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Original article

## Weight regain in patients with symptoms of post–bariatric surgery hypoglycemia

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### Abstract

**Background:** Weight regain (WR) and symptoms of post–bariatric surgery hypoglycemia (PBSH) are metabolic complications observed in a subset of postbariatric patients. Whether hypoglycemic symptoms are an important driver of increased caloric intake and WR after bariatric surgery is unknown.

**Objective:** This study aims to determine whether patients with PBSH symptoms have greater odds for WR.

**Setting:** Tertiary academic hospital.

**Methods:** Patients who underwent Roux-en-Y gastric bypass or sleeve gastrectomy at our tertiary academic hospital from August 2008 to August 2012 were mailed a survey, from which weight trajectory and PBSH symptoms were assessed. Percent WR was calculated as  $100 \times (\text{current weight} - \text{nadir weight}) / (\text{preoperative weight} - \text{nadir weight})$  and was compared between dates of survey completion and bariatric surgery. The primary outcome was  $\text{WR} \geq 10\%$ , as a reflection of the median WR among respondents. Multivariable logistic regression was used to determine clinical factors that indicate greater odds for  $\text{WR} \geq 10\%$  at the  $P < .05$  level.

**Results:** Of 1119 potential patients, 428 respondents (40.6%) were eligible for analysis. WR was observed in 79.2% ( $n = 339$ ), while 20.8% ( $n = 89$ ) experienced either weight loss or no WR at a mean of  $40.6 \pm 14.5$  months. Median WR was 10.8% (interquartile range, 5.6–19.4). Odds of  $\text{WR} \geq 10\%$  was significantly increased in those who experienced PBSH symptoms (odds ratio [OR] = 1.66; 95% confidence interval [CI]: 1.04–2.65), reported less adherence to nutritional guideline (OR = 2.36; 95% CI: 1.52–3.67), and had a longer time since surgery (OR = 1.05; 95% CI: 1.03–1.07).

**Conclusions:** We found evidence that the presence of PBSH symptoms was associated with WR. Future studies should elucidate the role of hypoglycemia among other factors in post–bariatric surgery WR. (Surg Obes Relat Dis 2017;■:00–00.) © 2017 American Society for Metabolic and Bariatric Surgery. All rights reserved.

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Bariatric surgery is a highly effective treatment for patients with severe obesity and obesity-related co-morbidities, such as diabetes, hypertension, and dyslipidemia [1]. However, the amount of weight loss and its successful maintenance varies for individual patients. Although most patients achieve maximum weight loss within the first postoperative year, defined as loss of at least 50% of preoperative excess weight, many regain a proportion of their weight in subsequent years [2–5]. Indeed, bariatric surgery is proven to be effective for weight loss in the short term [1,2,4], but the long-term efficacy of postsurgical weight maintenance and the driving factors for weight regain (WR) are less clear.

In addition to promoting weight loss, Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) affect glucose homeostasis in a rapid and durable manner [6]. Postbariatric surgery hypoglycemia (PBSH) is an increasingly recognized complication associated with the inappropriate secretion of insulin and gastrointestinal hormones [7–9]. PBSH is also known as late dumping syndrome, an entity that differs from early dumping syndrome in its delayed onset of 1–2 hours after a meal without vasomotor symptoms [10]. Although most cases are self-limited, some patients experience severe and potentially life-threatening hypoglycemia, associated with seizures, loss of consciousness, and motor vehicle accidents [8]. Although the prevalence of PBSH is thought to be low, we have previously reported that up to one third of patients who have undergone RYGB or SG report symptoms of PBSH [11].

Both RYGB and SG cause changes in glucose metabolism, but the mechanism through which they achieve these changes is thought to be different. Hypoglycemia after RYGB is thought to be mediated partly by expedited gastric emptying and by an increase in glucose-mediated glucagon-like peptide-1 secretion and subsequent insulin secretion [12,13]. The mechanism behind hypoglycemia after SG is unknown. Regarding the prevalence of hypoglycemia after each procedure, we have previously reported that undergoing RYGB was associated with risk for symptoms of PBSH, whereas no association was seen after SG [11]. However, the lack of evidence for PBSH after SG may be because the procedure is newer, with less longitudinal outcome data.

Other clinical factors reported to be associated with WR after bariatric surgery include low physical activity, poor dietary adherence, psychosocial stress, and low energy metabolism [3,14]. To our knowledge, whether the presence of PBSH contributes to WR has not yet been explored; however, several studies have reported that patients with hypoglycemia also present with weight gain [15–18]. The

risk for weight gain in diabetic patients, who experience hypoglycemia while receiving insulin therapy, is common [1,16]. Similarly, weight gain is a known complication in patients with insulinoma due to the increased frequency and amount of food eaten to avoid or prevent hypoglycemia, in combination with insulin's anabolic effects [17]. Finally, there is preclinical evidence to support the hypothesis that insulin-induced hypoglycemia stimulates peripheral and central nervous system responses that lead to increased hunger, food intake, and weight gain [18,19].

The plausible link between hypoglycemia and weight gain, in addition to the fact that WR and hypoglycemia are recognized metabolic complications after bariatric surgery, led to the hypothesis that postbariatric hypoglycemia may be an important contributor to WR. Thus, this study sought to determine whether patients with PBSH demonstrate greater odds for WR after bariatric surgery.

## Methods

As previously described, we collected survey data from the patients who underwent bariatric surgery at our institution [11].

### Participants

Patients who underwent either RYGB or SG between August 2008 and August 2012 at our tertiary academic center were identified. We collected data by mailing a questionnaire to 1119 patients regarding hypoglycemic symptoms, demographic characteristics, and weight data between August 2013 and April 2014. Multiple attempts were made to follow up with each subject using 2 additional questionnaire mailings and 2 reminder postcards. The institutional review board of the tertiary academic center exempted this study from further review. Completion of the questionnaire was assumed to indicate consent [11].

### Hypoglycemia questionnaire

We used modified questions from the Edinburgh Hypoglycemia questionnaire to assess hypoglycemic symptoms in this study's postbariatric patients [10,20]. The 11 key hypoglycemic symptoms included in the questionnaire include sweating, palpitation, shaking, hunger, confusion, drowsiness, odd behavior, speech difficulty, incoordination, nausea, and headache [20]. As reported previously, we dichotomized patients into either a low- or high-suspicion group for PBSH based on the number of symptoms or self-report of diagnosed, severe hypoglycemia [11]. The low-suspicion group was defined as those who experienced at most 2 of the 11 key validated hypoglycemic symptoms [10];

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