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Does Body Mass Index associate with the endoscopic severity of gastroesophageal reflux disease?

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Abstract

To evaluate the association between body mass index (BMI) and gastroesophageal reflux disease (GERD) severity in the group of patients frequently suffering from moderate/severe gastroesophageal reflux symptoms, one hundred and fifty eight previously untreated patients underwent upper panendoscopy as indicated by typical moderate/severe reflux symptoms, occurring three or more times per week. Patients' BMI values were tabulated and compared to the severity of endoscopic findings (according to Savary-Miller/modified by Siewert). Association between reflux disease activity and BMI was analyzed by Kruskall-Wallis test, while mild and severe group were compared using Mann Whitney test. Analyzing the whole group, including the patients who had no endoscopically verified erosions (Savary-Miller 0 stage = non erosive reflux disease/NERD) association was found at the level of perceivable statistical significance ($p=0.0501$). However subdividing the examined population into mild (Savary-Miller 0-1 stage) and severe (Savary-Miller 2-4 stage) groups according to the endoscopically verified mucosal lesions of the esophagus, there was a strong significant relationship between severity of GERD and BMI ($p=0.0056$). In the group of patients with moderate and severe GERD symptoms elevation of BMI can be a risk factor of increased severity of GERD particularly in those who already have erosive mucosal lesions at the time of examination.

Key words: *body mass index, gastroesophageal reflux disease, severity, association*

Introduction

Prevalence of GERD and obesity are both increasing in industrialized countries.[1] GERD is the manifestation of gastric acid exposure of the esophagus. Heartburn (a retrosternal burning sensation), acid regurgitation (a sour taste in the mouth) and dysphagia are considered typical and specific symptoms of GERD.[2] The relationship between overweight (BMI ≥ 25 kg/m^2 or obesity (BMI ≥ 30 kg/ m^2 and GERD is still controversial.

A German study (based upon a nationwide information campaign) of 1,296 patients with reflux episodes daily and several times a week[3] showed that BMI had no impact on the frequency of reflux symptoms. Similarly, a Swedish survey[4] based on 820 face-to-face interviews found no association between BMI at 20 years of age, BMI 20 years before the interview or maximum adult BMI and severity or duration of reflux symptoms.

On the other hand a strong correlation was found between BMI and severity of GERD, defined and quantified by DeMeester (pH-metric) score.[5] In the Bristol Helicobacter Project the relationship between BMI and severity of GERD reached conventional statistical significance.[6] In a 2003 Swedish study of 3113 patients who reported on severe heartburn or regurgitation, a dose-response association was detected between BMI and reflux in both sexes with even stronger significance among women especially premenopausally.[7]

Increased intra-abdominal pressure impairs the „second sphincter" function of crural diaphragm, which determines anatomical and functional impairments. Such displacement of the lower esophageal sphincter leads to increased esophageal acid exposure, subnormal lower esophageal sphincter (LES) pressure[8] and reflux symptoms. There are evidences that obese subjects have elevated gastro-esophageal pressure gradient from the mechanical burden of excessive fat with significantly prolonged esophageal transit time.[9] Obese persons with higher prevalence of hiatal hernia are also more sensitive to the presence of acid in the esophagus. Obesity seems to be a strong risk factor for gastroesophageal reflux[10] with high prevalence of asymptomatic esophageal motility disorders (in morbidly obese) suggesting abnormal visceral sensation.[11] Furthermore, obesity associated vagal abnormalities promote higher output of bile and pancreatic enzymes, which makes the refluxate more toxic and irritating to the esophageal mucosa than in lean patients.[12]

In addition to the many comorbidities of obesity, there are evidences that intestinal and extraintestinal symptoms (like abdominal pain, reflux, irritable bowel, sleeping disturbances, obstructive sleep apnea) are more common

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Table 1: Statistical characteristics of BMI in mild (Savary-Miller stage 0-1) and severe (Savary-Miller stage 2-4) patient groups of GERD

	Mild (0-1) GERD	Severe (2-4) GERD
Number of patients	69	89
Minimum (BMI)	17.54	17.63
25% percentile	21.1	23.58
Median	24.34	26.79
75% percentile	28.06	30.71
Maximum	38.87	57.63
Mean	25.24	28.25
Std. Deviation	4.76	7.16
St. Error	0.57	0.76

and more intense in this population.[13,14]

Previously most studies examined the correlation between the degree of obesity and the existence/frequency of GERD symptoms using surveys, esophageal sphincter manometry or 24 h pH monitoring.

In our study we analyzed the association between BMI and the severity of endoscopically verified mucosal lesions in patients with moderate/ severe GERD symptoms. This is thought to be essential since we know that obesity and GERD are both increasingly common conditions, overweight increases the risk of GERD hospitalization,[15] BMI and the presence of oesophagitis at initial examination independently predict long-term acid suppression therapy,[16] and GERD symptom severity is associated with impaired health-related quality of life.[17]

In addition we must not forget about the possible development of Barrett's esophagus, the strongest independent risk factor of esophageal adenocarcinoma together with obesity.[18]

Patients and methods

A gastroenterological team in the Szent János Hospital, Budapest, Hungary, conducted a representative population-based study; on 158 untreated patients with typical symptoms of GERD who were selected consecutively and referred for upper panendoscopy.

Mean age of the patients was 53.2 years (SD: 16.4); male/female ratio was 71/87 (45/55 %) and the mean BMI of 26.9 (SD: 6.39).

Definitions: GERD symptoms were defined as heartburn (a burning feeling arising from the stomach or lower part of the chest up towards the neck) and acid regurgitation (flow of sour or bitter fluid into the mouth). Symptoms were defined as moderate (if discomfort was sufficient to cause interference with normal activities) and severe (if incapacitating, with inability to perform normal activities). The diagnosis and Savary-Miller staging[19] was verified by upper panendoscopy findings.

Inclusion criteria: history of episodes of heartburn for one month or longer and with episodes of moderate/severe heartburn for 3 or more days during the last 7 days prior to examination.

Exclusion criteria: Those with ongoing treatment for peptic ulcer with anti-secretory or anti-Helicobacter pylori therapy (proton pump inhibitors, H2- blockers, prokinetics, antibiotics) were excluded.

Concurrent diagnosis of IBS, other erosive or ulcerative gastric or duodenal lesions at the time of endoscopy, other significant medical or surgical diseases which could explain the symptoms, daily use of ASA or NSAIDS, major psychiatric illness or dementia were also excluded.

The classification of GERD was based on endoscopic findings and the severity of oesophagitis. We used the conventional Savary-Miller classification of the disease modified by Sievert.[19]

Statistics

Patient data, including the severity grades of GERD (0-4), age, gender and Body Mass Index (BMI) were collated on an Excel 9.0 worksheet. Statistical analysis was performed using Graph Pad Prism3 and SPSS 9.0 computer programs. Results are expressed as median and 25-75 percentile as well as mean ± SD or SEM. Differences between groups were estimated with non-parametric Mann-Whitney U test and one-way ANOVA (Kruskall-Wallis) test. $P < 0.05$ was considered to be statistically significant.

Results

The total number of available patients was one hundred and fifty eight. Using the Savary-Miller definitions as modified by Sievert, our patients displayed the following distribution alongside the endoscopic classification of reflux disease: 23 (14.6 %) GERD 0 subjects, 46 (29.1 %) GERD 1 subjects, 60 (38%) GERD 2 subjects, 16 (10.1 %) GERD 3 subjects, 13 (8.2.%) GERD 4 subjects.

Relationship between BMI and severity of GERD for the sample covering GERD 0-4 groups are shown in Figure 1. In this case relationship between BMI and GERD severity was at the limit of significance by ANOVA test ($p = 0.0501$).

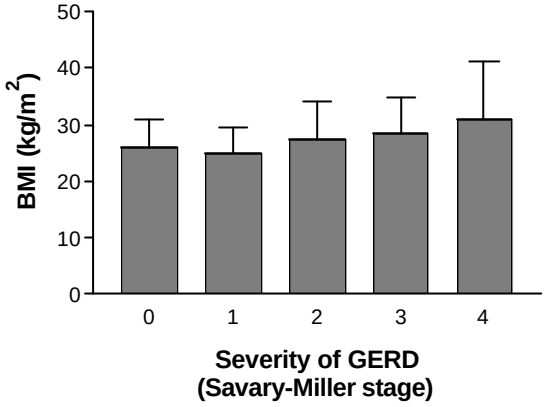

Fig 1: BMI (mean ± SD) in different severity groups of GERD

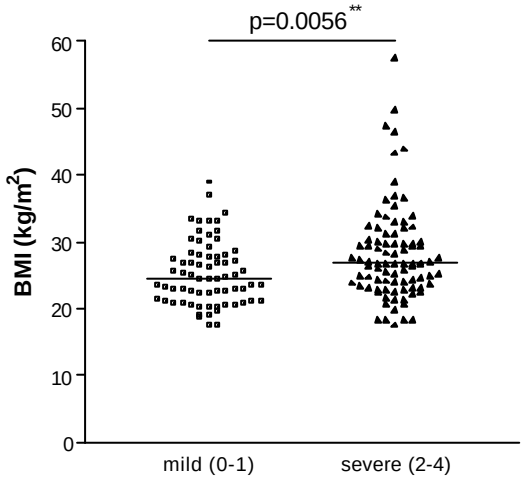

Fig. 2: Patients' BMI distribution in mild (Savary-Miller stage 0-1) and severe (Savary-Miller stage 2-4) groups of GERD (horizontal lines indicate median value of the groups)

There was a strong significant difference between two subgroups based on endoscopic findings, namely patients with non-erosive GERD 0 stage (NERD) and mild (GERD 1 stage) lesions versus well identified erosive lesions (GERD 2-4 stages) (Table 1.) detected by Mann-Whitney test (p=0.0056) (Figure 2.)

Discussion

In our study on a representative group of patients with untreated GERD, we have found an association between BMI and the severity of GERD. Reviewing the results and information published in the past few years, a definite cause-effect relationship has not yet been established in the literature.[3-7]

There is still no generally agreed standard definition on measurement of the occurrence of GERD. Even if we were to accept the evaluation based on the reflux symptoms due to lack of other gold standard, endoscopy is still needed to measure severity.

In the present population with typical and frequent GERD symptoms, the BMI showed just a borderline significant relationship with GERD severity when we analyzed the whole population (Savary-Miller 0-4 stage). Nevertheless, dividing the same population into two subgroups on the grounds of endoscopic findings as a non/mild lesion group (Savary-Miller stage 0-1) and moderate/severe erosive lesion group (Savary-Miller 2-4 stage) a strong correlation was detected between BMI and GERD severity. This finding suggests that obesity and increased BMI is not necessarily the primary cause of GERD but it could be a risk factor for more serious mucosal lesions in the esophagus increasing the possibilities of intestinal and extraintestinal complications of the higher stages of GERD.

In a population of 85 GERD and 100 Barrett patients Korn et al.[20] found no significant correlation between overweight and GERD but patients with Barrett esophagus had significantly higher body mass index than the normal controls. GERD and obesity are known risk factors of Barrett's esophagus[21] and it is estimated that 8-14 % of chronic GERD patients may develop Barrett's metaplasia, which should be considered a primary etiologic factor of esophageal adenocarcinoma (EAC).[22]

Since the incidence of EAC has been increasing faster than any other cancer in developed countries, approximately by 5-10 % per year, identifying these risk factors is essential.[23,24,25]Evaluation of a large population-based case control study[26] in the mid 1990s showed that BMI>30 increased the risk of EAC by 16-fold compared to persons with BMI <22. In the Swedish nationwide Case-control study (SECC) (2000)[18] higher severity of reflux symptoms together with elevated BMI increased the risk of EAC in a dose dependent manner. They found GERD and obesity as strong and independent risk factors of esophageal adenocarcinoma.

From a more practical point of view these two conditions pose social and financial burdens since overweight increases the risk of GERD hospitalization[15] and GERD symptom severity is associated with impaired health-related quality of life (HRQL).[17] On the other hand weight loss as the cheapest and a simple way of therapy has independent beneficial effect on GERD symptoms.[27]

Summarizing our results, higher BMI seems to be associated with higher degree of endoscopic GERD severity, which may worsen HRQL, elevating the risk of Barrett's esophagus,

predisposing to the development of esophageal adenocarcinoma.

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