Metabolic outcomes 2 years following gastric bypass surgery in people with type 2 diabetes: an observational cohort study

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Summary

Background: Gastric bypass surgery induces early remission or significant improvement in type 2 diabetes (T2D).

Aim: To assess effectiveness of stopping glucose-lowering treatment at the time of surgery.

Design: Observational cohort analysis.

Methods: We identified 101 patients (62 women) with T2D who had undergone gastric bypass surgery at a mean (SD, standard deviation) age of 51.4 (9.0) years. We recorded weight, body mass index (BMI), glycosylated haemoglobin (HbA1c), blood pressure (BP), total and high-density lipoprotein (HDL) cholesterol preoperatively and at a median 4, 12 and 24 months postoperatively, and changes to glucose-lowering therapy.

Results: Mean (SD) baseline BMI was 50.3 (6.3) kg/m², HbA1c 65.3 (18.5) mmol/mol, systolic BP 146.0 (18.0) mmHg, diastolic BP 87.0 (10.8) mmHg and total cholesterol-to-HDL cholesterol ratio 4.0 (1.2). Mean (95% confidence interval) reduction in BMI was 16.4 (14.1–18.7) kg/m², HbA1c 23.6 (17.6–29.6) mmol/mol, systolic BP 12.9 (5.9–19.8) mmHg, diastolic BP 6.1 (1.8–10.5) mmHg and total cholesterol-to-HDL cholesterol ratio 1.1 (0.6–1.5) at 24 months (P<0.001 for all measures). Although 91% of patients were receiving glucose-lowering therapies preoperatively, complete (HbA1c < 42 mmol/mol) and partial (HbA1c 42–48 mmol/mol) remissions of T2D were seen in 62.1% and 5.2% at 2 years postoperatively.

Conclusions: Cessation of glucose-lowering therapies in people with T2D at the time of gastric bypass surgery was clinically effective. The majority of patients remained in complete or partial remission of diabetes up to 2 years postoperatively.

Introduction

The global obesity epidemic, by increasing the risk of acquiring type 2 diabetes (T2D) several fold1,2 is fuelling the worldwide prevalence of diabetes in adults, with a projected increase of 69% in developing countries and 20% in developed countries between 2010 and 2030.3 Although lifestyle and dietary measures and anti-obesity pharmacotherapy are widely recommended as the primary treatment approach for obesity, bariatric surgery remains the most clinically effective and cost-effective intervention for people with morbid obesity compared with non-surgical interventions.4,5 Thus, the global
uptake of bariatric surgery has increased exponentially in the past decade. Bariatric surgery reduces mortality in people with a body mass index (BMI) ≥ 35 kg/m² and results in resolution or improvement in the severity of several co-morbid conditions including T2D, hyperlipidaemia and hypertension. Following an earlier audit at our centre which confirmed early remission or improvement in T2D following gastric bypass surgery, we introduced a protocol of cessation of glucose-lowering treatment in the immediate post-operative period with subsequent monitoring of glycaemic control. We now report a cohort analysis of weight loss and metabolic outcomes of gastric bypass surgery in people with T2D to assess the clinical effectiveness of this strategy.

Methods
We carried out an observational cohort analysis of bariatric surgical patients in the setting of a National Health Service university teaching hospital that serves the population of Greater Manchester in northwest England. Data were gathered prospectively in an automated database. We identified people with T2D who had undergone gastric bypass surgery since the time of the previous audit. Data extracted for this analysis included preoperative and postoperative body weight, glycosylated haemoglobin (HbA1c), blood pressure (BP), total and high-density lipoprotein (HDL) cholesterol, and changes to glucose-lowering therapies. Weight loss outcomes were reported as reduction in BMI and/or percent excess weight loss (%EWL). Remission of diabetes was defined as complete (HbA1c < 42 mmol/mol) or partial (HbA1c 42–48 mmol/mol) in the absence of active pharmacologic therapy. Comparisons of means were performed by Student’s t-test, and contingency tables of categorical variables were analysed by Fisher’s exact test. Comparisons among groups were done by one-way analysis of variance followed by Tukey’s multiple comparison test. P < 0.05 was considered statistically significant and 95% confidence interval (95% CI) was reported as a measure of precision. Data were analysed with SPSS 20.0 (IBM Corp., New York, NY) and Prism 4.03 (GraphPad Software Inc., La Jolla, CA). Permission was obtained from the Caldicott Guardian of our institution.

Results
We identified 62 women (61.4%) and 39 men with T2D with an overall mean (SD, standard deviation) baseline age of 51.4 (9.0) years and BMI 50.3 (6.3) kg/m² who had undergone gastric bypass surgery. There were no significant differences between men and women in age, BMI, duration of diabetes, systolic and diastolic BPs, total cholesterol and total cholesterol-to-HDL cholesterol ratio at baseline (Table 1). Following gastric bypass surgery there was significant weight loss with a mean (95% CI) reduction in BMI of 16.4 (14.1–18.7) kg/m² (P < 0.0001 for trend) at 24 months (Figure 1a). The mean (standard error) %EWL was 65.2 (2.2) % (P < 0.0001 for trend) at 24 months (Figure 1b). The mean (95% CI) reduction in HbA1c was 23.6 (17.6–29.6) mmol/mol (P < 0.0001 for trend) at 24 months (Figure 1c). HbA1c was ≥ 48.0 mmol/mol in 83.8% patients preoperatively and 20.7% patients by 4 months (P < 0.001) and maintained up to 24 months postoperatively (Figure 1d).

Table 1 Baseline mean (SD) measurements in people with T2D who had undergone gastric bypass surgery

<table>
<thead>
<tr>
<th></th>
<th>All (n = 101)</th>
<th>Men (n = 39)</th>
<th>Women (n = 62)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.4 (9.0)</td>
<td>52.2 (7.8)</td>
<td>50.8 (9.7)</td>
<td>ns</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>139.3 (23.2)</td>
<td>153.4 (20.8)</td>
<td>130.4 (20.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>50.3 (6.3)</td>
<td>49.9 (6.5)</td>
<td>50.6 (6.2)</td>
<td>ns</td>
</tr>
<tr>
<td>Duration of diabetes (months)</td>
<td>76.6 (64.0)</td>
<td>78.6 (56.3)</td>
<td>75.4 (68.9)</td>
<td>ns</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>65.3 (18.5)</td>
<td>70.2 (19.0)</td>
<td>62.3 (17.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>146.0 (18.0)</td>
<td>145.5 (17.6)</td>
<td>146.3 (18.4)</td>
<td>ns</td>
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<tr>
<td>Diastolic BP (mm Hg)</td>
<td>87.0 (10.8)</td>
<td>87.6 (12.9)</td>
<td>86.7 (9.3)</td>
<td>ns</td>
</tr>
<tr>
<td>Total cholesterol (mM)</td>
<td>4.6 (1.1)</td>
<td>4.5 (1.0)</td>
<td>4.6 (1.1)</td>
<td>ns</td>
</tr>
<tr>
<td>HDL cholesterol (mM)</td>
<td>1.2 (0.3)</td>
<td>1.1 (0.2)</td>
<td>1.3 (0.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total cholesterol:HDL cholesterol</td>
<td>4.0 (1.2)</td>
<td>4.2 (1.2)</td>
<td>3.8 (1.2)</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns, non-significant. *Men vs. women, Student’s t-test.
of 51 years as the cutoff, was similar at baseline but there were greater reductions in younger compared with older individuals by 4 months after gastric bypass surgery and maintained up to 24 months (Table 2). Likewise, there were significantly greater reductions in HbA1c in patients with shorter duration of diabetes in a two-group analysis using the median duration of 59 months as the cutoff (Table 2). There were no significant differences in HbA1c reduction based on greater or lesser degree of weight loss in a two-group analysis using the median BMI at 24 months of 33.35 kg/m² as the cutoff.

Ninety-one percent of patients were receiving glucose-lowering therapies preoperatively, including...
67% on oral hypoglycaemic agents (OHAs) and 24% on insulin ± OHAs. Glucose-lowering therapies were stopped completely in 80 patients at the time of surgery. Of those patients who continued treatment, 12 were on metformin, two on sulphonylureas and four on insulin ± OHA (unknown in three patients). Complete and partial remissions of T2D were seen in 66.2% and 4.4% of patients at 1 year and 62.1% and 5.2% at 2 years postoperatively. Of 24 patients who were on insulin ± OHAs preoperatively, 20 (83%) came off insulin treatment, of whom eight (40%) achieved complete withdrawal of glucose-lowering treatment; the remaining four (17%) of patients had reduced insulin requirements.

The mean (95% CI) reduction in systolic BP was 12.9 (5.9–19.8) mm Hg ($P < 0.0001$) and diastolic BP 6.1 (1.8–10.5) mm Hg ($P < 0.0001$) (Figure 1e) and non-HDL cholesterol 0.54 (0.10–0.98) mmol/l ($P = 0.001$) (Figure 1f). Systolic BP was $> 140$ mm Hg in 60.4% of patients preoperatively compared with 30.0% at 2 years postoperatively ($P = 0.001$). Total-to-HDL cholesterol ratio was $> 4.0$ in 44.7% of patients preoperatively compared with 10.5% at 2 years postoperatively ($P < 0.0001$).

### Discussion

We assessed the clinical effectiveness of stopping glucose-lowering therapies on the day of gastric bypass surgery in obese people with T2D and report that two-thirds of patients remained in complete or partial remission of T2D up to 2 years postoperatively. This is consistent with previous studies that have reported resolution or improvement of diabetes in 80% of gastric bypass patients at two or more years of follow-up.

Factors that predict remission of diabetes following bariatric surgery include younger age, shorter duration of diabetes and greater weight loss. We also confirmed that there were greater reductions in glycosylated haemoglobin in individuals who were younger or had shorter diabetes duration. These findings support the argument for considering bariatric surgery sooner rather than later in the management of T2D associated with morbid obesity. The degree of weight loss, however, did not influence the amount of reduction in HbA1c in our study. This lends further credence to the weight-independent mechanisms of improvement in glycaemic control by gastric bypass surgery. Studies have also
shown benefits in terms of reduction in cardiovascular events and mortality on long term follow-up of bariatric patients. The Swedish Obese Subjects study, which compared 2010 post-bariatric surgery patients with 2037 non-surgical patients matched for age, sex, BMI and co-morbidities, demonstrated a reduction in myocardial infarction rate of 43% and all cause mortality rate of 31% up to 15 years postoperatively.\textsuperscript{20}

Despite prospectively filled automated, electronic database for data collection, our study was restricted by the retrospective nature of the cohort analysis. We were unable to examine the influence of specific preoperative anti-diabetic therapies such as GLP-1 receptor agonists on postoperative clinical outcomes due to small numbers in sub-group analyses. Although glycosylated haemoglobin reflects sub-acute glycaemic control, we were unable to collect capillary blood glucose data or undertake continuous glucose monitoring due to the constraints of routine clinical care and logistical challenges. Similarly, in the absence of clinical utility, measurement of hormones involved in the regulation of the entero-insular axis was beyond the scope and means of this work.

Despite these limitations, our pragmatic, observational study confirms significant weight loss and early remission or improvement in T2D following gastric bypass surgery as reported previously. In addition, we report that our protocol for stopping glucose-lowering treatments in the immediate postoperative period in people with T2D prior to discharge from hospital was safe and effective. To our knowledge, this is the first report of such an approach of immediate discontinuation of glucose-lowering therapies at the time of gastric bypass surgery. As patients have markedly reduced food intake following gastric bypass surgery, our protocol minimizes the risk of post-operative hypoglycaemia. Patients were advised intensive monitoring of capillary blood glucose concentrations and review by specialist nurses and/or their primary diabetes care providers. In patients who continue to manifest hyperglycaemia, glucose-lowering therapies may be re-introduced in a phased manner as clinically indicated.

**Conclusion**

We conclude that cessation of glucose-lowering therapies in people with T2D at the time of gastric bypass surgery was clinically effective. The majority of patients remained in complete or partial remission of diabetes up to 2 years postoperatively.

**Acknowledgements**

This work was presented as an Oral Communication at the Diabetes UK annual professional conference (2013).\textsuperscript{21}

**Conflict of interest:** None declared.

**References**


