Gastroesophageal Reflux Before Metabolic Surgery

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Rezumat

Refluxul gastroesofagian înainte de operația metabolică

Introducere: Prevalența obezității a crescut semnificativ în ultimele decenii, iar chirurgia metabolică (bariatrică) a fost extinsă în consecință. Manifestările clinice ale bolii de reflux gastroesofagian (BRGE) sunt frecvente la populația obeză, dar prezența semnelor sau complicațiilor BRGE la pacienții asimptomatici supuși unei intervenții chirurgicale metabolice este neclară.

Obiective: (1) identificarea refluxului gastroesofagian sau a complicațiilor acestuia la pacienții supuși unei intervenții chirurgicale metabolice. (2) Studiarea corelațiilor simptomelor clinice ale BRGE cu constatările radiologice și endoscopice preoperatorii.

Metoda: Toți pacienții consecutivi (BRGE simptomatici sau nu) candidați pentru o intervenție chirurgicală metabolică într-un centru de excelență Bariatric între decembrie 2015 și mai 2016 au fost incluși într-un studiu prospectiv. O echipă multidisciplinară a evaluat toți pacienții din cadrul programului de chirurgie bariatrică. Evaluarea clinică, investigațiile radiologice și endoscopice au fost efectuate la toți pacienții incluși. Pacienții care au avut anterior un tratament anti-reflux sau bariatric au fost excluși.

Rezultate: Patru sute patruzeci și opt de pacienți consecutivi au fost înscrși în studiu. Vârsta medie a pacienților a fost de 41,04 ($\pm$ 11,15) ani, iar 29% dintre aceștia au fost bărbați. Valoarea medie a IMC a fost de 39,96 ($\pm$ 8,17) kg/m². Simptome BRGE au fost înregistrate numai la 93 pacienți (20,76%), în timp ce examinarea endoscopică a evidențiat esofagită la 139 (31,03%) pacienți (107 grade A, 28 grade B, 3 grade C, 1 grad D). Esofagul Barrett a fost suspectat la 5 pacienți, dar confirmarea histologică (metaplazia gastrică) a fost înregistrată numai la 2 pacienți (0,44%). Hernia hiatală a fost descoperită prin endoscopie și radiologie la 119 (26,56%) și 112

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pacienți (25%). 62% dintre pacienții care prezentau esofagită (86/139) nu au avut nici un simptom preoperator al BRGE, ceea ce înseamnă că un număr semnificativ de pacienți asimptomatici supuși unei intervenții chirurgicale metabolice pot prezenta consecințe ale refluxului gastro-esofagian.

Concluzii: Studiul demonstrează că BRGE este mai frecventă decât se așteaptă la pacienții obezi asimptomatici supuși unei intervenții chirurgicale metabolice. Impactul clinic al acestor constatări este important pentru selectarea corectă a procedurii și pentru o evaluare corectă a evoluției post-operatorii.

Cuvinte cheie: reflux gastroesofagian, endoscopie preoperatorie, chirurgie bariatrică, esofag Barrett

Abstract

Background: Obesity has significantly increased in the last decades and metabolic (bariatric) surgery has been extended accordingly. Clinical manifestations of Gastroesophageal reflux disease (GERD) are frequent in the obese population but the presence of GERD premises (i.e. Hiatal hernia) or complications in asymptomatic patients undergoing metabolic surgery is unclear.

Aim: (1) to identify gastroesophageal reflux condition or complications in patients undergoing metabolic surgery. (2) Study the correlations of the clinical symptoms of GERD with the preoperative radiological and endoscopic findings.

Methods: All the consecutive patients (GERD symptomatic or not) undergoing metabolic surgery in a Bariatric Center of Excellence between December, 2015 and May 2016 were included in a prospective study. A multidisciplinary team evaluated all the patients within the bariatric surgery program. Clinical evaluation, radiological and endoscopic investigations were performed to all the included patients. The patients who previously had anti-reflux or bariatric surgery were excluded.

Results: Four-hundred-forty-eight consecutive patients were enrolled into the study. The mean age of patients was 41.04 (± 11.15) years, and 29% of them were men. The mean BMI was 39.96 (± 8.17) kg/m². Symptoms of GERD were recorded only in 93 of the patients (20.76%) while endoscopic examination revealed esophagitis in 139 (31.03%) patients (107 Grade A, 28 Grade B, 3 Grade C, 1 Grade D. Barrett esophagus was suspected in 5 patients but histologic confirmation (gastric metaplasia) was recorded only in 2 patients (0.44%). Hiatal hernia was revealed by endoscopy and radiology in 119 (26.56%) and 112 patients (25%). 62% of the patients presenting esophagitis (86/139) had no pre-operative symptom of GERD, meaning that a significant number of the asymptomatic patients undergoing metabolic surgery may present consequences of gastro-esophageal reflux.

Conclusions: The study demonstrates that GERD is more frequent than expected in asymptomatic obese patients undergoing metabolic surgery. The clinical impact of these findings is important for the proper procedure selection and for a correct evaluation of the postoperative evolution.

Key words: gastro-esophageal reflux, preoperative endoscopy, bariatric surgery, Barrett esophagus

Introduction

The prevalence of gastroesophageal reflux disease in the general population is between 5% and 20% (1,2). Overweight and obesity are recognized as important risk factors for gastroesophageal reflux disease (GERD) (3).

Consequently, in the last decades, the considerable increase in the number of people with obesity was followed by the more frequent reporting of gastroesophageal reflux disease. Along with patients who are addressing the physician, due to the presence of typical symptoms (retrosternal heartburn, regurgitation,

epigastric pain), a significant number of obesity patients have premise or consequences of GERD outside of clinical manifestations (patients with asymptomatic reflux). This situation can be explained by the fact that obesity generates a particular situation by altering the sensitivity and diminishing the esophageal symptoms (4,5). Therefore, there was no correlation between clinical signs and the presence of imaging or endoscopic changes, a circumstance that may cause underestimation of the prevalence of GERD in obese patients (5). On the other hand, in the context of epidemic obesity, we find a significant increase in the use of metabolic surgery, especially of laparoscopic gastric sleeve (LSG) procedures (6), and the influence of these operations on GERD is of concern and a lot of debate in literature (7-11). Consequently, preoperative extensive evaluation of GERD in bariatric patients is mandatory for establishing surgical treatment (type of metabolic surgery, hiatal hernia repair), but also for accurate reporting of BRGE progression following such operations and postoperative weight loss. This will create the premises for correct assignments of the remissions, as well as the "de novo" incidence of GERD.

Aim

The objectives of this study are:

1. Identification of GERD in candidates for metabolic treatments.
2. Analysis of correlation of symptomatology with preoperative radiological and endoscopic aspects in these patients.

Material and Methods

The study looks prospectively for consecutive patients, with or without BRGE symptomatology, evaluated for the treatment of obesity by endoscopic or surgical bariatric procedures (regardless of the type of surgery subsequently established). This study was conducted between December 2015 and May 2016 at the Ponderas Academic Hospital - Center of Excellence in Bariatric and Metabolic Surgery. All patients were investigated by a multidisciplinary team

according to a protocol implemented in the bariatric surgery program that provided data obtained from: clinical examination, symptomatology, medical history, treatments, laboratory analysis, oral contrast study, upper digestive endoscopy, 24-hour pH monitoring. Patients who had a medical history of bariatric surgery or antireflux, endoscopic or surgical procedures were excluded from the study.

Clinical and Anamnestic Data

Symptoms characteristic of reflux disease have been reported: heartburn, regurgitation, epigastric pain, dysphagia as well as the existence and therapeutic effects of acid reflux medication (when appropriate).

Oral Contrast Study

For each patient was noted the presence of radiological signs of GERD and the identification of radiographic signs of hiatal hernia. The device used was Siemens Luminos Fusion - Fluorospot Compact (Siemens Healthcare GmbH, Erlangen, Germany).

Upper Gastrointestinal

Upper gastrointestinal endoscopy recorded the presence of esophagitis and its staging was made after the Los Angeles classification (12); It was also noted the presence of hiatal hernia, Barrett's esophagus and other esogastro-duodenal changes identified during these explorations. The biopsy was performed in all cases of metaplasia. The investigation was performed under i.v. sedation with midazolam using the Olympus Exera III system.

24-h Impedance pH Monitoring

24-h impedance pH monitoring - has been performed selectively only in patients who have identified suggestive changes for the Barrett esophagus. Catheter with 1 pH sensor placed above the upper LES edge according to catheter variation ph and 6 impedance sensors (placed at 3, 5, 7, 9, 15, 17 cm towards the upper edge of LES), (Given Imaging, Medtronic, U.S.).

All the data has been introduced in Excel Microsoft Office 2016, vs 1801, Microsoft

Corporation. Statistical analyses were carried out by SAS University Edition v 9.2, (c) SAS Institute Inc. 100 SAS Campus Drive Cary, NC 27513-2414, USA. The data are presented in Average Arithmetic ($\pm$ D.S) D.S. = standard deviation for continuous variables and absolute frequency and relative frequency for the category variables. A P-value lower than 0.05 was considered to be statistically significant.

Information regarding the study was provided to the patients and their written informed consents were taken in accordance with the Helsinki Declaration. The hospital ethics committee approved the study.

Results

Four-hundred-forty-eight consecutive patients were enrolled into the study between December, 2015 and May, 2016. The mean age of patients was 41.04 ($\pm$ 11.15) years, and 29% of them were men (m/f: 134/314). The mean patients' weight and abdominal circumference was 115.82 ($\pm$ 28.82) kg and 121.45 (19.20) cm, while the mean BMI was 39.96 ($\pm$ 8.17) kg/m². As expected, comorbidities were found in a significant number of the patients: hypertension 33,48%, Type2 Diabetes mellitus 14,95%, Dyslipidemia 56,3% and OSA in 10,93% of the patients. 183 patients were smokers (Table 1).

Typical symptoms of GERD were recorded only in 93 of the patients (20.76%) and only five of them were on PPI therapy, while the rest of the patients (79.24%) had no reflux complain. Endoscopic examination revealed esophagitis in 139 (31,03%) patients (107 Grade A, 28 Grade B, 3 Grade C, 1 Grade D). Barrett with histologic confirmation (gastric metaplasia) was recorded in 2 patients (0.44%). Endoscopy demonstrated hiatal hernia in 119 of the patients (26,56%). Upper GI radiological study revealed gastro-esophageal reflux in 163 the patients (36.38%), and radiological signs of hiatal hernia were noticed in 112 patients (25%) (Table 2).

The results showed the presence of esophagitis in a significant number of the asymptomatic patients, with an increase of more than 50% of the cohort affected by GERD

Table 1. Demographic characteristics of the patients

Age	41.04 ($\pm$ 11.15)
Gender	
M / Total (%)	134 / 448 (29.91)
F / Total (%)	314 / 448 (70.09)
Weight av. (kg)	115.82 ($\pm$ 28.82)
Abdominal circumference (cm)	121.45 (19.20)
Comorbidity	
Hypertension	150 / 448 (33.48)
Diabetes type II	67 / 448 (14.95)
Dyslipidemia	251 / 448 (56.03)
Obstructive Sleep Apnea (OSA)	49/448(10.93)
Smoking	183 / 448 (40.85)

within the group of the patients undergoing metabolic surgery (20.76% vs 31.3%). For the patients with endoscopic findings of esophagitis (139 pts), we found a significant correlation with the GERD clinical symptoms, the presence of hiatal hernia (endoscopy and radiology) and the contrast gastroesophageal reflux (Table 3). More interesting was to discover that 62% of the patients presenting esophagitis (86/139) had no preoperative symptom of GERD, meaning that a significant number of the patients undergoing metabolic surgery may present consequences of gastro-esophageal reflux (Graphic 1).

We demonstrated that gastroesophageal reflux may significantly occur even in asymptomatic

Table 2. GERD symptoms, endoscopic and radiological findings in the preoperative investigations of metabolic patients

Symptoms	
Heartburn, regurgitation, epigastric pain (5 patients on IPPs)	93 / 448 (20.76%)
Endoscopy	
Esophagitis	139 / 448 (31.03%)
Los Angeles A esophagitis	107 / 448 (23.88%)
Los Angeles B esophagitis	28 / 448 (6.42%)
Los Angeles C esophagitis	3 / 448 (0.6%)
Los Angeles D esophagitis	1 / 448 (0.2%)
Barrett with histologic confirmation (gastric metaplasia)	2/448 (0.44%)
Hiatal hernia	119 / 448 (26.56%)
Radiological aspects	
GE reflux	163 / 448 (36.38%)
Hiatal Hernia	112 / 448 (25%)

Table 3. Correlations between esophagitis Symptoms, Weight, BMI, Abdominal Circumference, Smoking, Type 2 DM, radiological signs of hiatal hernia, reflux and endoscopic relevance of hiatal hernia

	Spearman's correlation coefficient							
	P-value							
	Number of cases							
	Symptoms	Weight	BMI	Abd. circ.	Smoking	DZ II	RX Reflux	RX HH
Esophagitis	0.28725	0.12903	0.09539	0.09947	0.07088	0.00224	0.36533	0.22363
	<.0001	0.0062	0.0436	0.0353	0.1341	0.9623	<.0001	<.0001
	448	448	448	448	448	447	448	445
								HH endoscopy
								447

matic obese patients undergoing metabolic surgery. Therefore, patients should be carefully evaluated before surgery even in the absence of symptoms. The clinical impact of these findings is very important for the candidates to metabolic surgery in order to select the proper procedure and have a correct evaluation of the postoperative evolution.

Discussions

Obesity is often associated with gastro-esophageal reflux disease (GERD) and hiatal hernia (HH) (13,14). Pathophysiology includes several mechanisms. In the obesity-GERD relationship, both anatomical and hormonal changes are caused by fat excess. The link between obesity and GERD is direct through increased weight, but especially through the distribution of adipose tissue. Thus patients

with abdominal obesity have a higher risk of developing gastro-oesophageal reflux (15,16). In our study we confirm a positive correlation between the GERD and weight, BMI and abdominal circumference. This also happens as a result of the increase (table 3) in intra-abdominal pressure which will lead to changes of the anatomical elements of the gastro-esophageal junction, resulting in the occurrence of hiatal hernias much more frequently than in the normoponderal population (17,18). Once the phrenoesophageal membrane is thinned, the intraabdominal pressure will move the lower esophageal sphincter (LES) towards the mediastinum, making it incompetent and allowing acid reflux at the terminal esophagus. Esophageal motility disorders (LES malfunction and / or inappropriate body activity of the esophagus) are part of the mechanisms for producing GERD irrespective of body weight, but in the case of obese patients these are found in 61% of them (19). This finding is based on the hypothesis that leptin is a hormone synthesized mainly by adipocytes, is found in larger amounts in obese people and could cause hypomotility of the gastrointestinal tract (20,21). One of the main factors involved in the occurrence of GERD in obese patients is the increase in the frequency of transient relaxation of LES, achieved by mechanical stimulation by distention of the gastric fundus, but also by activation of chemoreceptors at the junction of the gastro-esophageal junction and the proximal portion of the stomach. The way in which patients with obesity (often compulsive and with high volume of food) are eating, is the one that can lead to increased postprandial intragastric pressure, with more frequent

Patients presentig esophagitis

Graphic 1. Correlations between esophagitis and GERD symptoms in patients undergoing metabolic surgery.

relaxation of LES and, implicitly, the onset of GERD (22). In addition to these particular mechanisms, there are also independent weight factors such as smoking, alcohol consumption, food preferences like as a high fat diet, and how these patients are feeding. Poor weight control, including the mechanisms involved, causes the evolution of reflux disease to complicated forms such as erosive esophagitis, Barrett's esophagus or even esophageal adenocarcinoma. Barrett's esophagus has been reported at a 3-fold higher frequency than in the normoponderal population (23,24,25), but in our group we met it in only 2 cases (0.44%). The characteristic symptoms of GERD (heartburn, regurgitation, epigastric pain, dysphagia) are described in other studies varying from 22% to 70% of obese patients (26); we recorded a lower percentage of symptomatic patients, around 20%. A large number of obese patients addressing bariatric and metabolic surgery centers have no esogastric symptoms at the time of the investigations. This discordance between symptomatology and the proven existence of GERD is based on the hypothesis that obese patients have impaired visceral sensitivity. The increased percentage of fatty tissue in the human body results in decreased sympathetic and parasympathetic autonomic nervous system function, resulting in altered esophageal sensitivity transmitted vagal and decreased esophageal symptoms. In our study 62% of the patients with endoscopically diagnosed esophagitis had no preoperative symptoms of GERD. In this situation, guiding diagnosis according to the Montreal Consensus rules suggesting that GERD should be investigated only in the presence of symptoms that affect quality of life may lead to omission of a significant proportion of asymptomatic patients with gastro-oesophageal reflux. Therefore, for obese patients who will benefit from bariatric surgery, preoperative assessment of the esogastric function should be performed independently of the presence or absence of GERD symptoms, each patient should be evaluated according to a protocol including the eso-gastro-duodenal radiology study, superior

digestive endoscopy or 24-h pH monitoring. The adequate preoperative identification of GERD with or without hiatal hernia in these patients is very important as it guides the surgeon in choosing the optimal type of bariatric surgery. Considering that obesity can cause GERD, ideal surgical treatment should control both body weight and gastric reflux (27). Roux – en – Y Gastric bypass follows these two mandatory requirements (28). Bariatric surgery is the most effective method of weight-loss and long-term maintenance, reducing comorbidities associated with obesity, and acting better on GERD mechanisms than strictly anti-reflux procedures (Nissen, Toupet, Dor funduplications) (29).

Limitations of study: 24-h impedance-pH monitoring was used only for the patients with the endoscopic suspicion of Barrett (5 patients) and only in 2 of them had significant reflux (DeMeester score >14) and histological confirmation (gastric metaplasia). We consider that the absence of the 24-h impedance-pH monitoring in all the patients as the main limitation of the present study. However, the study enrolled a significant group of patients consecutively operated within six months in a Bariatric Center of Excellence.

Conclusions

20% of the candidates for metabolic surgery reported typical GERD symptoms while one third had endoscopic and radiologic evidence of GERD. 62% of the patients with esophagitis were asymptomatic prior to surgery. Since typical reflux symptoms are not able to predict objective findings, endoscopy and radiologic investigations should be a must component of the preoperative work-up before metabolic procedures.

The study demonstrates that GERD is more frequent than expected in asymptomatic obese patients undergoing metabolic surgery. The clinical impact of these findings is important for the proper procedure selection and have a correct evaluation of the postoperative evolution.

Conflict of Interest

No conflict of interest for any of the authors.

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