

Identifying predictors of long-term effects of bariatric surgery

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Sahlgrenska sjukhuset, Vita stråket 12, Göteborg. Onsdagen den 4 december 2024, klockan 09:00.

av Felipe M Kristensson

Fakultetsopponent: Docent Mikael Wirén
Linköpings Universitet, Sverige

Avhandlingen baseras på följande delarbeten

- I. **Long-term effects of bariatric surgery in patients with obesity and chromosome 16p11.2 microdeletion.** Kristensson FM et al. *Surgery for Obesity and Related Diseases*, 2017. 13(8): p.1321-1326.
- II. **Effects of Bariatric Surgery in Early- and Adult-Onset Obesity in the Prospective Controlled Swedish Obese Subjects Study.** Kristensson FM et al. *Diabetes Care*, 2020. 43(4): p. 860-866.
- III. **Breast Cancer Risk After Bariatric Surgery and Influence of Insulin Levels – A Nonrandomized Controlled Trial.** Kristensson FM et al. *JAMA Surgery*, 2024. 159(8): p. 856-863.
- IV. **FTO rs9939609 genotype and breast cancer risk after bariatric surgery in the Swedish Obese Subjects study.** Långegård E*, Kristensson FM* et al.
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**SAHLGRENKA AKADEMIN
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Felipe M Kristensson

Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden, 2024.

Abstract

Aim of the thesis: To identify predictors of long-term treatment outcomes after bariatric surgery.

Material and methods: The Swedish Obese Subjects (SOS) study is a prospective controlled intervention study comparing bariatric surgery (n=2010) and conventional obesity treatment (n=2037). Data on anthropometry, biochemical variables, and questionnaires are available from over 20-years of follow-up. Data on mortality and morbidity were obtained from national registers. DNA for genetic analysis was extracted from samples of whole blood.

Results: In *Paper I*, carriers of the chromosome 16p11.2 microdeletion, which is strongly associated with obesity, had significantly higher BMI, insulin levels, and systolic blood pressure at baseline compared to non-carriers. However, long-term weight loss and changes in risk factors were similar in both groups. *Paper II* showed that individuals with obesity at the age of 20 had greater initial weight reduction following bariatric surgery compared to those who developed obesity later in life. However, the effects of surgery on cardiometabolic health were similar across subgroups defined by obesity onset. In *Paper III*, we found that bariatric surgery was associated with a reduced risk of breast cancer in women with obesity, with the greatest treatment benefit observed in women with hyperinsulinemia at baseline. *Paper IV* found an association between the A-allele in rs9939609 in the fat mass and obesity-associated protein (*FTO*) gene, and breast cancer risk in women with obesity after bariatric surgery.

Conclusion: In conclusion, the presence of a microdeletion on chromosome 16p11.2 or the age of obesity onset did not affect treatment outcomes following bariatric surgery. In contrast, baseline insulin levels and a risk allele in the *FTO* gene were associated with treatment benefits on cancer risk after bariatric surgery in women with obesity.

Keywords: Bariatric surgery, obesity, predictor, cancer, CVD, *FTO*, insulin