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RESEARCH ARTICLE

Early Changes in Postprandial Gallbladder Emptying in Morbidly Obese Patients Undergoing Roux-en-Y Gastric Bypass: Correlation with the Occurrence of Biliary Sludge and Gallstones

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Abstract
Background Gallstones have been frequently diagnosed after Roux-en-Y gastric bypass (RYGBP). Gallbladder stasis associated with duodenal exclusion may play a role in their pathogenesis.
Methods Gallbladder emptying was studied before and on the 30th and 31st postoperative days (POD) after RYGBP in 20 morbidly obese patients. Gallbladder volume after fasting and every 15 min during a 2-h period following administration of a standard liquid meal was determined by sonography. On the 31st POD, the meal was administered through the gastrostomy in order to promote its transit through the duodenum. Fasting volume (FV), maximum ejection fraction (Max EF), and residual volume (RV) were determined. Biliary sludge and calculi were investigated after 1 and 6 months, respectively.
Results FV was 39.4±20.2 ml, 50.1±22.7 ml, and 47.9±23.4 ml, respectively, for the preoperative and two postoperative assessments (P=0.09). RV was 7.6±8.7 ml, 25.1±20.0 ml, and 24.6±20.9 ml; and Max EF was 80.5±20.9%, 54.3±21.4%, and 50.5±29.0%, respectively, for the pre-, postoral, and postgastrostomy infusion measurements. There was only a significant difference between the preoperative value and the two postoperative values (P<0.001). Biliary sludge was detected in 65% of the patients and 46% of them subsequently developed gallstones.
Conclusions Gallbladder emptying became significantly compromised after RYGBP. This impairment was unrelated to duodenal exclusion but it was associated with biliary sludge and stone formation.

Keywords Morbid obesity · Cholelithiasis · Gallbladder emptying · Gastroplasty · Ultrasonography · Bariatric surgery

Introduction

Gallstones represent the third most common disease observed among obese patients [1]. Moreover, about 30% of the patients who are candidates for bariatric surgery either have undergone prior cholecystectomy or are found to present gallstones at the time of surgery [2].

On the other hand, newly formed gallstones may be diagnosed in 27% to 43% of patients who have undergone bariatric surgery within a very short period of time [3]. Recently, it was found that the risk of developing gallstones can be as high as 52.8% in patients undergoing Roux-en-Y

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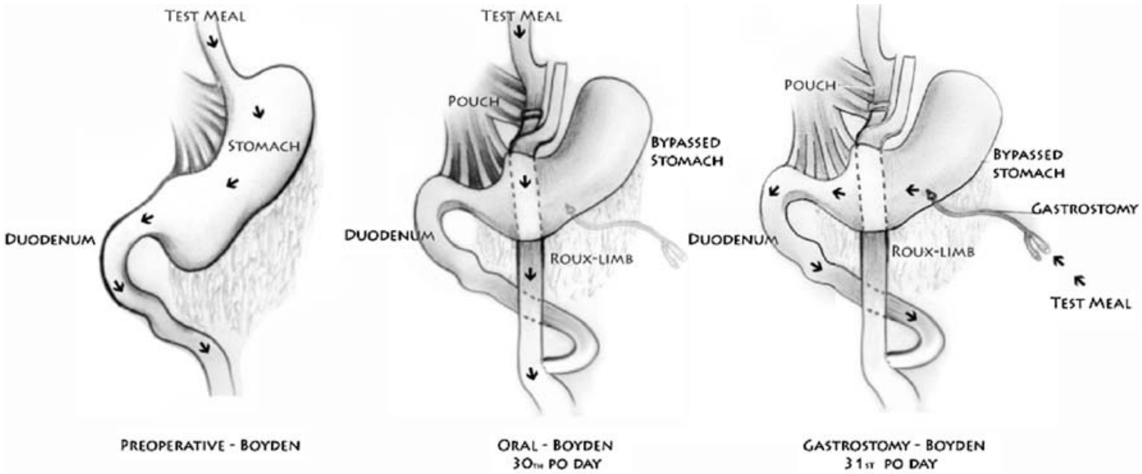

Fig. 1 Pre- and postoperative transit of the Boyden test meal

gastric bypass (RYGBP) who are followed up for 1 year afterwards [4].

Three factors are considered to be important in cholesterol gallstone formation: cholesterol supersaturation in the bile, presence of factors that shorten nucleation time (time taken for cholesterol crystals to form), and gallbladder hypomotility, which offers the time and conditions necessary for cholesterol crystals to grow into macroscopic stones [5–10].

Patients undergoing rapid weight loss, following bariatric surgery, experience increased cholesterol saturation in the bile [11] and also present increased concentrations of mucin in the gallbladder, which is the most important pronucleating factor [6]. The altered anatomy created by surgery, such as when RYBGP is performed, may induce changes in postprandial gallbladder emptying secondary to decreased circulating cholecystokinin levels [12], thus representing the third factor potentially involved.

The purpose of this study was to assess the early occurrence of changes in postprandial gallbladder emptying, their association with duodenal exclusion, and their potential influence on the process of biliary sludge and gallstone formation.

Materials and Methods

Sample

Twenty morbidly obese patients of both genders (16 females) who had previously been selected for bariatric surgery were invited to enter this study. All of these patients met the 1991 National Institutes of Health Consensus Conference criteria for bariatric operations [13]. Additional inclusion criteria included absence of gallbladder disease, as assessed by sonography, and no previous surgery involving

Table 1 Pre- and postoperative gallbladder volumes while fasting and at the different time points after administering the test meal orally and through the gastrostomy

	Gallbladder volume (Boyden test)									
Observation times	Minutes	F	15	30	45	60	75	90	105	120
Preoperative	Mean	39.43	22.50	13.48	10.56	10.25	10.99	11.65	14.56	16.09
Oral	Mean	50.13	37.59	34.39	32.01	32.03	30.17	29.48	29.22	32.44
Gastrostomy	Mean	47.94	40.17	33.54	32.89	30.97	31.19	29.93	33.19	32.75
Pre×oral×gastrostomy	F	2.55	7.86	13.64	15.27	14.50	11.05	11.18	7.10	6.00
ANOVA	*P*	NS	*	*	*	*	*	*	*	*
Tukey test										
Pre×Oral	*P*		*	*	*	*	*	*	*	*
Pre×Gastrostomy	*P*		*	*	*	*	*	*	*	*
Oral×Gastrostomy	*P*		NS	NS	NS	NS	NS	NS	NS	NS

Values are expressed as means

F Fasting, *Pre* preoperative Boyden test, *Oral* postoperative oral Boyden test, *Gastrostomy* postoperative gastrostomy Boyden test, *NS* not significant

*$P<0.05$ (significant; ANOVA and Tukey tests)

the digestive or biliary tracts. Diabetes mellitus, Chagas disease, use of nonsteroidal anti-inflammatory agents, or hormonal contraceptives were considered to be exclusion criteria, as were occurrences of any clinical or surgical complications that would require a change in the study protocol. The patients' mean age was 39.3 years (range 28 to 59) and their mean body mass index (BMI; ±standard deviation (SD)) was 46.1±5.2 kg/m^2 (range 35.7 to 58.3).

Study Design

Gallbladder emptying was assessed by sonography 1 week before surgery for all patients. The surgical treatment involved an open RYGBP procedure performed by the same surgical team for all cases (MB and FGB), as previously described by Fobi et al. [14] and Capella et al. [15]. A gastrostomy tube was inserted into the excluded stomach by means of a standard procedure. For the entire first postoperative month, the patients were kept exclusively on a liquid diet that was started on the first postoperative day. Gallbladder emptying was reassessed on the 30th postoperative day: on this day, a test meal was administered orally. The assessment was repeated on the next day (31st postoperative day): on this day, the same test meal was infused through the gastrostomy tube in order to allow its transit into the duodenum (Fig. 1). On these latter two occasions, the presence of biliary sludge was investigated. Sonographic assessment in order to diagnose any newly formed gallstones started at least 6 months after RYGBP and continued up to a maximum of 35 months.

Sonographic Measurement of Gallbladder Volume and Emptying

Gallbladder emptying was assessed utilizing real-time ultrasonography (HDI 5000, ATL; 2–5 MHz convex transducer) performed by a single investigator (JBF). From the fasting subjects, sagittal and transversal images of the gallbladder at its largest diameters were obtained and its length, width, and height were registered. Subsequently, sequential images of the gallbladder were obtained every 15 min over a 120-min period following the administration of a 200-ml liquid test meal (25 g carbohydrate, 19.1 g fat, and 13.1 g protein), which was used to trigger gallbladder contraction (Boyden test) [16, 17]. The gallbladder volume (GV) while fasting and at each postprandial time point (15th, 30th, 45th, 60th, 75th, 90th, 105th, and 120th min) was calculated using a formula for the volume of an ellipsoid: volume (ml)=0.52×length (cm)×width (cm)×height (cm) [18]. The following measurable variables were studied: fasting volume (FV), residual volume (RV), and ejection fraction (EF) [19]. For each subject, the smallest of the postprandial gallbladder volumes measured was accepted as the RV. The EF was calculated as follows: $EF(\%)=([FV-GV \text{ at the corresponding time point}]/FV)\times 100$. The maximum ejection fraction was also established as follows: $\text{Max } EF(\%)=([FV-RV]/FV)\times 100$. [19, 20].

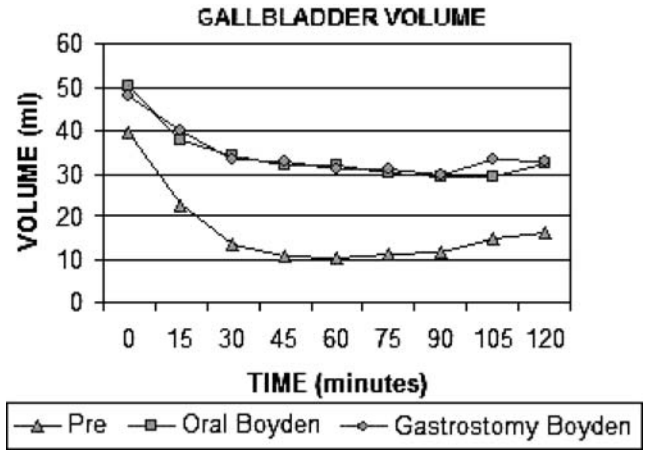

Fig. 2 Pre- and postoperative gallbladder volume curves with the Boyden test meal administered orally and through the gastrostomy

Table 2 Pre- and postoperative ejection fractions at the different time points after administering the test meal orally and through the gastrostomy

	Ejection fraction (Boyden test)								
Observation times	Minutes	15	30	45	60	75	90	105	120
Preoperative	Mean	42.10	64.98	72.77	74.40	73.69	71.17	62.85	60.25
Oral	Mean	27.56	33.91	40.22	40.42	44.51	44.62	44.25	37.73
Gastrostomy	Mean	19.15	31.77	33.42	36.66	36.79	37.59	28.28	28.78
Pre×Oral×Gastrostomy	F	4.76	12.18	15.87	15.39	12.45	10.11	4.18	3.43
ANOVA	*P*	*	*	*	*	*	*	*	*
Tukey test									
Pre×Oral	*P*	NS	*	*	*	*	*	NS	NS
Pre×Gastrostomy	*P*	*	*	*	*	*	*	*	*
Oral×Gastrostomy	*P*	NS	NS	NS	NS	NS	NS	NS	NS

Values are expressed as means

Pre Preoperative Boyden test, *Oral* postoperative oral Boyden test, *Gastrostomy* postoperative gastrostomy Boyden test, *NS* not significant

*$P<0.05$ (significant; ANOVA and Tukey tests)

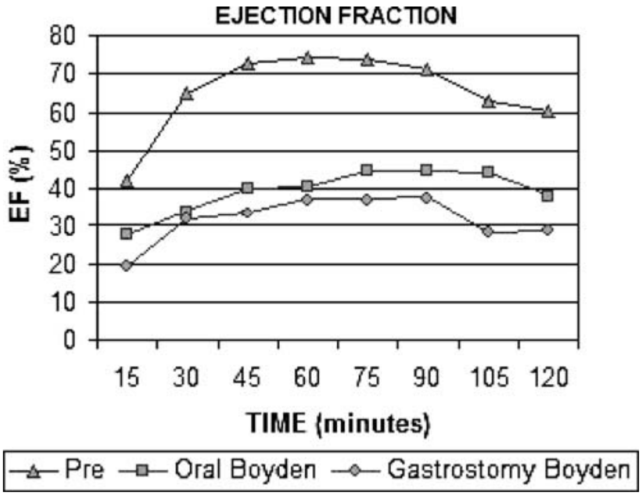

Fig. 3 Pre- and postoperative ejection fraction curves with the Boyden test meal administered orally and through the gastrostomy

Ultrasonographic Diagnosis of Biliary Sludge and Gallstones

On ultrasonography, sludge appeared as low-amplitude echoes without acoustic shadowing that formed layers in the dependent portions of the gallbladder. Sludge was also observed in suspension in the bile [21, 22]. Gallstones were recognized as hyperechogenic images that were associated with posterior shadowing and movement occurring as patient shifted in their decubitus position.

Statistical Analysis

All data are expressed as mean±SD. The statistical analyses were carried out using Statistica for Windows (StatSoft Inc.) release 7.0, 2004, and SPSS for Windows (SPSS Inc., Chicago, IL, USA), release 10.01, 1999. The paired *t*-test was used to analyze variations in weight and BMI between the pre- and postoperative measurements for the same individuals. When these variables were compared between two different groups, the nonparametric Mann–Whitney test was used. Differences between the three observation times (preoperative, 30th postoperative day, and 31st postoperative day) for the same individuals were analyzed using analysis of variance (ANOVA). The Tukey test or Wilcoxon test was applied to establish differences between pairs, as appropriate. Differences were considered to be significant at a P value<0.05.

Results

There was a significant change in the patients' weights (preoperative 125.4±22.3 kg versus postoperative 113.0±20.3 kg) and BMI (preoperative 46.2±5.2 kg/m^2 versus postoperative 41.6±5.1 kg/m^2). The difference between the preoperative values and the values observed on the 30th postoperative day was approximately 10%. The GVs and EFs relating to the pre- and postoperative assessments of gallbladder emptying are shown in Tables 1 and 2, respectively. The corresponding curves are demonstrated in Figs. 2 and 3. Except for the volume while fasting, statistically significant differences were observed between the preoperative values and both postoperative volumes at each time point (P<0.001). Performing the Boyden test through the gastrostomy evoked a response regarding gallbladder volume reduction that was similar to what was observed with in the test performed orally. No significant difference was found between the EFs from the preoperative and postoperative oral Boyden tests with regard to the first 15 min (preoperative Boyden 42.1% versus postoperative oral Boyden 27.5%; P=0.14), but significant differences were found at all other time points (P<0.001). All time points in the postoperative gastrostomy Boyden test presented significantly reduced EFs in relation to the preoperative value.

The pre- and postoperative FV, RV, and Max EF values from the gallbladder emptying assessments are shown in Table 3. The postoperative FV was greater than the preoperative value, but the difference did not reach statistical significance (P=0.09). The postoperative RV was significantly greater than the preoperative value (preoperative Boyden 7.6±8.7 ml versus postoperative oral Boyden 25.0±19.9 ml and postoperative gastrostomy

Table 3 Pre- and postoperative fasting volume, residual volume, and maximum ejection fraction from the gallbladder emptying assessment

N=20	Pre	Oral	Gastrostomy	Pre×Oral	Pre×Gastrostomy	Oral×Gastrostomy
FV (ml)	39.4±20.1	50.1±22.7	47.9±23.4	NS	NS	NS
RV (ml)	7.6±8.7	25.0±19.9	24.6±20.9	*	*	NS
Max EF (%)	80.4±20.9	54.3±21.4	50.5±28.9	*	*	NS
ΔT (min)	80.8±23.8	84.7±29.3	92.8±28.1	NS	NS	NS

Values are expressed as mean±SD

FV Fasting volume, *RV* residual volume, *Max EF* maximum ejection fraction, ΔT time taken to reach residual volume, *Pre* preoperative Boyden test, *Oral* postoperative oral Boyden test, *Gastrostomy* postoperative gastrostomy Boyden test, *NS* not significant

*P<0.05 (significant; Tukey test)

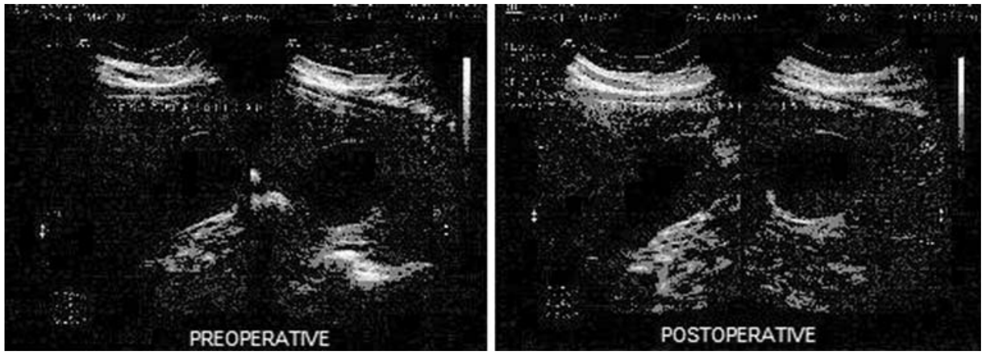

Fig. 4 Normal ultrasonographic image of the gallbladder before the operation and image presenting biliary sludge after the operation

Boyden 24.6±20.9 ml; $P<0.001$). No significant difference was observed between values relating to administration of the test meal orally and through the gastrostomy ($P=0.99$). Max EF decreased from a preoperative value of 80.4±20.9% to postoperative values of 54.3±21.4% and 50.5±28.9% for administration of the test meal orally and through the gastrostomy, respectively ($P<0.001$). No significant difference was found between the two postoperative values ($P=0.78$).

The presence of biliary sludge was diagnosed in 13 of the 20 patients on the 30th postoperative day (65%; Fig. 4). The patients who developed biliary sludge had an initial mean BMI that was similar to the BMI of those who did not develop sludge (46.8±6.2 kg/m^2 versus 44.9±2.5 kg/m^2, respectively; $P=0.44$), and the percentage weight losses experienced during the first postoperative month were also similar (10.1±2.1% versus 9.4±1.6%; $P=0.47$).

No significant differences between pre- and postoperative fasting volumes were observed in either subgroup of patients (with or without sludge). However, the patients in the subgroup that developed sludge showed a significant increase in RV volume ($P=0.001$) and a significant decrease in Max EF after the operation ($P=0.001$). For both subgroups, the RV and Max EF values from performing the Boyden test with infusion of the test meal through the gastrostomy were not significantly different from those observed after oral administration (Table 4).

Six patients developed gallstones that were diagnosed after the sixth postoperative month (Fig. 5). All of these patients were derived from the subgroup that developed biliary sludge. This represents an incidence of 46% if only the subgroup of sludge-positive patients is taken into account, or an incidence of 30% if the whole sample is considered. All of the patients who developed gallstones were asymptomatic.

Table 4 Pre- and postoperative fasting volume, residual volume, and maximum ejection fraction in the subgroups with and without biliary sludge from gallbladder emptying assessment

		With sludge ($N=13$)	Without sludge ($N=7$)
FV (ml)	Pre	43.7	31.4
	Oral	55.3	40.5
	Gastrostomy	54.1	36.4
RV (ml)	Pre	7.9	6.9
	Oral	30.7*	14.5NS
	Gastrostomy	29.9*	14.8NS
Max EF (%)	Pre	83.5	74.8
	Oral	48.7*	64.6NS
	Gastrostomy	46.0*	58.7NS

Values are expressed as means

FV Fasting volume, *RV* residual volume, *Max EF* maximum ejection fraction, *Pre* preoperative Boyden test, *Oral* postoperative oral Boyden test, *Gastrostomy* postoperative gastrostomy Boyden test, *NS* no significant difference between oral and gastrostomy Boyden in either subgroup

*$P<0.05$ (significantly different from Pre value; Wilcoxon)

Discussion

Bariatric surgery has been associated with increased incidence of cholesterol gallstones because of the rapid and significant weight loss that is induced. Cholesterol supersaturation of the bile is considered to be of funda-

Fig. 5 Sonographic image of gallstones at a late postoperative stage

mental importance in gallstone formation, but it is not the sole factor involved. Decreased gallbladder emptying may increase the risk of gallstone disease by giving time for cholesterol precipitation and the aggregation and growth of cholesterol crystals from supersaturated bile to form stones [23]. This process may also be favored by the retention of mucin within gallbladder bile caused by the sluggishness of the gallbladder [24].

The present study revealed significantly impaired postprandial gallbladder emptying 30 days after RYGBP was performed, as demonstrated by the increased RV and decreased Max EF, in comparison with preoperative values. These changes may be secondary to decreased levels of circulating postprandial cholecystokinin, which are associated with surgical exclusion of the duodenum. In an attempt to elucidate this question, we studied the gallbladder emptying response to the Boyden test, with infusion of a test meal through the gastrostomy tube in order to allow its transit through the duodenum and thus simulate the preoperative condition. Surprisingly, contradicting to our prior expectations, we were unable to reproduce the preoperative gallbladder emptying parameters that had previously been observed. This could in part be interpreted as a result from eliminating the cephalic and oral cholinergic stimuli for gallbladder emptying [24], as occurs when the test meal is directly infused into the stomach. Retention of the test meal inside the excluded part of the stomach for a prolonged period of time could be another reason. However, we presume that, after RYGBP, the excluded part of the stomach may behave as it does after proximal gastric vagotomy, with regard to the emptying of liquids, which may be in fact accelerated and not retarded [25]. Decreased H^+ ion concentrations at the duodenal level secondary to denervation of the proximal excluded part of the stomach and the routine use of H2 blockers following RYGBP may compromise pancreatic lipase secretion, which is fundamental for releasing free fatty acids from ingested triglycerides [26]. In this way, the secretion of cholecystokinin from the I cells may be reduced [27, 28]. Finally, based on previous reports that confirm the deleterious effect of cholesterol bile supersaturation on the mechanisms for gallbladder smooth muscle cell contraction [29, 30], we accept that supersaturation of gallbladder bile, as reported following RYGBP [31–33], may be the main explanation for our findings.

We found a much higher incidence of biliary sludge (65%), associated with significantly impaired gallbladder emptying, at the end of the first postoperative month than was previously reported by Shiffman et al. (12%) [34] and Sugerman et al. (11%) [35]. These discrepancies are probably related to the fact that these two previous studies were conducted 6 months after RYGBP was performed. This may have given enough time for gradual recovery of gallbladder contractile function to take place, as demonstrated by Inoue et al. in gastrectomized patients [36].

The present study revealed that the incidence of gallstones diagnosed after the sixth postoperative month was 30%. This is comparable with the rates reported by Wattchow et al. (33%) [37], Amaral and Thompson (27.5%) [38], Shiffman et al. (38%) [34], Sugerman et al. (32%) [35], and Guadalajara et al. (24.7%) [39]. The highest reported incidence was 52.8%, by Iglézias Brandão de Oliveira et al. [4], after a follow-up period of 1 year.

There is controversy in the literature regarding the approach of performing prophylactic cholecystectomy together with RYGBP. While advocated by Fobi et al. [40], Czendes et al. [41], Liem and Niloff [42], and Guadalajara et al. [39], other authors have not agreed that this approach should be routine practice [43–47]. The observation that all of our patients who developed gallstones had previously been diagnosed as presenting biliary sludge may represent an opportunity to take a conservative approach regarding gallstone prevention. In this respect, we propose that there should be a gallbladder sonographic assessment at the end of the first postoperative month after RYGBP and that prophylactic use of oral bile salts should be started whenever biliary sludge is detected to be used for a 6-month period.

Based on the results from the present study, we concluded that gallbladder emptying became significantly compromised after RYGBP. This impairment was unrelated to duodenal exclusion but it had a significant influence on gallstone development.

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