

University of Groningen

## Hypoglycaemia after bariatric surgery

van Beek, André

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*

Publisher's PDF, also known as Version of record

*Publication date:*

2022

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

van Beek, A. (2022). *Hypoglycaemia after bariatric surgery*. 13-14. Abstract from ESE Clinical Update on Obesity 2021 online webinars. [https://www.es-hormones.org/media/4320/es-cu-obesity-webinar-report-2021\\_v9-web.pdf](https://www.es-hormones.org/media/4320/es-cu-obesity-webinar-report-2021_v9-web.pdf)

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Table. Current treatment modalities for people with overweight or obesity, based on BMI and co-morbidities.

Treatment	BMI category (kg/m <sup>2</sup> )				
	≥25	≥27	≥30	≥35	≥40
Diet, physical activity and behaviour therapy	+	+	+	+	+
Pharmacotherapy		With co-morbidities	+	+	+
Bariatric surgery				With co-morbidities	+

Around 70% of variability in post-surgery weight loss is heritable, affected by the patient's circulating levels of appetite-suppressing or -stimulating hormones, such as peptide YY, glucagon-like peptide-1 (GLP1) and ghrelin.

#### Predicting weight loss response

A poor weight loss response can be identified at around 3 months post-surgery. This means there is an opportunity to intervene with other measures and avoid losing the patient to follow-up. It can be disheartening for patients to experience a poor response, so early intervention and support are important.

Studies are underway to try to predict surgical outcomes preoperatively.

#### Approaches to inadequate weight loss/weight regain

We can maximise the health benefits of bariatric surgery by using a polymodal approach, adding lifestyle interventions and pharmacotherapy after surgery. Optimising lifestyle factors should be the first step, followed by a review of any weight gain-promoting medications.

There may be options to revise or enhance surgical therapy. For example, with bypass, it may be possible to extend the limb length, decrease the size of the pouch, or decrease the diameter of the gastrojejunal anastomosis. Converting from one surgery to another, such as converting from a sleeve gastrectomy to a single anastomosis duodeno-ileal bypass, is also quite common.

Bariatric surgery is safe, but revisional surgery carries double the mortality and morbidity of primary surgery, and data to show improved outcomes are lacking.

#### Anti-obesity medications

The availability of anti-obesity drugs varies by region. Naltrexone/bupropion, phentermine and phentermine/topiramate cause an average weight loss of 7% in people prior to bariatric surgery. Studies for every anti-obesity medication show similar efficacy before and after bariatric surgery.

A 2019 study showed that 1.8mg liraglutide caused a significant reduction in glycated haemoglobin and a significant reduction in body weight in patients who still had type 2 diabetes after bariatric surgery.<sup>5</sup> Real world

evidence suggests that 3mg liraglutide leads to similar weight loss in those who have had prior surgery and those who have not.

#### New pharmacotherapies

In people with overweight or obesity without type 2 diabetes, the GLP1 receptor agonist semaglutide (2.4mg), injected subcutaneously once per week, resulted in 14.9% weight loss, compared with 2.4% with placebo.<sup>6</sup>

Tirzepatide is a dual glucose-dependent insulinotropic polypeptide and GLP1 receptor agonist, which has been shown to help patients with type 2 diabetes and obesity achieve up to 15% weight loss.

With more efficacious pharmacotherapy, we will be able to further improve the health of people with weight regain after bariatric surgery.

In discussion, it was suggested that knowing when to offer surgery to maximise outcomes for people with obesity is challenging, and is likely to change, as new, more efficacious drugs become available. Younger patients may choose to wait for a forthcoming drug that could help them achieve 20% weight loss without surgery. However, this also becomes more challenging, as obesity is a chronic progressive disease.

#### REFERENCES

1. Garvey *et al.* 2016 *Endocrine Practice* **22** 1–203.
2. Mann *et al.* 2007 *American Psychologist* **62** 220–233.
3. Sjöström *et al.* 2012 *JAMA* **307** 56–65.
4. Manning *et al.* 2015 *Surgical Endoscopy* **29** 1484–1491.
5. Miras *et al.* 2019 *Lancet Diabetes & Endocrinology* **7** 549–559.
6. Wilding *et al.* 2021 *New England Journal of Medicine* **384** 989–1002.

## Hypoglycaemia after bariatric surgery

André van Beek Groningen, The Netherlands



The prevalence of post-bariatric hypoglycaemia is not completely understood. Only a few patients are seen in hospital with hypoglycaemia each year. Around 12% of patients issued with post-surgical questionnaires report moderate to severe complaints, though it is unclear if these would

meet the cut-off values for hypoglycaemia. However, investigation with an oral glucose tolerance test (OGTT) or mixed meal test (MMT) tends to show that around 30–80% of patients have hypoglycaemia. Sensors show an even higher prevalence, which means many patients may be unaware that they have hypoglycaemia.

Post-bariatric hypoglycaemia can have a major impact on quality of life. Patients with hypoglycaemia are more likely to experience anxiety and depression after surgery.

#### Case study

A 31-year-old woman underwent gastric bypass surgery 2 years ago. Prior to surgery, she weighed 110kg, with a body mass index (BMI) of 43kg/m<sup>2</sup> and no co-morbidities. At 1 year after surgery, her weight was 75kg (a BMI of 29kg/m<sup>2</sup>), which represented a weight loss of 32%. She reported experiencing tremors, perspiration, loss of concentration and hunger over several weeks. These symptoms appeared around an hour

after eating and lasted for an hour. They disappeared after eating sweets but recurred quickly afterwards.

This is a classic description of post-bariatric hypoglycaemia.

#### Diagnosis of post-bariatric hypoglycaemia

Diagnosis is confirmed where:

- Whipple's triad is present
- symptoms occur as a post-prandial event (1–3 hours after eating)
- the patient had prior Roux-en-Y gastric bypass surgery (or other surgery of the upper intestinal tract)
- there are no atypical findings, such as fasting hypoglycaemia or late nocturnal hypoglycaemia.

Testing with OGTT, MMT or glucose sensor analysis is recommended.

The Whipple's triad includes the presence of symptoms of hypoglycaemia, which



may be autonomic (such as weakness, tremors, perspiration or palpitations) or neuroglycopenic (such as dizziness, drowsiness or confusion). Secondly, these symptoms are found in combination with a low plasma glucose concentration. Finally, the symptoms are relieved when plasma glucose is increased.

There is no absolute cut-off point for plasma glucose, though the lower the level, the more likely a diagnosis will be. A 2021 study suggests glucose below 3.0mmol/l would be consistent with post-bariatric hypoglycaemia.<sup>1</sup> Others have suggested a cut-off of 2.8mmol/l.<sup>2</sup> The Figure (right) shows a very fast glucose resorption in the absence of the native stomach and pyloric function within around 30min of eating, with hypoglycaemia occurring within 60–120min of eating.

A highly fluctuating glucose concentration throughout the day would also be indicative of post-prandial hypoglycaemia.

#### Patients at risk

Hypoglycaemia is associated with both increased insulin sensitivity and  $\beta$  cell function. Further research has shown that those who undergo revisional gastric bypass surgery are at higher risk of developing hypoglycaemia, perhaps due to vagus nerve damage. Altered bile metabolism following cholecystectomy may also increase risk. Patients with early dumping may also show an increased likelihood.

There are few therapeutic options to address insulin sensitivity, but  $\beta$  cell function can be influenced. In a recent study, blocking the glucagon-like peptide-1 (GLP1) receptor prevented a high insulin response and low glucose nadir, which led to a reduction in symptoms.<sup>3</sup>

#### Treating hypoglycaemia

Post-bariatric hypoglycaemia treatments focus on taming the L cell by reducing the rate of glucose absorption by diet or acarbose, or

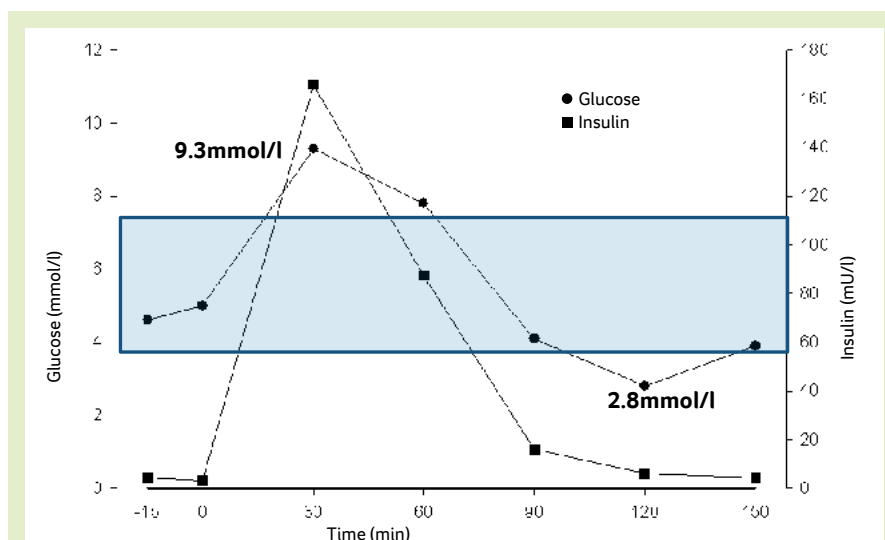


Figure. Results of OGTT showing very fast post-prandial glucose resorption in the absence of the native stomach and pyloric function ( $t_{max}$  is  $\pm 30$ min). Hypoglycaemia is usually between 60 and 120min after the meal.

by decreasing GLP1 and insulin production by use of somatostatin analogues.

Treatment often needs escalation, requiring a combination of diet and medical treatment. A low carbohydrate diet has been shown to be hugely effective. Grade B recommendations include:

- eliminating rapidly absorbable carbohydrates from the diet
- eating six small meals per day
- allowing 30min between eating and drinking
- prioritising high fibre and high protein foods, eaten slowly.<sup>2</sup>

Pharmacological treatment usually begins with acarbose, which slows the rate of glucose absorption. Next, somatostatin analogues may be tried, which are more expensive. These reduce the secretion of GLP1 and insulin. GLP1 analogues have little effect on post-prandial hypoglycaemia, but seem to prompt changes in dietary habits and preferences.

Surgical treatments may include tube feeding into the remnant stomach, which causes almost no glucose fluctuations compared with oral feeding. Banded bypass is no longer recommended. Gastric bypass reversal is an option, shown in a literature review to resolve 88% of cases.<sup>4</sup> Full or partial pancreatectomy should be avoided.

#### Future treatment options

Avexitide is a new GLP1 receptor blocker, which has shown promising results in a study of 18 patients. New research pointing to the role of glucagon in hypoglycaemia could also lead to potential therapeutic targets, such as the closed-loop glucagon system. SGLT-2 inhibitors are another new option.

#### REFERENCES

1. Craig *et al.* 2021 *Surgery for Obesity & Related Diseases* **17** 1865–1872.
2. Scarpellini *et al.* 2020 *Nature Reviews Endocrinology* **16** 448–466.
3. Craig *et al.* 2017 *Diabetologia* **60** 531–540.
4. Xu *et al.* 2021 *Obesity Surgery* **31** 1801–1809.

## Management of nutritional deficiencies

Stephan Bischoff Stuttgart, Germany



The pathophysiology of obesity is characterised by excess fat, but reduced muscle mass is also important. An active patient with obesity may have enhanced muscle mass, because they are carrying more weight. Should they become less mobile, they are likely to experience muscle loss. This is associated with poor outcomes, such as physical disabilities and increased insulin resistance.

Obesity treatments can also cause nutrient deficiency and muscle mass reduction.

#### Micronutrient deficiency before and after treatment

Obesity is associated with micronutrient deficiencies including iron, ferritin,

haemoglobin, thiamine and vitamin D. In one study, patients with obesity were found to have increased stores of vitamin D in fat, which could explain a vitamin D deficiency.<sup>1</sup> These deficiencies may aggravate weight reduction therapy, and need adequate diagnosis and therapy.

Very low calorie diets (VLCD) and bariatric surgery are both associated with a risk of micronutrient deficiency. The Figure on page 15 shows changes in micronutrient deficiencies before and after treatment with a VLCD. Vitamin D deficiency decreased after treatment, while deficiencies in vitamin C, selenium, iron, zinc and calcium all increased.<sup>2</sup>