

On the effects of obesity treatment

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs Universitet kommer att offentligen försvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Vita stråket 12, Göteborg den 16. Juni 2021, kl. 9:00 av

Gudrún Höskuldsdóttir

Fakultetsopponent:

Professor Mikael Rydén

Karolinska Institutet, Huddinge, Stockholm

Avhandlingen baseras på följande delarbeten

- I. Höskuldsdóttir G, Ekelund J, Miftaraj M, Wallenius V, Ottosson J, Näslund I, Gudbjörnsdóttir S, Sattar N, Svensson AM, Eliasson B. Potential Benefits and Harms of Gastric Bypass Surgery in Obese Individuals with Type 1 Diabetes: A Nationwide, Matched, Observational Cohort Study. *Diabetes Care* 2020;43(12):3079-85.
- II. Höskuldsdóttir G, Sattar N, Miftaraj M, Näslund I, Ottosson J, Franzén S, Svensson AM, Eliasson B. Potential Effects of Bariatric Surgery on the Incidence of Heart Failure and Atrial Fibrillation in Patients with Type 2 Diabetes Mellitus and Obesity and on Mortality in Patients with Preexisting Heart Failure: A Nationwide, Matched, Observational Cohort Study. *J Am Heart Assoc.* 2021;10(7):e019323.
- III. Höskuldsdóttir G, Mossberg K, Wallenius V, Al Nimer A, Björkvall W, Lundberg S, Behre CJ, Werling M, Eliasson B, Fändriks L. Design and baseline data in the BAriatic surgery SUBstitution and Nutrition study (BASUN): a 10-year prospective cohort study. *BMC Endocr Disord* 2020 Feb 14;20(1):23.
- IV. Höskuldsdóttir G, Engström M, Rawshani A, Wallenius V, Lenér F, Fändriks L, Mossberg K, Eliasson B. The BAriatic surgery SUBstitution and Nutrition (BASUN) population: a data-driven exploration of predictors for obesity. Manuscript.
- V. Höskuldsdóttir G, Engström M, Rawshani A, Lenér F, Wallenius V, Fändriks L, Mossberg K, Eliasson B. Effects two years after medical and surgical treatments of obesity: prospective cohort study. Manuscript.

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Aim: In this thesis the effects of bariatric surgery in individuals with type 1 diabetes (T1D) will be assessed as well as the effects of surgery on risk for heart failure (HF) and atrial fibrillation (AF) in individuals with type 2 diabetes (T2D). Intensive medical treatment of obesity will be compared with the most common surgical methods and factors predicting obesity and treatment outcomes evaluated.

Methods: Study I included effects of Roux-en-Y gastric bypass (RYGB) on cardiovascular outcomes, mortality, serious hypo- and hyperglycemia, substance abuse, psychiatric health, kidney function and amputation in individuals with T1D and obesity. In study II the effects of RYGB on the incidence of HF and AF in individuals with T2D and obesity was evaluated as well as effects on mortality in individuals with preexisting HF. COX proportional hazards regressions were applied. Studies III-V included individuals from the BASUN study that received non-surgical treatment of obesity or surgical treatment with RYGB or sleeve gastrectomy. Study III includes a description the population at baseline. In study IV, machine learning algorithms were used to rank individual variables and variable domains with regard to predictive value on BMI. Study V describes the results from the three treatments at two-year follow-up. Outcomes included were changes in anthropometric measures and metabolic parameters (analyzed using linear regression models) and composite variables for successful and unsuccessful treatment (analyzed using a logistic regression model). Clinical variables were divided into domains and their impact in predicting treatment success was computed using conditional random forest with conditional permutation.

Results: We found that RYGB reduced risk for cardiovascular disease and mortality in individuals with T1D and obesity but increased risk for serious hyperglycemic events and substance abuse. Surgically treated individuals with T2D and obesity that underwent RYGB had significantly lower risk for hospitalization for AF and HF in comparison with those that did not undergo surgery. Lower mortality was observed in individuals with known HF that had undergone surgery. Domains including socioeconomic status, age, sex, lifestyle and habits as well as potential anxiety and depression were shown to have strong predictive value on BMI levels. Bariatric surgery is more effective than medical treatment of obesity, although medical treatment was also shown to be effective. There was no difference in safety measures between the treatment groups. Domains including anthropometry at baseline, metabolic disease, lifestyle and habits and socioeconomic status had predictive value on treatment success and domains including mental well-being and psychiatric disorders were also important in success of the different treatment options.

Conclusion: Bariatric surgery may be considered in individuals with T1D after consideration of risk for serious hypo- and hyperglycemia. This treatment option is effective in individuals with T2D and obesity to reduce risk for HF and AF and may even be considered in a selected population of individuals with known HF. Mental well-being and not only diagnosed psychiatric disorders could be an important factor in the treatment and follow-up with individuals with obesity. Although surgical treatment of obesity is more effective with regard to weight loss, medical treatment can also lead to meaningful weight loss. Deficiencies of vitamins and minerals or complications of treatment are not necessarily more common after bariatric surgery given good compliance to supplementary treatment and careful choice of treatment option.

Keywords: Obesity, diabetes, bariatric surgery

ISBN 978-91-8009-314-9 PRINT

ISBN 978-91-8009-315-6 PDF

<http://hdl.handle.net/2077/68054>