoms to participate in the study: 221 signed informed consent and 215 patients (male/female: 110/105, mean age 52.6 ± 14.7 years) were finally included (six patients did not show up for the endoscopy). The majority of patients (203/215, 94%) reported day symptoms; heartburn was present in 195 (91%) patients, while regurgitation was reported by 118 (55%) of patients. Nocturnal symptoms were present in 139 (65%) of patients; about half of patients reported heartburn (110, 51%) or regurgitation (106, 49%). Patients had symptoms for a mean of 63.8 ± 68.1 months (range 2–360).

Hiatal hernia was identified in 103 (48%) patients with a mean size of 2.9 ± 1.0 cm (range 2–7 cm). Patients with hiatal hernia were significantly older (55.8 ± 14.3 vs. 49.6 ± 14.5 years, $p = 0.002$) and had a higher body mass index (28.1 ± 3.5 vs. 26.8 ± 4.0 kg/m², $p = 0.015$). The prevalence of erosive oesophagitis was 73% in the total study population and patients with hiatal hernia were more likely to have any grade of erosive oesophagitis (81.6 vs. 65.2%, $p = 0.007$). Moreover, patients with hiatal hernia had evidence of severe oesophagitis (grade C and D) compared to those without hiatal hernia (18.4 vs. 2.7%, $p < 0.001$). Table 1 summarizes the characteristics of patients with and without hiatal hernia.

Hiatal hernia and prevalence of night and day symptoms

Patients with hiatal hernia were more likely to have nocturnal symptoms as a whole compared to those without hiatal hernia (78.6 vs. 51.8%, $p = 0.0001$); each nocturnal symptom was also reported by significantly more patients with hiatal hernia; night heartburn was reported by 59.2% of patients with hiatal hernia compared to 43.8% of patients without hiatal hernia ($p = 0.033$), whereas night regurgitation was reported by 60.2% of patients with hiatal hernia compared to 39.3% of patients without hiatal hernia ($p = 0.003$).

There was no statistical difference between patients with and without hiatal hernia for day heartburn (89.3

vs. 92%, $p = 0.665$). There was a trend, which did not reach significance, for higher prevalence of day regurgitation in patients with hiatal hernia compared to those without hiatal hernia (61.6 vs. 47.6%, $p = 0.054$).

Hiatal hernia and frequency of night and day symptoms

The median frequency of nocturnal heartburn in patients with hiatal hernia was 2–3 nights/week compared 0 nights/week to those without hiatal hernia ($p = 0.004$). Sixty-two patients with hiatal hernia reported at least one episode of nocturnal heartburn compared to 51/112 (45%) of those without hiatal hernia ($p = 0.0162$). The same pattern of frequency was found for nocturnal regurgitation (Table 1); at least one episode of regurgitation was reported by almost 50% (51/103) of patients with hiatal hernia compared to 30% (35/112) of patients without hiatal hernia ($p = 0.0238$). Presence of hiatal hernia had no effect on the frequency of day heartburn or regurgitation, although a trend for more frequent heartburn in patients with hiatal hernia was observed (Table 1).

Table 1. Demographic and clinical characteristics of patients with and without hiatal hernia

	With hiatal hernia ($n = 103$)	Without hiatal hernia ($n = 112$)	p -value
Age (years)	55.8 ± 14.3	49.6 ± 14.5	0.002
Gender (male/female)	58/45	52/60	NS
Body mass index (kg/m ²)	28.1 ± 3.5	26.8 ± 4.0	0.015
Erosive oesophagitis	84 (81.6)	73 (65.2)	0.007
Grade A	24 (23.3)	45 (40.2)	
Grade B	41 (39.8)	25 (22.3)	
Grade C	16 (15.5)	2 (1.8)	
Grade D	3 (2.9)	1 (0.9)	
Day symptoms			
Heartburn			
Frequency	4 (3–5)	4 (3–5)	NS
Severity	6.1 ± 2.8	6.1 ± 2.5	NS
Regurgitation			
Frequency	1 (1–2)	1 (1–3)	NS
Severity	1.8 ± 2.9	2.1 ± 2.8	NS
Night symptoms			
Heartburn			
Frequency	3 (1–5)	1 (1–3)	0.004
Severity	4.9 ± 4.2	3.2 ± 3.7	0.002
Regurgitation			
Frequency	1 (1–3)	1 (1–2)	0.008
Severity	3.8 ± 4.2	2.2 ± 3.5	0.001

Values are mean $\pm$ SD, n , n (%), or median (range).

Hiatal hernia and severity of night and symptoms

Patients with hiatal hernia graded their night heartburn as significantly more severe than those without hiatal hernia at the visual analogue scale (4.9 ± 4.2 vs. 3.2 ± 3.7 , $p = 0.002$). Significantly higher severity scores were also reported for night regurgitation in hiatal hernia presence group at the visual analogue scale (3.8 ± 4.2 vs. 2.2 ± 3.5 , $p = 0.001$). Severity scores for day heartburn and day regurgitation were similar between patients with and without hiatal hernia (6.1 ± 2.8 vs. 6.1 ± 2.5 , $p = 0.94$ and 1.8 ± 2.9 vs. 2.1 ± 2.8 , $p = 0.41$, respectively).

Factors associated with the length of hiatal hernia

In the univariate analysis, a statistically significant relationship between length of hiatal hernia and age ($p < 0.00001$), grade of oesophagitis ($p < 0.00001$), and severity of nocturnal heartburn ($p = 0.006$) and regurgitation ($p = 0.0008$) was observed. In the multiple regression analysis, only an association between length of hiatal hernia and grade of oesophagitis ($p < 0.00001$) was identified.

Discussion

Although hiatal hernia is strongly associated with GORD, there are few data for the putative association of hiatal hernia with different manifestations of GORD, such as nocturnal symptoms. Nocturnal symptoms have gained attention over the past years because they affect one-half to three-quarters of patients with GORD and produce greater burden of illness than similar symptoms that occur primarily during the daytime.^{1-3,17} Our study showed that GORD patients with hiatal hernia were more likely to have nocturnal symptoms compared to those without hiatal hernia. Moreover, nocturnal symptoms were more frequent and intense when hiatal hernia was present.

The association between presence of hiatal hernia and nocturnal symptoms seems logical. The presence of hiatal hernia has been shown to be predictive of oesophagitis presence and severity.^{13,18,19} We indeed found that patients with hiatal hernia were more likely to have any grade of erosive oesophagitis and a severer grade of it. The gastro-oesophageal junction in GORD patients with hiatal hernia has been found to be more distensible and shorter than in patients without hiatal hernia, contributing in a way to increased liquid reflux.⁸ Moreover, presence of hiatal hernia influenced the unbuffered acid pocket that exists just above the gastro-oesophageal junction.^{20,21} As patients with hiatal hernia have a reduced threshold for TLOSRS,

the presence of the acid pocket may increase the risk for reflux during those TLOSRS.^{9,21} The presence of combined hiatal hernia and acid pocket could deteriorate gastric reflux in the recumbent position leading to nocturnal symptoms. Our study supported the idea that hiatal hernia is a major risk factor for the generation of nocturnal GORD symptoms. We did observe that almost 80% of patients with hiatal hernia reported nocturnal GORD symptoms compared to 50% of patients without hiatal hernia. Significantly more patients with hiatal hernia were also noted with nocturnal heartburn or regurgitation as independent symptoms than those without hiatal hernia.

Our results are in agreement with a recent study that identified a significant association between the presence of hiatal hernia and nocturnal reflux.²² However, our study population was balanced between male and female, whereas in the forementioned study the population consisted almost exclusively of veteran male. Moreover, we evaluated frequency and severity of nocturnal reflux symptoms. We found that nocturnal reflux symptoms were more frequently reported by GORD patients with hiatal hernia. Nocturnal heartburn or regurgitation for at least 1 day per week was reported by 60 and 50% of patients with hiatal hernia. Furthermore, nocturnal reflux symptoms were graded as significantly more severe in patients with presence of hiatal hernia rather than in those without hiatal hernia. Our finding strengthens the hypothesis that presence of hiatal hernia predisposed for nocturnal GORD symptoms.

Once refluxate has entered the oesophagus, the removal of the noxious agents as quickly as possible is achieved by either primary or secondary peristalsis.²³ Chemical clearance by salivary bicarbonate acts to neutralize the oesophageal pH.⁷ The absence of primary peristalsis induction, due to cessation of swallowing during sleeping, means that the main role in clearing the oesophagus in supine position is played by secondary peristalsis. However, secondary peristalsis in GORD patients was deteriorated resulting in impairment of acid clearance during supine reflux.^{24,25} The lack of gravity in recumbent position also reduced the clearance of gastric contents.²⁶ Thus, nocturnal gastric reflux is associated with increased contact time with the mucosa. The contact time of the oesophageal mucosa with gastric refluxate will be more prolonged considering that presence of hiatal hernia also increased oesophageal acid exposure and predicted more prolonged proximal oesophageal acid exposure.^{10,27} It is well known that the prolonged effect of gastric reflux on oesophageal mucosa leads to a longer duration of reflux episodes.⁴ This long duration of supine reflux events may explain the fact that nocturnal reflux symptoms are perceived as more severe than daytime.

We indeed found that patients with hiatal hernia graded their nocturnal heartburn or regurgitation significantly more severe than those patients without hiatal hernia. Presence of hiatal hernia had no effect on the severity of daytime reported symptoms.

Possible limitations of this study should be considered. First, symptoms were assessed through a self-reported questionnaire; therefore, there is a possibility of recall bias. Moreover, evaluation of severity and frequency was based on investigator-developed non-validated questionnaire. However, we prospectively enrolled more patients than those that our sample size estimation indicated and we have no reason to suspect bias concerning differential response among cases with versus without hiatal hernia. Another limitation is the fact that we did not assess quality of life in our study population, although the fact that the patients do recall and grade nocturnal symptoms implies significant sleep disturbance. Finally, measurement of hiatal hernia size by any method is difficult. Although barium radiology is considered the 'gold standard' method for the diagnosis, in our study hiatal hernia was diagnosed and measured using endoscopic criteria. We used a standard protocol measuring the size at the end of examination after deflation of the stomach in order to avoid any amount of variability. We also used a modified endoscope, marked at 1 cm-interval, that showed 95% overall accuracies in measuring lengths ≥ 2 cm.¹⁵

In conclusion, we found that more GORD patients with hiatal hernia reported nocturnal reflux symptoms compared to those with normal oesophagogastric junction position. Furthermore, nocturnal reflux symptoms were significantly more frequent and graded as significantly more severe in patients with presence of hiatal hernia rather than in those without hiatal hernia. Our findings suggest that patients with hiatal hernia could be benefit with a change in their lifestyle (avoiding sleep early after dinner). Moreover, in patients with hiatal hernia and nocturnal regurgitation despite PPIs therapy, the choice of early surgical treatment should be offered at the early stage of GORD.

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Conflict of interest

The authors declare that there is no conflict of interest.

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