ORIGINAL ARTICLE

Esophageal pH and impedance reflux parameters in relation to body mass index, obesity-related hormones, and bariatric procedures

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KEY WORDS

adipokines, bariatric surgery, esophageal pH monitoring, gastric balloon, obesity

ABSTRACT

INTRODUCTION Obese patients have a higher risk of gastroesophageal reflux disease (GERD), but obesity-related hormonal changes associated with GERD and the effects of bariatric therapy on reflux are unclear.

OBJECTIVES The aim of the study was to assess reflux parameters in relation to bariatric therapy and hormonal changes in obese patients.

PATIENTS AND METHODS This prospective observational study with a 1-year follow-up included 53 obese patients undergoing bariatric therapies. Esophageal pH and impedance monitoring tests were performed and circulating hormone levels were analyzed.

RESULTS Esophageal acid exposure time (%AET) and the number of refluxes correlated positively with body mass index. There were several significant, although weak, correlations of pH and impedance parameters with ghrelin and omentin levels. Patients with abnormal %AET had lower ghrelin levels and those with abnormal reflux number had lower omentin levels than patients with normal parameters. Although we observed certain changes including increased %AET and bolus clearance time (BCT) after laparoscopic sleeve gastrectomy, a reduced BCT and number of refluxes after gastric band, and nonsignificant changes after intragastric balloon, the overall bariatric therapy did not significantly impact on the final GERD diagnosis. GERD before and after therapy was present in 42% of patients. De novo GERD developed in 17.8% of patients, while a similar percentage of patients with initial GERD had normal pH and impedance after therapy. Patients with de novo or persistent GERD had a similar percentage of weight loss as patients without GERD.

CONCLUSIONS Bariatric therapy and percentage of weight loss do not significantly affect GERD. The observed hormonal changes alone do not fully explain the high prevalence of GERD in obese patients.

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INTRODUCTION The increasing prevalence of obesity in adults in developing countries, and in children and adolescents globally, is a major public health challenge.[1,2] In Poland, every fourth inhabitant is obese and abdominal obesity is observed in every third man and nearly every second women.[2] The estimated health care costs attributable to excessive body weight are high because obesity is associated with increased risks of major chronic conditions including diabetes, cardiovascular diseases, depression, and cancers.[1] In addition, people with obesity are at a higher risk of gastroesophageal reflux disease (GERD) and its complications such as Barrett esophagus and esophageal adenocarcinoma. Body mass index (BMI), waist-to-hip ratio, or visceral adiposity are linked to GERD symptoms, Barrett esophagus, or esophageal adenocarcinoma.[3-6]

A variety of pathophysiologic mechanisms have been proposed to link obesity with GERD, including increased abdominal pressure and gastroesophageal pressure gradient, anatomic alterations of the esogastric junction, an increased rate of hiatal hernias, slower esophageal acid clearance, and gastric compression from visceral adiposity.[3-5]

Hormones that regulate food intake, such as ghrelin, and adipokines produced by visceral fat, such as adiponectin, leptin, and omentin, are also an important area of research. We previously reported high levels of leptin and low levels of adiponectin, ghrelin, and omentin in patients with obesity and described hormonal changes in relation to bariatric procedures.[7] Hormones and adipokines may be one of many complex mechanisms linking obesity and GERD and may explain the higher risk of reflux disease in obese patients. Adiponectin deficiency or increased leptin levels were found to be independent risk factors for Barrett esophagus and esophageal adenocarcinoma, and several potential mechanisms promoting carcinogenesis were found.[4] Certain hormonal changes, including lower ghrelin levels, have been described in GERD patients, but the data are sparse.[8,9]

The primary focus in patients with obesity is the achievement of sustained weight loss, which is also important for patients with GERD.[10,11] The beneficial effects of endoscopic and surgical bariatric procedures on weight loss and amelioration of comorbidities are due to the resulting anatomic, physiologic, and hormonal changes.[12-18] However, these therapies may have unintended effects on the esophagus, and the main concern is the possible development of de novo GERD or worsening of existing reflux symptoms after treatment. The available data are conflicting, and the effects of bariatric procedures on esophageal motility and gastroesophageal reflux are still unclear. Most studies investigated GERD by assessing symptoms or the use of proton pump inhibitors only. The use of pH-metry, endoscopy, and esophageal manometry is also quite rare.[12-14,18-20] Furthermore, there is a shortage of prospective studies that would investigate GERD preoperatively and postoperatively or studies that would assess esophageal reflux based on pH and impedance monitoring, which is the most accurate method for esophageal reflux analysis.[21-23]

The purpose of this prospective observational study was to assess gastroesophageal reflux on the basis of pH and impedance monitoring, symptoms, and endoscopic evaluation, in relation to body weight changes, bariatric procedures, and hormone and adipokine levels in patients with obesity undergoing bariatric procedures.

PATIENTS AND METHODS We conducted a prospective observational study of 53 consecutive patients with obesity referred for bariatric endoscopic or surgical therapies (the type of the procedure was in accordance with patients' preferences). We included patients with a BMI of 40 kg/m^2 or higher or a BMI of 35 kg/m^2 or higher with at least 1 obesity-related disease, a history of failed conservative treatment of obesity, and a written informed consent. Exclusion criteria included the following: contraindication to surgery or anesthesia, severe cardiac or chronic renal disease, malignancies, active or chronic infections, secondary causes of obesity, esophageal hiatal hernia (>3 cm), untreated neuropsychiatric disorders, alcohol intake, drug addiction, and lack of collaboration with the patient. Only patients without conventional esophageal manometry abnormalities were included in the study. The study protocol was approved by the Ethics Committee of the Medical University in Bialystok (Białystok, Poland).

An intragastric balloon (IGB, Orbera, Allergan, Irivine, California, United States) was placed and successfully removed after 6 months in 25 patients at the Department of Gastroenterology and Internal Medicine, Medical University of Bialystok. Surgical procedures including laparoscopic adjustable gastric banding (LAGB, 8 patients) and laparoscopic sleeve gastrectomy (LSG, 20 patients) were successfully performed in all patients at the Department of General and Endocrine Surgery, Medical University of Bialystok. Outpatient follow-up visits were scheduled every 1 to 2 months. All patients were followed for 1 year.

Baseline and control (10–12 months posttreatment) evaluations included clinical (reflux symptom assessment, gastroesophageal reflux disease questionnaire [GerdQ])[24] and physical examination (body weight, BMI, percentage of initial body weight [%IBW], and percentage of excess weight loss), upper gastrointestinal endoscopy (presence of reflux esophagitis and grade of esophagitis according to Los Angeles [LA] classification),[25] and 24-hour multichannel pH-metry and impedance monitoring.

We used 24-hour multichannel esophageal pH and impedance monitoring (Sleuth system, Sandhill Scientific Inc., Highland Ranch, Colorado, United States), which was successfully performed in all 53 patients referred for bariatric therapy and repeated at 10 to 12 months after the procedures in 45 patients (85%, the test was not repeated in 2 patients due to technical problems; the data were incomplete in 2 patients, and 4 patients refused to repeat the test). Patients were instructed to eat 3 meals during the measurement and encouraged to maintain normal daily activities. They were asked to mark meals, periods spent in a supine position, and press the event marker button on the data logger whenever they experienced symptoms. The data were analyzed using a semiautomated software system (BioView, Sandhill Scientific) and then verified manually. The following pH and impedance monitoring data were analyzed: esophageal acid exposure time (%AET,

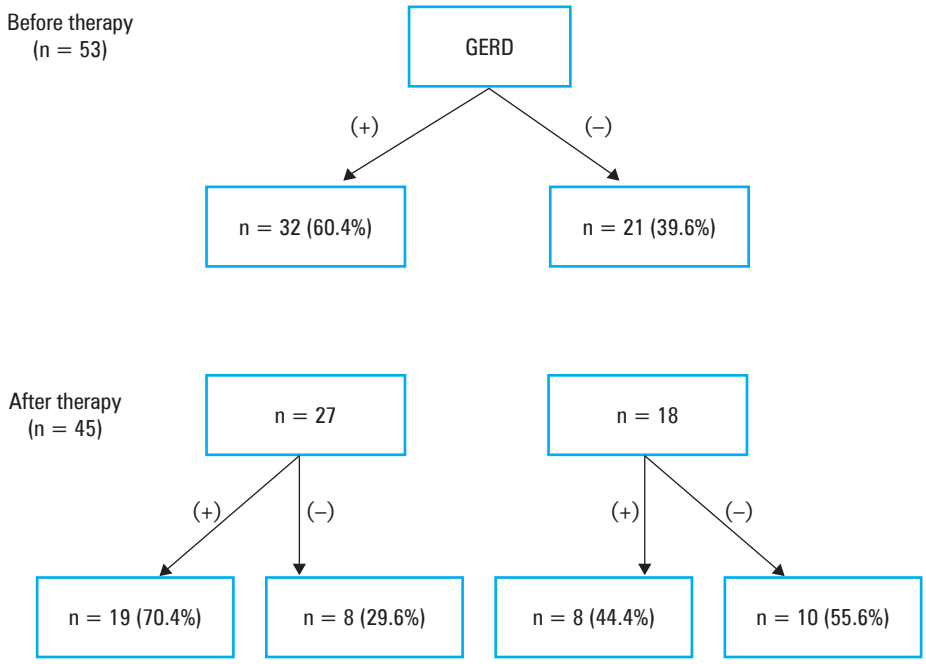

FIGURE 1 Presence of gastroesophageal reflux disease (GERD) after bariatric therapy among patients with and without GERD before therapy

the percentage of time that pH was below 4), acid clearance time (ACT), bolus clearance time (BCT), total number of reflux episodes, number of acid reflux episodes (impedance-detected reflux with nadir, pH <4), number of weakly acidic reflux episodes (impedance-detected reflux with nadir, pH 4–7), number of weakly alkaline reflux (impedance-detected reflux with nadir, pH >7), number of proximal reflux episodes (reaching 15 cm above the lower esophageal sphincter [LES]), number of reflux episodes in upright or recumbent positions, and the number of reported symptoms (typical: heartburn and regurgitation; atypical: belching, abdominal pain, cough, other).

Diagnosis of GERD was made on the basis of abnormal pH with impedance test. %AET higher than 4.2% and a total number of reflux episodes exceeding 73 were considered pathological. A reflux episode was considered to be associated with reflux symptoms if the experienced symptoms followed within 2 minutes after the onset of the reflux episode. This association was analyzed using symptom association probability (SAP) as previously described, and a SAP exceeding 95% was considered positive.[26-28] All patients with endoscopic reflux esophagitis were considered to have GERD and had abnormal pH with impedance monitoring. All pH with impedance tests were performed at least 8 weeks off reflux inhibitor therapy (proton pump inhibitors and H_2-receptor antagonists).

Blood samples were collected from a peripheral vein before and at 10 to 12 months after therapy to assess the levels of adiponectin (Human Adiponectin, RIA, Millipore, Burlington, Massachusetts, United States), ghrelin (Human Ghrelin Total, RIA, Millipore), and omentin-1 (Human Omentin-1, Elisa, Biovendor, Brno, Czech Republic). All measurements were performed according to the manufacturers' instructions.

Statistical analysis All statistical analyses were performed using the STATISTICA 10.0 package. Results were presented as a median and interquartile range (IQR) or percentage. The Mann–Whitney test was used for comparison of quantitative variables and the χ^2 test for comparison of qualitative variables. Dependent variables were compared using the Wilcoxon matched-pairs signed-rank test and McNemar tests. Multiple variables were analyzed using the analysis of variance Kruskal–Wallis test. Correlations were shown by means of the Spearman coefficient. A P value of less than 0.05 was considered significant.

RESULTS

Baseline characteristics of patients

A total of 53 patients (21 men, 32 women) at a median age of 41.6 years (range, 20–70 years) were included in the study. The median body weight was 134 kg (IQR, 119–146 kg) and the median BMI was 47.3 kg/m^2 (IQR, 42.2–50.4 kg/m^2).

Overall, pH-metry and impedance monitoring confirmed GERD in 32 patients (60.4%) referred for bariatric therapies (FIGURE 1). Endoscopic findings before any bariatric procedures were as follows: normal endoscopy in 42 patients (79%) and reflux esophagitis in 11 (21%) (grade A in 8 patients and grade B in 3 patients according to the LA classification). The median GerdQ score at baseline did not correlate with body weight and BMI.

Correlation of pH-metry and impedance parameters with body weight, reflux esophagitis, and hormone levels

We found a positive correlation of body weight and BMI with the %AET in the upright position (Rs = 0.305; P = 0.03 and Rs = 0.275;

TABLE 1 Twenty-four–hour multichannel esophageal pH-metry and impedance parameters and hormone levels in patients with and without reflux esophagitis before bariatric therapies

Parameter		Reflux esophagitis (n = 11)	No reflux esophagitis (n = 42)	*P* value
Body weight, kg		130 (119–145)	139 (119–150)	0.76
BMI, kg/m^2		42.9 (41.2–48.3)	45.3 (42.2–50.8)	0.46
%AET	Total	6.1 (3.0–9.7)	3.8 (1.6–5.5)	0.02
	In recumbent position	3.4 (1.1–10.8)	0.8 (0.2–2.6)	0.01
	In upright position	5.7 (4.1–8.8)	5.5 (2.9–7.9)	0.44
ACT, s		119 (87–215)	78 (65–109)	0.02
BCT, s		10 (7–12)	12 (9–16)	0.14
Total reflux episodes, n		66 (53–101)	70.5 (46–109)	0.90
Acid reflux, n		50 (38–79)	47 (25–72)	0.64
Weakly acidic reflux, n		15 (11–26)	23 (12–32)	0.26
Proximal reflux, n		33 (30–45)	29.5 (19–62)	0.68
Adiponectin, ng/ml		6205.5 (3319–14 025.5)	7270 (4160–10 479.5)	0.65
Ghrelin, pg/ml		494 (450–630.2)	584.1 (507.3–765.2)	0.08
Omentin, ng/ml		327.2 (264.4–659.2)	438.7 (305.4–588.8)	0.88

Data are presented as median (interquartile range) unless otherwise indicated.

Abbreviations: ACT, acid clearance time;%AET, acid exposure time; BCT, bolus clearance time; BMI, body mass index

P = 0.046, respectively) and the number of proximal reflux episodes (*Rs* = 0.358; *P* = 0.01 and *Rs* = 0.279; *P* = 0.049, respectively). There were weak but significant correlations between the total GerdQ score and the %AET in the upright position (*Rs* = 0.271; *P* = –0.0499) and the number of reflux episodes in the upright position (*Rs* = 0.276; *P* = 0.046).

Patients with reflux esophagitis had a significantly higher median total %AET and ACT than patients without reflux esophagitis (TABLE 1), whereas there were no differences between groups in median body weight and BMI.

Previously, we found that patients with obesity compared with controls had lower adiponectin, ghrelin, and omentin levels and described their variation after bariatric therapies.[5] In the current study, we assessed the correlation of hormone levels with reflux parameters of pH with impedance monitoring. We did not observe significant correlations between the median levels of adiponectin and pH-metry and impedance parameters. However, we found weak but significant correlations between median ghrelin levels and the total %AET (*Rs* = –0.311; *P* = 0.02), %AET in the upright position (*Rs* = –0.390; *P* = 0.004), and the median number of proximal reflux episodes (*Rs* = –0.303; *P* = –0.03). Patients with pathological %AET had significantly lower median ghrelin levels than patients with normal %AET (504.4 pg/ml [IQR, 456.3–663.6 pg/ml] and 669.4 pg/ml [IQR, 521.9–700.4 pg/ml], respectively, *P* = 0.04). We found that median omentin levels correlated with the total number of reflux episodes (*Rs* = –0.447; *P* <0.001), the number of acid reflux episodes (*Rs* = –0.419; *P* <0.001), the number of reflux episodes in the upright position (*Rs* = –0.401; *P* = 0.002) and recumbent position (*Rs* = –0.297, *P* = 0.03), and the number of reflux episodes reaching the proximal esophagus (*Rs* = –0.386; *P* = 0.004). Patients with a pathological total number of reflux episodes had lower median omentin levels than patients with normal number of reflux episodes (<73) (367.7 ng/ml [IQR, 220.8–472.1 ng/ml] and 508.4 ng/ml [IQR, 373.9–629.1 ng/ml], *P* = 0.006, respectively).

In this study, patients with obesity and reflux esophagitis on endoscopy as compared with patients with obesity and without reflux esophagitis did not show significant differences in the median levels of adiponectin, ghrelin, and omentin (TABLE 1).

Characteristics of patients after bariatric procedures Bariatric therapies resulted in significant weight loss. Overall, the median body weight at 12 months after the procedure was 108.6 kg (IQR, 92–121 kg; *P* <0.001 vs body weight before the procedure) and the median BMI was 38.5 kg/m^2 (IQR, 33.2–43.3 kg/m^2; *P* <0.001 vs BMI before the procedure). The median %IBW was 78% (IQR, 71.4%–86.1%) and percentage of total weight loss (%TWL) was 22% (IQR, 51.1%–13.9%).

No significant abnormalities on control endoscopy after the bariatric procedure were detected in 46 patients (86.8%) and esophagitis was found in 7 patients (13.2%) (grade A in 6 patients and grade B in 1 patient according to the LA classification). In general, 37 patients (69.8%) had normal endoscopy before and after the procedure. Normal endoscopy results after therapy were found in 9 patients (17%) with initially observed reflux esophagitis (IGB, 5 patients; LSG, 3 patients; and LAGB, 1 patient). In contrast, control endoscopy revealed reflux esophagitis in 7 patients (13.2%) including 5 patients in

TABLE 2 Weight loss in relation to the presence of gastroesophageal reflux disease (GERD) after therapy

Parameter		No GERD (n = 18)	Persistent or de novo GERD (n = 27)	*P* value
Body weight, kg	Before therapy	121.5 (112.0–142.0)	140.0 (126.0–143.0)	0.14
	After therapy	99.0 (85.0–113.0)	102.0 (92.0–125.0)	0.32
%IBW		76.7 (72.4–84.3)	77.1 (71.4–91.4)	0.74
%TWL		23.3 (15.7–27.6)	22.9 (8.6–28.6)	0.74

Data are presented as median (interquartile range).

Abbreviations: %IBW, percentage of initial body weight; %TWL, percentage of total weight loss

TABLE 3 Twenty-four–hour multichannel esophageal pH and impedance parameters before and after bariatric therapy

Parameter		Before bariatric therapy	After bariatric therapy	*P* value
%AET	Total	3.8 (2.0–5.9)	2.8 (1.1–7.8)	0.58
	Upright position	5.7 (3.1–7.9)	3.3 (0.7–8.2)	0.24
	Recumbent position	1.1 (0.2–2.8)	0.9 (0.1–7.4)	0.15
ACT, s		82.0 (65.0–119.0)	68.0 (32.0–226.0)	0.65
BCT, s		12.0 (8.0–14.0)	12.0 (8.0–17.0)	0.08
Reflux episodes, n	Total	70.0 (49.0–105.0)	54.0 (41.0–84.0)	0.02
	Acid	49.0 (32.0–72.0)	40.0 (23.0–59.0)	0.11
	Weakly acidic	21.0 (12.0–31.0)	14.0 (10.0–31.0)	0.11
	Weakly alkaline	0.0 (0.0–2.0)	0.0 (0.0–20.0)	0.82
	Gas	11.0 (7.0–25.0)	10.0 (5.0–16.0)	0.02
	Proximal	30.0 (22.0–53.0)	31.0 (14.0–50.0)	0.16
	Upright position	55.0 (41.0–77.0)	42.0 (29.0–56.0)	0.002
	Recumbent position	14.0 (5.0–27.0)	13.0 (7.0–31.0)	0.94
Symptoms, n		8.0 (3.0–14.0)	8.0 (3.0–24.0)	0.12
Positive SAP, n (%)		34 (73.9)	28 (75.7)	0.85

Data are presented as median (interquartile range).

Abbreviations: SAP, symptom association probability; others, see TABLE 1

whom the endoscopy before therapy was normal (IGB, 3 patients; LSG, 1 patient; and LAGB, 1 patient) and 2 patients with esophagitis at baseline (LAGB, 1 patient; LSG, 1 patient).

The median GerdQ score before and after the procedures was similar (6.5, [IQR, 6–7] vs 6.7 [IQR, 6–8]; $P = 0.15$).

After treatment, pH and impedance monitoring was repeated in 45 patients, of whom 27 (60%) were diagnosed with GERD, including 19 patients with preoperative GERD and 8 patients without preoperative GERD. After therapy, 18 of 45 patients (40%) did not have a GERD diagnosis, including 10 patients without preoperative GERD and 8 patients with preoperative GERD (FIGURE 1). In summary, 19 of the 45 patients (42.2%) had GERD before and after therapy and 10 of the 45 patients (22.2%) did not have GERD before and after therapy. In contrast, 8 of the 45 patients (17.8%) had de novo reflux disease, while 8 of the 45 patients (17.8%) with GERD at baseline had normal pH with impedance monitoring after therapy ($P = 1.00$).

Next, we analyzed if there were differences in the amount of weight loss after therapy between patients with persistent or de novo GERD and patients without GERD. The %IBW and %TWL were similar in both groups (TABLE 2).

Overall, the analysis of the parameters of pH with impedance monitoring showed that bariatric therapy did not significantly change the median %AET, ACT, or BCT but reduced the total number of reflux episodes. In addition, there were no significant differences in the median number of reflux symptoms before and after therapy as well as in the median number of patients with positive SAP (TABLE 3).

Parameters of multichannel pH-metry with impedance monitoring in relation to bariatric procedures We analyzed the parameters of pH-metry with impedance monitoring before and after treatment in relation to the procedure type. Specifically, IGB therapy resulted in nonsignificant changes of pH and impedance monitoring parameters. Only a decreasing trend in the median total %AET and number of reflux episodes was

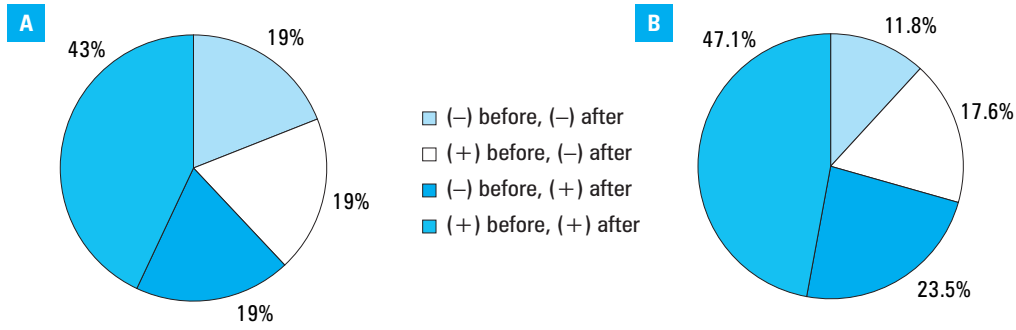

FIGURE 2 Percentage of patients with diagnosis of gastroesophageal reflux disease before and after intragastric balloon (**A**) and laparoscopic sleeve gastrectomy (**B**)

observed. Four patients treated with IGB developed de novo GERD, while 4 patients with GERD diagnosis before therapy had a normal control pH and impedance test (FIGURE 2).

A nonsignificant decrease in the %AET in patients after the LAGB was observed, but these patients were found to have a lower median BCT, lower median number of reflux episodes (total, acid, and weakly acidic), especially in the upright position, and a lower number of reflux episodes reaching the proximal esophagus (TABLE 4).

In contrast to the changes observed after IGB placement and LAGB, the LSG led to a significant increase of the %AET, especially in the recumbent position, and the BCT (TABLE 3). Among patients treated with LSG, 4 patients developed de novo GERD and 3 patients with a GERD diagnosis before therapy had a normal pH and impedance test after therapy (FIGURE 2).

Although we observed changes of some pH and impedance parameters after therapy compared with the parameters at baseline, the final diagnosis of GERD based on pH with impedance monitoring before and after IGB placement and LSG did not change significantly (TABLE 4, FIGURE 2).

Overall, among 27 patients with persistent or de novo GERD after therapy, there were 13 patients treated with IGB (13/21, 62%), 12 patients treated with LSG (12/17, 70.6%), and 2 patients treated with LAGB (2/7, 28.6%) (FIGURE 2). In a subgroup of patients treated with IGB, the weight loss expressed by the %IBW was not different between patients with persistent or de novo GERD and patients without GERD (91.4% [83.0%–93.4%] vs 74.2% [71.9%–88.6%], $P = 0.06$). Similarly, among patients treated with LSG, the %IBW was similar in patients with persistent or de novo GERD and patients without GERD (71.1% [66.2%–74.1%] vs 76.2% [67.2%–77.3%], $P = 0.33$).

DISCUSSION The prevalence of GERD is estimated to be between 10% and 20% in the Western world and is higher in a given population with obesity.[5,6,11] We diagnosed GERD based on a pH and impedance test in more than half of the patients referred for bariatric therapy, and reflux esophagitis was found in 21% of patients. The risk of GERD symptoms and its complications were linked to BMI, waist-to-hip ratio, and visceral adiposity, and patients with obesity were found to have increased rates of esophageal dysmotility, acid reflux, and impairment of esophageal acid clearance.[4,13,29-32] In our paper, BMI correlated with esophageal acid exposure time and number of proximal reflux episodes. In addition, patients with obesity and reflux esophagitis had a significantly higher median esophageal %AET and ACT than patients without reflux esophagitis.

Hormonal changes may be one of several mechanisms responsible for the increased risk of GERD in patients with obesity, but this association is unclear as the current data are limited.[4,8,9,33] To the best of our knowledge, this study is the first to assess the levels of ghrelin, adiponectin, and omentin in patients with obesity in relation to reflux parameters of pH and impedance monitoring. Ghrelin, which is secreted mainly by the gastric fundus, stimulates appetite, promotes gastric emptying, enhances growth hormone secretion, and may modify inflammatory pathways.[9,14,33] We believe that low levels of ghrelin may influence reflux in patients with obesity, perhaps through decreasing gastric emptying and increasing stasis of gastric contents. This mechanism may be responsible for an increase in gastric pressure and LES relaxations and promote the reflux of gastric contents to the esophagus. In addition, impaired ghrelin signaling was found to be associated with gastrointestinal dysmotility in an experimental study of surgically induced GERD.[34,35] Omentin-1 is a fat depot-specific secretory protein produced by the stromal vascular cells from adipose tissue. The role of omentin in the context of reflux and esophageal mucosa is not known and needs to be evaluated at the cellular and tissue levels. We think that omentin can have impact on esophageal reflux by affecting the LES, gastrointestinal motility, and esophageal mucosa. In our study, the median ghrelin levels were significantly lower in patients with a pathological esophageal %AET than in patients with a normal esophageal %AET, while omentin levels were significantly lower in patients with abnormal number of reflux episodes than in patients with a normal number of reflux episodes. Although we found several significant correlations of ghrelin and omentin levels with reflux parameters, most of these correlations were weak. Therefore, hormonal changes itself cannot explain the high prevalence of GERD in obese patients

TABLE 4 Twenty-four–hour multichannel esophageal pH-metry and impedance parameters in relation to the type of bariatric therapy

Parameter		Intragastric balloon (n = 25)	Sleeve gastrectomy (n = 20)	Gastric band (n = 8)	*P* value
Total %AET	Before procedure	3.8 (1.6–5.6)	4.6 (2.6–6.0)	3.4 (1.3–5.6)	0.69
	After procedure	2.8 (1.4–5.9)	5.4 (1.7–11.1)	0.2 (0.2–2.9)	
	P value	0.42	0.07	0.5	
%AET in upright position	Before procedure	5.3 (2.9–7.7)	6.4 (4.1–8.3)	3.8 (2.7–9.9)	0.48
	After procedure	5.2 (0.9–7.2)	5.0 (1.7–8.4)	0.4 (0.3–6.9)	
	P value	0.33	0.48	0.61	
%AET in recumbent position	Before procedure	0.9 (0.3–2.6)	1.6 (0.3–4.5)	0.8 (0.2–2.2)	0.49
	After procedure	1.1 (0.4–4.3)	7.4 (0.2–14.7)	0.1 (0.0–0.4)	
	P value	0.97	0.02	0.45	
ACT, s	Before procedure	78.0 (55.0–151.0)	102.0 (69.0–119.5)	84.5 (54.5–114.0)	0.73
	After procedure	68.0 (32.0–119.0)	133.0 (59.0–238.0)	24.0 (10.0–91.0)	
	P value	0.44	0.07	0.61	
BCT, s	Before procedure	12.0 (10.0–14.0)	17.0 (11.0–25.0)	9.5 (8.0–14.0)	0.65
	After procedure	12.0 (9.0–16.0)	11.5 (8.0–13.5)	7.0 (4.0–7.0)	
	P value	0.82	0.002	0.02	
Total reflux, n	Before procedure	62.0 (41.0–89.0)	71.5 (58.5–118.0)	86.0 (58.0–95.0)	0.26
	After procedure	54.0 (41.0–78.0)	72.0 (52.0–115.0)	30.0 (16.0–51.0)	
	P value	0.15	0.64	0.02	
Acid reflux, n	Before procedure	42.0 (19.0–68.0)	63.0 (38.5–78.0)	54.5 (35.5–68.5)	0.20
	After procedure	42.0 (23.0–59.0)	47.0 (30.0–67.0)	15.0 (10.0–40.0)	
	P value	0.58	0.57	0.046	
Weakly acidic reflux, n	Before procedure	19.0 (12.0–29.0)	22.0 (11.5–31.5)	27.0 (13.0–31.5)	0.77
	After procedure	13.0 (10.0–25.0)	29.0 (14.0–37.0)	10.0 (1.0–23.0)	
	P value	0.08	0.55	0.03	
Weakly alkaline reflux, n	Before procedure	0.0 (0.0–2.0)	0.5 (0.0–2.5)	0.0 (0.0–1.5)	0.79
	After procedure	1.0 (0.0–4.0)	0.0 (0.0–2.0)	0.0 (0.0–1.0)	
	P value	0.37	0.63	0.79	
Gas reflux, n	Before procedure	11.0 (5.0–19.0)	21.0 (10–33.0)	10.5 (7.0–14.5)	0.04
	After procedure	10.0 (6.0–16.0)	11.0 (5.0–17.0)	5.0 (2.0–10.0)	
	P value	0.34	0.07	0.24	
Proximal reflux, n	Before procedure	30.0 (18.0–44.0)	40.5 (26.5–65.5)	26.0 (18.5–38.5)	0.09
	After procedure	30.0 (14.0–44.0)	42.0 (30.0–67.0)	10.0 (4.0–18.0)	
	P value	0.17	0.74	0.02	
Upright reflux, n	Before procedure	47.0 (31.0–77.0)	58.0 (50.0–77.0)	55.0 (44.5–73.5)	0.29
	After procedure	42.0 (27.0–55.0)	50.0 (35.0–80.0)	29.0 (10.0–37.0)	
	P value	0.1	0.19	0.02	
Recumbent reflux, n	Before procedure	9.0 (5.0–20.0)	17.0 (9.0–43.0)	12.0 (7.0–29.0)	0.39
	After procedure	10.0 (7.0–27.0)	17.0 (10.0–34.0)	6.0 (1.0–14.0)	
	P value	0.59	0.82	0.18	
Symptoms, n	Before procedure	8.0 (3.0–17.0)	8.0 (3.0–10.0)	8.0 (1.0–13.0)	–
	After procedure	7.0 (2.0–26.0)	12.0 (5.0–24.0)	11.5 (6.5–29.0)	
	P value	0.43	0.26	0.72	

Data are presented as median (interquartile range).

Abbreviations: see TABLE 1

and confirm the complex mechanism linking obesity and GERD.

Data on the effects of bariatric therapy on esophageal motility and gastroesophageal reflux are conflicting, and there is little known on how to manage patients with obesity and GERD or to avoid GERD development after bariatric procedures.[12-14] We performed a detailed analysis of reflux parameters based on pH with impedance monitoring. The bariatric procedures taken together did not significantly change the final GERD diagnosis after therapy compared with

before therapy. De novo GERD was detected in about 18% of patients, while a similar number of patients with preoperative GERD had normal pH-metry with impedance test postoperatively. In about 42% of patients GERD was present before and after therapy. In addition, patients without GERD after the procedure had a percentage of weight loss similar to those with de novo or persistent GERD after an operation, although the last group had a slightly but nonsignificantly higher baseline body weight. In our previous study, LSG provided better weight loss compared with LAGB and IGB.[7] In this study, the development of de novo GERD or persistence of GERD after therapy in all patients as well as in the subgroups treated with IGB and LSG were not associated with the amount of weight loss. However, the size of the analyzed subgroups was small and varied and we do not exclude the possibility of significant changes in a larger subgroup of patients.

The effects of different bariatric techniques on reflux parameters are still unclear and debated. We observed certain differences between the procedure types in pH and impedance parameters before and after therapy. The LAGB decreased the number of reflux episodes and tended to decrease the median esophageal acid exposure time. In contrast, the LSG caused a significant increase in the BCT and esophageal %AET in the recumbent position. However, when analyzing the final diagnosis based on pH-metry with impedance monitoring, the percentage of patients with GERD before and after therapy as well as the percentage of patients with de novo or resolved GERD after LSG or IGB were similar. Currently, the available data on LAGB shows improvement of reflux symptoms, a decreased use of proton pump inhibitors, and resolution of esophageal lesions shortly after therapy (up to 2 years). However, the lesions can recur in a longer follow-up. Gastric banding may have an antireflux effect by augmenting the LES through creation of a longer intra-abdominal pressure zone and by prevention of hiatal hernias through creation of a physical barrier below the diaphragm. Worsening of GERD after LAGB may result from esophageal dilation due to esophageal outlet narrowing, which reduces the flow and esophageal clearance, and results in stasis of food and refluxate, incomplete LES relaxation and increased LES pressure, or pouch formation caused by inaccurate band placement.[12-14,36-38] Studies regarding the effects of IGB therapy on GERD are sparse. The incidence of GERD following balloon placement was 18.3%.[39,40] Several studies have shown improvement of GERD after sleeve gastrectomy, while other authors described worsening of GERD symptoms or development of de novo GERD symptoms or reflux esophagitis.[12-15] LSG may decrease GERD by reversing weight and visceral adiposity, increasing gastric emptying, and decreasing stomach pressure. In contrast, the development of GERD, observed usually a few years after LSG, may be caused by anatomic changes such as the alteration of the angle of His, hiatal herniation, decrease in LES pressure, migration of the proximal sleeve above the level of the hiatus, and the formation of a neofundus.[12-15] An increased occurrence of reflux after LSG may be due to low ghrelin levels as a consequence of gastric fundus resection. In contrast, the LAGB procedure promotes increased ghrelin plasma levels.[16,17]

The present study has several limitations that can result in statistical bias. A direct comparison of the bariatric therapies on reflux parameters was not performed as the number of patients that underwent particular bariatric procedures was different and the number of patients who underwent LAGB was small. In addition, this was an observational nonrandomized study with a short follow-up, and the type of the performed procedure was in accordance with patients' preferences. However, the strength of this study is its prospective design and a comprehensive investigation of GERD by the assessment of pH with impedance monitoring, which is the most accurate method of reflux analysis as well as symptom and endoscopic evaluation. We did not observe significant impact of bariatric therapy on GERD in the whole study population, but we excluded patients with esophageal dysmotility (by conventional manometry) and large hiatal hernias (>3 cm). It is known that proper patient selection, complete preoperative assessment to identify the presence of esophageal dysmotility, LES abnormalities, hiatal hernias, and good surgical techniques are the key to achieve optimal outcomes.[41] We did not perform a detailed analysis concerning the necessity of on-demand therapy with proton pump inhibitors in the periods between control visits. However, all tests including endoscopy and pH and impedance monitoring were performed at least 8 weeks off reflux inhibitor therapy. In addition, we cannot exclude the possible spontaneous intraindividual variability of pH with impedance parameters. All tests (endoscopy, pH and impedance monitoring) before and after therapy were performed by one experienced endoscopist and gastroenterologist to diminish the potential interobserver variability. Other study limitations are the lack of a direct assessment of the impact of ghrelin and omentin on the esophageal mucosa and their concentrations in the stomach and unknown data on the levels of hormones in GERD patients without obesity, which needs further evaluation.

In conclusion, GERD was recognized in about half of obese patients referred for bariatric therapies, and pH and impedance monitoring parameters showed significant correlations with BMI. The hormonal changes alone do not fully explain the high prevalence of GERD among obese patients as most of observed significant correlations of ghrelin and omentin levels with reflux parameters were weak. These observations confirm a more complex mechanism linking obesity and GERD. We observed some changes between particular bariatric procedures in pH and

impedance parameters before and after therapy, but overall bariatric therapy did not significantly impact on GERD development. Less than half of patients had persistent GERD after therapy. De novo GERD after therapy developed in one-fifth of patients, while a similar number of patients with initial GERD had a normal pH--metry with impedance monitoring after therapy. In addition, patients with de novo or persistent GERD had a percentage of weight loss similar to patients without GERD after therapy. Therefore, the persistence of GERD or development of de novo GERD after therapy does not seem to depend on the amount of weight loss but on proper patient selection and bariatric technique. Longer follow-up and a larger group of patients are needed to assess the development of de novo GERD after different bariatric therapies independently from sustained weight loss or progressive weight gain.

SUPPLEMENTARY MATERIAL Supplementary material is available with the article at www.pamw.pl.

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