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Utility of Bile Acid Scintigraphy in the Diagnosis of Remnant Gastropathy in Patients with Roux-en-Y Gastric Bypass

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Introduction

Roux-en-Y gastric bypass (RYGB) is one of the most commonly performed surgical procedures for obesity(1–3). This procedure involves stapling of the proximal stomach to create a small gastric pouch that is separated from the distal stomach, known as the gastric remnant. The gastric pouch is then anastomosed to a Roux limb of small bowel, creating a gastrojejunal anastomosis. In so doing, the biliopancreatic digestive enzymes are diverted more distally in the small bowel having a metabolic effect that leads to weight loss. Additionally, the remnant stomach does not participate in digestive process and is excluded from nutrients.

In light of this altered anatomy, gastric bypass patients are prone to a variety of complications, many of which are known to cause abdominal pain(4,5). Work-up of potential etiologies typically includes upper endoscopy and abdominal computed tomography (CT) to evaluate for possible ulceration or stenosis of the gastrojejunal anastomosis, gastrogastic fistula, gastroesophageal reflux disease, internal hernias or cholelithiasis(6).

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Thompson CC: study concept and design; critical revision of the manuscript for important intellectual content; study supervision

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study formal consent is not required.

These studies, however, are frequently unremarkable. Oftentimes, in patients with RYGB anatomy referred for diagnosis of chronic abdominal pain with negative initial work-up, examination of the remnant stomach with device-assisted enteroscopy may be considered, and often confirms the presence of erythema, pooled bile and gastropathy on histologic evaluation(7).

Anatomic changes following RYGB predispose to gastropathy of the excluded stomach in part due to a lack of nutrient contact with the gastric mucosa. Moreover, acid production continues in the remnant stomach without the buffering effects of food. Finally, the pooling of bile due to the proximity of the papilla to the remnant, coupled with a lack of antegrade flow and potentially altered motility, all contribute to mucosal damage and resultant abdominal pain.

Treatment with ursodiol, a secondary bile acid, may alter the composition of bile, halting the caustic damage and allowing the mucosa to heal. Elimination of symptoms and resolution of gastropathy on repeat histologic examination have been demonstrated in small series(7). Unfortunately, device-assisted enteroscopy is technically challenging, poses significant risk, and is performed by few centers. As such, a less invasive and more readily available method of establishing this diagnosis is needed. Cholescintigraphy (99mTc-hepato-iminodiacetic acid [HIDA] scanning) allows for a radiolabeled substance to be taken up selectively by hepatocytes and excreted into bile, thereby providing information about bile flow. This imaging can detect retrograde flow and pooling of bile in the excluded stomach, predisposing to remnant gastropathy. We sought to determine the sensitivity of this finding on HIDA scan in predicting response to ursodiol therapy for the treatment of unexplained abdominal pain in RYGB patients with suspected remnant gastropathy.

Methods

Patient characteristics

This is a prospective registry study, with retrospective analysis, occurring at a single tertiary care center. All consecutive patients referred to our center for chronic abdominal pain following RYGB, with a negative work-up, including but not limited to physical examination, serologic studies, endoscopy, and abdominal computed tomography, were included. HIDA scans were performed to assess for bile pooling in the gastric remnant. Patient demographics were collected from the medical record and included age, sex, pre-RYGB body mass index (BMI), and time since RYGB. All patients were maintained on proton pump inhibitors.

Intervention

Upon the finding of bile pooling in the gastric remnant, therapy with ursodiol 500mg BID was initiated. The dose of this medication was escalated to 1000mg BID if only partial or no improvement of clinical symptoms occurred after twelve weeks. Instructions were given to crush tablets and take separately from other medications. Patients were then followed for six months for improvement of abdominal pain.

Outcomes

The primary outcome was the sensitivity of HIDA scan in predicting response to ursodiol therapy for treatment of abdominal pain due to suspected remnant gastropathy in patients with RYGB.

Statistical analysis

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Proportional comparisons between groups were performed with Fisher's Exact test. Continuous variables were compared using Student's *t*-test or Wilcoxon Signed Rank test for parametric and non-parametric data, respectively. All statistics are reported as mean $\pm$ SEM or median[IQR]. A two-tailed *p*-value of 0.05 was considered statistically significant.

Results

Patient characteristics

Twenty-five patients with chronic abdominal pain and unrevealing work-up underwent HIDA scan. Eighty-eight percent of these patients were female. Baseline characteristics of this cohort are shown in Table 1. Mean time since RYGB was 6.1 ± 0.6 years and mean BMI was 32.7 ± 1.3 kg/m².

The left upper quadrant and mid-abdomen regions were the most common reported locations for pain. The quality of the pain was variable, and was described as burning, gnawing, dull or sharp, inconsistently worse with meals, and occasionally accompanied by nausea.

Sensitivity of HIDA scan

Eighty percent (20/25) of patients demonstrated pooling of bile in the gastric remnant (Figure 1).

Ursodiol therapy

Ursodiol 500 mg twice a day was initiated in patients with positive HIDA scans. Eighty percent (15/20) of patients reported complete resolution in abdominal pain at next scheduled follow-up visit which was 9.2 ± 1.6 weeks after starting medication.

In the five patients with only partial or no relief, ursodiol was increased to 1000 mg twice a day, and this escalation was successful in 2/5 of patients, for a total response rate of 88%. In the three patients who did not respond to maximum dose of ursodiol, one patient was later found to have a distal small bowel obstruction that was not visualized on prior CT scan but identified on surgical exploration. The second patient was found to have an esophageal motility disorder refractory to medical therapy and was ultimately referred to thoracic surgery, and the third was thought to have an abdominal wall pain syndrome and was referred for trigger point injection with resolution of her symptoms.

Discussion

Chronic abdominal pain following RYGB is a common presenting symptom leading to a substantial number of clinic visits and hospital admissions annually(4,5,8,9). Typically, upper endoscopic evaluation and abdominal CT are performed. If these studies are unrevealing, device-assisted enteroscopy is often recommended to rule out pathology in the remnant stomach. However, this procedure is technically challenging, only performed in specialized centers, and poses a risk of perforation that is not insignificant(10).

The present study established that 80% of gastric bypass patients with abdominal pain and an exhaustive unrevealing evaluation were found to have a HIDA scan demonstrating pooling of bile in the remnant stomach. Previous studies have demonstrated that bile reflux to the remnant stomach is associated with chemical gastropathy and abdominal pain(7). Treatment with ursodiol may alter the composition of bile, thereby leading to cessation of mucosal damage. Preliminary studies have demonstrated elimination of symptoms and resolution of gastropathy on repeat histologic examination in patients with biopsy proven gastropathy treated with ursodiol therapy(7). As a large referral center for post-bariatric surgery patients, we have a standard protocol for diagnostic evaluation, management, and follow-up of abdominal pain. In our clinic, patients with this type of pain and unrevealing work-up are typically scheduled for a two month return visit. In this case, patients who were started ursodiol and in whom response was not complete, the dose was increased.

In the present study, ursodiol initiation in those patients with bile pooling demonstrated on HIDA scan was successful 80% of the time, and increased to 88% with dose escalation. Considering the high prevalence of a positive HIDA scan in this patient population, and the relatively high sensitivity in predicting symptom resolution with ursodiol treatment, empiric therapy with ursodiol should be considered. In patients who have an incomplete response or who are non-compliant with medication, HIDA scans may prove to be useful in clarifying the diagnosis. Current studies are underway.

A limitation of this study is that the percentage of patients without abdominal pain who would have a positive HIDA scan is unknown. The HIDA scan does not make a diagnosis, however, is a surrogate for the diagnosis as it merely identifies patients at risk for the condition. Nevertheless, there was a high percentage of patients who responded to treatment in this study, and a non-invasive imaging study is likely preferable to a more invasive and costly deep enteroscopy.

This is the first study to date investigating the use of HIDA scan for detecting bile pooling in the remnant stomach in patients with RYGB with chronic abdominal pain and negative evaluation. Given the invasiveness of device-assisted enteroscopy, HIDA scan should be considered in the evaluation of suspected remnant gastropathy.

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Figure 1.
HIDA scan demonstrating radiotracer uptake in the gallbladder (A) and later in the excluded portion of the stomach (gastric remnant) (B).

Table 1**Baseline characteristics**

Variable	Normal (n=25) n(%)
Age (mean $\pm$ SE)	50.0 $\pm$ 2.3
Sex (M) (%)	88%
BMI* m/kg ² (mean $\pm$ SE)	32.7 $\pm$ 1.3
Time since RYGB (years) (mean $\pm$ SE)	6.0 $\pm$ 0.6