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Original article

# The incidence and risk factors associated with developing symptoms of hypoglycemia after bariatric surgery

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## Abstract

**Background:** Hypoglycemia after bariatric surgery is an increasingly recognized metabolic complication associated with exaggerated secretion of insulin and gut hormones.

**Objective:** We sought to determine the incidence of hypoglycemic symptoms (hypo-sx) after bariatric surgery and characteristics of those affected compared with those unaffected.

**Setting:** University hospital.

**Methods:** We collected retrospective survey data from the patients who underwent bariatric surgery at a single center. Based on number and severity of postprandial hypo-sx in Edinburgh hypoglycemia questionnaire postoperatively, patients without preoperative hypo-sx were grouped into high versus low suspicion for hypoglycemia. We used multivariable logistic regression to examine potential baseline and operative risk factors for the development of hypo-sx after surgery.

**Results:** Among the 1119 patients who had undergone bariatric surgery who received the questionnaire, 464 (40.6%) responded. Among the 341 respondents without preexisting hypo-sx, 29% (n = 99) had new-onset hypo-sx, and most were severe cases (n = 92) with neuroglycopenic symptoms. Compared with the low suspicion group, the high suspicion group consisted of more female patients, younger patients, patients without diabetes, and those who underwent Roux-en-Y gastric bypass with a longer time since surgery and more weight loss. In multivariate analysis, factors independently associated with incidence of hypo-sx after bariatric surgery were female sex ( $P = .003$ ), Roux-en-Y gastric bypass ( $P = .001$ ), and absence of preexisting diabetes ( $P = .011$ ).

**Conclusions:** New onset postprandial hypoglycemic symptoms after bariatric surgery are common, affecting up to a third of those who underwent bariatric surgery. Many affected individuals reported neuroglycopenic symptoms and were more likely to be female and nondiabetic and to have undergone Roux-en-Y gastric bypass. (Surg Obes Relat Dis 2018;■:00–00.) © 2018 American Society for Metabolic and Bariatric Surgery. All rights reserved.

## Keywords:

Bariatric surgery; Gastric bypass; Glucose metabolism; Treatment outcomes; Questionnaire design

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While the benefits of bariatric surgery are well established, it is also important to recognize its risks given the rising utilization worldwide. Hypoglycemia after bariatric surgery is an increasingly recognized metabolic complication associated with exaggerated secretion of insulin and gut hormones, which can be observed after Roux-en-Y gastric bypass surgery (RYGB) and sleeve gastrectomy [1–4].

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Post-bariatric surgery hypoglycemia typically occurs postprandially with onset  $\geq 6$  months after surgery. Severe hypoglycemia, defined as requiring assistance, can lead to neuroglycopenic symptoms and subsequent serious adverse events, such as seizure, syncope, and motor vehicle accidents [1,2]. Perhaps not surprisingly, severe hypoglycemia is also associated with increased morbidity and mortality in patients with type 2 diabetes [5]. In contrast, nonsevere hypoglycemia, defined as asymptomatic hypoglycemia or hypoglycemia with mild symptoms, is less well understood in its clinical relevance. However, recent studies have highlighted its clinical importance with studies showing an increased risk of cardiac arrhythmia during hypoglycemia among insulin-treated patients with type 2 diabetes [6,7] and another study speculating that an increase in incident cardiovascular death in post-bariatric surgery patients compared with nonsurgical controls may be due to hypoglycemia [8].

The exact incidence of post-bariatric surgery hypoglycemia is unknown. Several studies have reported a  $< 1\%$  prevalence of post-gastric bypass hypoglycemia based on large database-driven studies using electronic health records for hospitalization or clinic visits for hypoglycemia or self-reported hypoglycemia [9–11]. In contrast, we have previously reported that the prevalence of hypoglycemic symptoms after bariatric surgery, which was defined as  $\geq 3$  symptoms of hypoglycemia, or a history of requiring assistance, seizure, or medical diagnosis of hypoglycemia, was 34% among those who underwent bariatric surgery at our institution [12]. Other studies reported similar rates of nonsevere hypoglycemia ( $< 60$  mg/dL without symptoms during mixed meal challenge or  $< 70$  mg/dL during continuous glucose monitoring in adults without diabetes), thus raising the concern that the prevalence may have been previously underestimated [3,13,14].

Such high prevalence of symptoms of hypoglycemia among our patients may be due, in part, to the nonspecific nature of the symptoms asked to determine the presence of hypoglycemia. Therefore, in this study we sought to understand the incidence of symptoms of postbariatric surgery hypoglycemia by focusing on the survey responders with no preexisting symptoms of hypoglycemia and compared the responses from those who went on to develop symptoms of hypoglycemia versus those who did not after bariatric surgery.

## Methods

### Subject/study design

As previously described, the questionnaire-based survey was conducted retrospectively in bariatric surgery patients between August 2013 and February 2014 to obtain data on new-onset symptoms of hypoglycemia. We identified 1174 patients who underwent either RYGB or vertical sleeve

gastrectomy at Johns Hopkins Bayview Bariatric Center between August 2008 and August 2012 using the hospital database. Inclusion criteria were English-speaking adults and history of the aforementioned bariatric surgery 9 months to 5 years before the administration of the survey. A total of 20 patients did not have valid addresses and were excluded from the study. Six patients directly declined to participate in the survey study by mailing back blank surveys. The institutional review board of the Johns Hopkins Hospital exempted the study from further review. Consent was assumed by the completion of the survey.

### Data collection

As previously reported, in August 2013, we mailed surveys to 1174 patients with a \$2 bill enclosed as an incentive. We asked each subject to complete the survey either on paper or online. Through February 2014, multiple attempts were made to follow up with each subject using 2 additional survey mails and 2 reminder postcards [12].

### Questionnaire design

The questionnaire included the Edinburgh hypoglycemia questionnaire, which identified and validated 11 key symptoms underlying hypoglycemia (see [Supplemental Materials](#)) [15]. The 11 symptoms are sweating, palpitations, shaking, hunger, confusion, drowsiness, odd behavior, speech difficulty, incoordination, nausea, and headache. We asked the participant about the presence of any of these symptoms before and after bariatric surgery and additional questions regarding the onset of symptom(s) in relation to the meal, frequency, previous experience with and awareness of hypoglycemia, and any severe episode of hypoglycemia requiring assistance from others. We also collected data on bariatric surgery history, current dietary history, presurgical weight, current weight, and height of the respondent. Respondents with diabetes were asked to provide further information including the duration of diabetes, current medication, and current hemoglobin A1C.

To exclude those with preexisting history of hypoglycemia, we excluded those with  $\geq 3$  preoperative symptoms of postprandial hypoglycemia or a preoperative history of requiring assistance because of hypoglycemia, seizure, or medical diagnosis of hypoglycemia. We categorized the remaining patients ( $N = 341$ ) into either a low or high suspicion group for symptoms of post-bariatric hypoglycemia; the group with low suspicion of hypoglycemia symptoms was defined as those with 0 to 2 postprandial symptoms consistent with hypoglycemia after bariatric surgery, whereas the group with high suspicion of having had hypoglycemic symptoms was defined as those with  $\geq 3$  symptoms of postprandial hypoglycemia after bariatric surgery or a history of requiring assistance, seizure, or medical diagnosis of hypoglycemia. We performed a

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