

Gastric surgery and the incidence of longer-term hypoglycaemic events

In this section, a panel of multidisciplinary team members give their opinions on a recently published paper. In this issue, the focus is on the results of a report on the longer-term incidence of hypoglycaemia among people who have undergone gastric surgery for obesity.



Professor Brian Frier,
Department of
Diabetes,
Royal Infirmary,
Edinburgh

With the increasing popularity of bariatric surgery to treat obesity, an increasing range of complications have emerged.

Hyperinsulinaemic hypoglycaemia is a late complication of gastric bypass surgery, occurring at any time from 18 months to several years after the procedure. It occurs mainly following Roux-en-Y gastric bypass, but – fortunately – is not a recognised consequence of adjustable gastric banding, which is currently the most common gastric weight-loss procedure in the UK (Burns et al, 2010).

Various putative mechanisms have been proposed for the pathogenesis underlying this postoperative hypoglycaemia (Patti and Goldfine, 2010), which is not simply a severe manifestation of postoperative dumping syndrome. It is essential to confirm, characterise and investigate this hypoglycaemia, partly to select appropriate therapeutic measures for its prevention but also to exclude an insulinoma (Zagury et al, 2004).

Marsk et al (2010; summarised alongside) have estimated the frequency of hypoglycaemia following different types of bariatric surgery and astutely measured surrogate indices of hypoglycaemia

(e.g. seizures, syncope, confusion) that are suggestive of severe neuroglycopenia. Although the relative risk of hypoglycaemia following gastric bypass surgery was higher than for controls, the absolute risk was small.

While few experience this problem, unexpected severe hypoglycaemia can have serious consequences. The mortality rate in those affected by post-gastric surgery hypoglycaemia was higher than comparators, with more deaths occurring from accidents than in the control group. This uncommon but serious postoperative complication may therefore be life-threatening in susceptible individuals and has implications for those who drive vehicles or operate machinery. The condition has been identified as a metabolic complication of bariatric surgery that will soon have to be reported to the Driver and Vehicle Licensing Agency (Frier, 2010).

Although severe hypoglycaemia is a relatively rare postoperative complication of gastric bypass surgery its impact is serious.

Burns EM et al (2010) *BMJ* **341**: c4296

Frier BM (Chairman) (2010) *Draft Minutes of the Secretary of State's Honorary Medical Advisory Panel on Driving and Diabetes Mellitus Held on Wednesday, 29 September 2010*. Driver and Vehicle Licensing Agency, Cardiff. Available at: bit.ly/eG3Zg4 (accessed 25.01.11)

Patti ME, Goldfine AB (2010) *Diabetologia* **53**: 2276–9

Zagury L et al (2004) *Obesity Surgery* **14**: 120–3



Roger Ackroyd,
Consultant Surgeon,
Sheffield Teaching
Hospitals NHS
Foundation Trust,
Sheffield

I read Marsk et al's (2010; summarised alongside) article with interest. It highlights the increased risk of late postoperative hypoglycaemia among people who have undergone Roux-en-Y gastric bypass surgery for obesity. A large cohort are followed-up over a long period of time and, as such, we are provided with useful data on this interesting group of people.

It is well known that gastric bypass surgery provides many useful health benefits, one of which is the remission of type 2 diabetes (Pournaras et al, 2010). However, there are adverse side-effects of gastric bypass surgery, one of which is symptomatic hypoglycaemia – in some cases requiring hospitalisation. It is important that people planning to undergo this surgery, and healthcare professionals involved in their care, are made aware of this risk.

On the other hand, it is only right to point out that this late complication of gastric bypass surgery is a relatively rare occurrence ($\leq 1\%$ of participants in the present study affected). Dumping syndrome, which may also be due to a reactive hypoglycaemia, is much more commonly seen, particularly in the early postoperative period (Padoin et al, 2009). It is also important to emphasise, as Marsk et al do, that this problem is only associated with gastric bypass surgery and not with gastric banding or vertical banded gastroplasty.

Marsk et al provide an important clinical reminder of an uncommon but potentially troublesome side-effect of gastric bypass surgery. However, this message should not be overemphasised and should not be used as a deterrent as the benefits of weight-loss surgery in appropriately selected people far outweigh the risks.

Padoin AV et al (2009) *Obes Surg* **19**: 1481–4

Pournaras DJ et al (2010) *Ann Surg* **252**: 966–71

Nationwide cohort study of post-gastric bypass hypoglycaemia including 5040 patients undergoing surgery for obesity in 1986–2006 in Sweden

Marsk R, Jonas E, Rasmussen F, Näslund E (2010) *Diabetologia* **53**: 2307–11

DIABETOLOGIA

Increased risk of hypoglycaemia, accidental death following gastric bypass surgery

- 1** A number of case reports have highlighted symptomatic hypoglycaemia as a complication of gastric bypass surgery for obesity, although the incidence is unknown.
- 2** The authors of this study sought to determine the incidence of post-surgical hypoglycaemia requiring hospitalisation among those who had undergone a gastric surgical procedure for obesity.
- 3** Data for 5040 people who underwent a gastric surgical procedure for obesity (i.e. gastric bypass, vertical banded gastroplasty or gastric banding) between 1 January 1986 and 31 December 2006, and 10 age- and sex-matched

randomly selected referents per surgical patient, were collected from Swedish national registries.

4 The incidence of hospitalisation for hypoglycaemia and a range of its surrogates (i.e. confusion, syncope, epilepsy or seizures) in both groups was recorded both before and after surgery.

5 Pre-surgery rates of inpatient care for hypoglycaemia and its surrogates were similar in the surgical and reference groups. Post-surgery the adjusted hazard ratio for hypoglycaemia and its surrogates was significantly elevated in the surgical group compared with the reference group (2.7; 95% confidence interval, 1.2–6.3).

6 Mean time from surgery to an episode of hypoglycaemia requiring inpatient care was 2.7 years (range, 1.0–14.8 years).

7 When analysed by surgery type, an increased risk of hypoglycaemia was seen only among those who underwent gastric bypass. Hypoglycaemia hazard ratios for those who underwent vertical banded gastroplasty or gastric banding were not significantly different to those of the reference group.

8 The absolute number of those affected by any of the endpoints investigated by the study was $\leq 1\%$.

9 Excluding the first 3 months after surgery, the mortality rate was greater in the surgery group than in the reference group (34.5 vs 19.2 per 10 000 person-years). Accidental death accounted for a greater percentage of total deaths in the surgery group (10.1%) than in the reference group (4.2%).

10 The authors call for future research to explore the underlying physiological mechanisms of symptomatic hypoglycaemia as a complication of gastric bypass surgery for obesity, but remind the reader that the overall incidence of this complication appears to be very low.



Tristan Richardson
Consultant
Physician,
Bournemouth
Diabetes and
Endocrine Centre,
Royal Bournemouth
Hospital,
Bournemouth

Yet again, the Scandinavians have put together a well-designed study to answer a clinical question (Marsk et al, 2010; summarised alongside). After a sensible fashion, this cohort study has investigated the question of post-gastric bypass hypoglycaemia – an increasingly (if anecdotally) reported phenomenon in the literature (Bantle et al, 2007; McLaughlin et al, 2010). The question

of whether this is a true association or not has been unclear – perhaps until now.

Marsk et al convincingly show an association between gastric bypass surgery and a 2- to 3-fold increased risk for hypoglycaemia manifesting 2–3 years postsurgical intervention. A clear relationship with its other clinical presentations such as confusion, seizure, syncope and even fatal accidents, seems evident. There was no evidence to suggest a link between hypoglycaemia and the simpler restrictive procedures such as gastric bands.

Marsk et al discuss possible underlying physiological reasons for the predisposition to hypoglycaemia in this group, further study into which is needed. The relationship is likely to be due to increased incretin hormones, increased islet-cell activity and increased insulin sensitivity,

which seem plausible but are, as yet, unproven.

So how do Marsk et al's findings help us in the clinical setting? The overall incidence of hypoglycaemic complications is small ($\leq 1\%$ of patients affected in Marsk et al's report) and this complication is unlikely to deter people from undergoing gastric surgery for weight reduction in view of the clear benefits of the intervention (Sjöström et al, 2007). However, these data may affect the choice of intervention.

Prior to any concerns being raised regarding post-bypass hypoglycaemia, the proportion of gastric bands has been rapidly increasing, while the number of gastric bypass procedures falls (Tice et al, 2008). This study provides more data on the complications associated specifically with gastric bypass, rather than the other available procedures, and may increase the swing away from gastric bypass.

This is a well-designed study answering the preliminary question of the frequency and association between gastric bypass surgery and hypoglycaemia. It is a valuable addition to the literature and may add to the rising proportion of banding procedures versus bypasses that is currently under way.

Bantle JP et al (2007) *Obes Surg* **17**: 592–4

McLaughlin T et al (2010) *J Clin Endocrinol Metab* **95**: 1851–5

Sjöström L et al (2007) *N Engl J Med* **357**: 741–52

Tice JA et al (2008) *Am J Med* **121**: 885–93



Professor Mike Lean
Professor of Human
Nutrition, Life-
Course Nutrition &
Health, University of
Glasgow, Glasgow

This unusual study from Marsk et al (2010) examines the frequency of post-gastric bypass hypoglycaemia – and episodes of confusion, syncope or seizures, which could be hypoglycaemia related – in a group of 5040 well-documented obese people.

The authors report that the frequency of these outcomes increased significantly following gastric bypass surgery (but not after purely restrictive banding procedures) from presurgical levels, with some 50 000 members of the general population used as a reference group. Hypoglycaemia may not explain all the syncope or seizures in the present study, but it is the most likely explanation for the increased frequency of their occurrence in this cohort.

Following gastric bypass surgery, hypoglycaemia doubled and syncope and seizures trebled (confusingly, seizures and epilepsy were coded separately in this study). The hazard ratios were substantially greater when people with preexisting diabetes were excluded, suggesting that the increase

in hypoglycaemia was not related to antidiabetes drug therapy and that people with diabetes are relatively protected from hypoglycaemia.

How serious a problem was hypoglycaemia for this cohort? Syncope and seizures are unpleasant, frightening and stigmatising. They can also cause serious accidents. In this study accidental deaths were 19.2/10 000 person-years. This rose to 34/10 000 following gastric bypass, to account for 10% of all deaths. Hypoglycaemia probably accounted for some of that increase.

The Swedish Obese Subjects study has already established that gastric bypass leads to greater weight loss than banding, but with increased mortality and more hypoglycaemia (Sjöström et al, 2007). Yet, it is difficult for an individual to weigh up the benefits and hazards from different bariatric procedures, and adhering to dietary control is always going to be difficult. Patients deserve to have their views heard, but a blind pursuit of greater weight loss now needs to be tempered by an understanding of the increased risk of hypoglycaemia and its impact on quality of life following gastric bypass procedures.

Sjöström L et al (2007) *N Engl J Med* **357**: 741–52