

# Effects of Gastric Bypass Surgery in Patients with Obesity and Type 2 Diabetes

Akademisk avhandling

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## Avhandlingen baseras på följande delarbeten

- I. Eliasson B, Liakopoulos V, Franzén S, Näslund I, Svensson AM, Ottosson J, Gudbjörnsdottir S. **Cardiovascular disease and mortality in patients with type 2 diabetes after bariatric surgery in Sweden: a nationwide, matched, observational cohort study.** *Lancet Diabetes Endocrinol.* 2015;3(11):847–54.
- II. Liakopoulos V, Franzén S, Svensson A-M, Zethelius B, Ottosson J, Näslund I, Gudbjörnsdottir S, Eliasson B. **Changes in risk factors and their contribution to reduction of mortality risk following gastric bypass surgery among obese individuals with type 2 diabetes: a nationwide, matched, observational cohort study.** *BMJ Open Diabetes Res Care.* 2017;5(1):e000386.
- III. Liakopoulos V, Franzén S, Svensson A-M, Miftaraj M, Ottosson J, Näslund I, Gudbjörnsdottir S, Eliasson B. **Pros and cons of gastric bypass surgery in individuals with obesity and type 2 diabetes: nationwide, matched, observational cohort study.** *BMJ Open.* 2018; 9(1):e023882.
- IV. Liakopoulos V, Franzén S, Svensson A-M, Sattar N, Miftaraj M, Björck S, Ottosson J, Näslund I, Gudbjörnsdottir S, Eliasson B. **Change in renal, cardiovascular and mortality outcomes after gastric bypass in type 2 diabetes - cardiorenal risk reductions exceed atherosclerotic benefits.** 2019 (submitted).

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## Abstract

**Background:** The effects of Roux-en-Y gastric bypass (GBP) have not been adequately explored in patients with concurrent obesity and type 2 diabetes mellitus (T2DM) to the same extent as has occurred for individuals with obesity alone. The overall aim of this thesis is to thoroughly examine the effects of GBP surgery in patients with obesity and T2DM in terms of cardiovascular disease and mortality, changes in various comorbidities, risk factors, and renal function as well as reporting adverse events.

**Method:** The reported studies are based mainly on merging data from two nationwide quality registries in Sweden (the National Diabetes Register and Scandinavian Obesity Surgery Register) as well as other national databases. Our study population of individuals with T2DM who had undergone GBP was matched with respect to baseline parameters such as sex, age, body mass index (BMI), and calendar year with controls who did not undergo surgery. The risks of postoperative outcomes were assessed using Cox regression models adjusted for various factors depending on endpoints.

**Results:** Assessing data for 6,132 patients in each group from 2007 to 2014, we found a 58% relative risk reduction in overall mortality, a 59% lower risk of cardiovascular death, and a 49% lower risk of fatal or non-fatal myocardial infarction in the GBP group compared to controls. Following GBP, there were beneficial changes in BMI, hemoglobin A<sub>1c</sub>, blood lipids, and blood pressure compared to controls despite less frequent use of antidiabetic, antihypertensive, and antihyperlipidemic medications. The improvements in risk factors might contribute to the reduction of mortality risk after GBP in individuals with obesity and T2DM, but the main effect seems to be mediated through the decrease in BMI.

New analyses of data for 5,321 individuals during 2007 to 2015 confirmed lower incidences of all-cause mortality and cardiovascular disease, demonstrated beneficial effects on severe kidney disease, and showed increased risks (2-fold to 9-fold) for several short-term postsurgical complications compared to controls. There were long-term adverse consequences of GBP compared to controls: there was a 92% higher risk of anemia, a 3-fold increase in nutritional deficiencies, a 33% higher risk for psychiatric diagnoses, and a 3-fold increase in alcohol abuse. The risk rates for most outcomes relating to renal function were lower after GBP. Risks of a composite of severe renal disease or halved estimated glomerular filtration rate (eGFR), and cardiovascular and renal mortality, were generally lower after GBP in all eGFR strata, even in patients with the lowest eGFR.

**Conclusion:** The benefits of GBP for patients with obesity and T2DM on mortality, cardiovascular risk, and a broad spectrum of clinical diagnoses might be associated to changes in several risk factors; however, the main effect seems to be mediated through weight reduction. Interestingly, the positive effects of GBP are found for almost all categories of renal function, at the same time delaying deterioration to end-stage renal disease. However, the panorama of both short- and long-term adverse events suggests a more effective selection of patients who genuinely are eligible for such an intervention.

**Keywords:** Gastric bypass; bariatric surgery; obesity; type 2 diabetes mellitus; cardiovascular disease; mortality; risk factors; renal disease; adverse events