

Søknadsinformasjon

Utlysning	Nordic Cancer Union Research Grant, 2015
Søknad	Influence of obesity surgery on cancer risk in a Nordic population-based cohort study
Søknadsid	176514
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Oppgave: Progress report

Tilordnet	Jesper Lagergren
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RAPPORT

Briefly describe the project in a language understandable to non-scientists

Obesity surgery is used increasingly often due to the increasing occurrence of obesity. The cancer risk following obesity surgery is uncertain, but the limited available literature has helped us to formulate two main hypotheses:

- 1) Obesity surgery decreases risk of obesity-related cancer
- 2) Obesity surgery increases risk of colorectal cancer

Data from nationwide Nordic registries for in-hospital care, cancer and mortality are used to assess how obesity surgery influences cancer risk. Data from all five Nordic countries are merged to create a large group of obesity surgery patients and estimate their cancer risk compared to a background population and to non-operated patients with a diagnosis of obesity. The two control groups consist of individuals of the corresponding age and sex distribution as the obesity surgery group.

If our hypotheses are proven true, tailored prevention and surveillance of high-risk individuals for cancer might be considered following obesity surgery.

Summarize the major findings of the project

It has been an extensive and very time-consuming work to get this all-Nordic cohort in place for final analyses. The main parts of the work has been: 1) to apply for and get all formal permissions from ethical committees and data inspectorates from all countries, 2) collecting, managing, checking, merging and analysing all data retrieved, including several complimentary data retrievals. However, we have now finalised the cohort.

The first study is a comprehensive description of the cohort. The cohort includes 506,826 individuals diagnosed with obesity, together contributing with 3,597,897 person-years of follow-up for cancer risk. Among these, 57,283 (11.3%) individuals have undergone obesity surgery during the study period, corresponding to 313,036 person-years of follow-up. Obesity surgery was mainly performed in Sweden during the 1980s and 1990s and occurred only rarely in the other Nordic countries. A rapid increase in the number of obesity surgery procedures per 100 000 inhabitants was observed in all Nordic countries during the 2000s, with Sweden and Denmark in the lead in the absolute number of procedures performed, while Iceland had a high volume of obesity surgery procedures in relation to its population size. Finland and Norway had intermediate levels of procedures. This paper has been submitted for publication.

Interestingly, preliminary results from the analyses of the studies examining the risk of obesity-related cancer and colorectal cancer indicate that the hypotheses are in fact correct, i.e. we see a clearly decreased risk of obesity-related cancer over time following surgery, while the risk of colorectal cancer is instead increased. We are currently working on completing these studies and they will be submitted for publication later this year.

During the work with collecting the Nordic cohort presented above, we have used the Swedish part of the cohort to conduct other studies of relevance for obesity surgery. The absolute risk of mortality following obesity surgery is low, but there is an increased relative risk of mortality associated with male sex, diabetes, congestive heart failure, and open surgical access (compared to laparoscopic procedures). A history of diabetes and peptic ulcer increases the risk of marginal ulcer following obesity surgery, while hyperlipidemia, hypertension, and chronic obstructive pulmonary disease do not. Lower doses of aspirin, nonsteroidal anti-inflammatory drugs, and selective serotonin reuptake inhibitors does not increase the risk, but higher doses of aspirin do. The risk of oesophageal adenocarcinoma might not decrease after obesity surgery, but larger studies with longer follow-up are needed. The prognosis in rectal cancer, but not in colon cancer, is worse following obesity surgery compared to in non-operated obese patients. Obesity surgery registration in the Swedish National Patient Registry has high accuracy and is a reliable source of data to identify patients having undergone obesity surgery. There is great value of recommending weight loss in the treatment of gastro-oesophageal reflux disease.

Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer

The seemingly strongly protective effects of obesity surgery in relation to the risk of developing obesity-related cancers in general suggests that weight loss might be a useful measure of preventing cancer, particularly in people with an increased risk of developing such cancers in the first place, e.g. those with cancer heredity, premalignant conditions, and those exposed to other risk factors.

The increased risk of colorectal cancer indicates a potential role for colonoscopic surveillance after obesity surgery to identify colorectal tumours at an early and curable stage, or at least an increased awareness of the risk, which should prompt early colonoscopy whenever symptoms that might be due to cancer development occur.

Additionally, this project shows that despite the initial obstacles and the work-load it is indeed possible to conduct all-Nordic studies for high quality cancer research, providing excellent statistical power and complete follow-up.

Outline how Nordic cooperation has added value to this project

This research could not have been conducted without Nordic collaboration and the goldmine of registry data available in these countries. These data are unique from an international perspective. Previous research attempting to address cancer risk after obesity surgery has been clearly under-powered. By merging data from all Nordic countries, we could include as many as 57,283 patients having undergone obesity surgery and 506,826 non-operated obese patients. This provided a most powerful basis for the studies. Detailed sub-group analyses are possible, e.g. assessment of specific types of cancer, and thorough risk assessments in follow-up of time periods after surgery. No previous studies on these topics are close to the statistical power of this project.

We should add that this well-working Nordic collaboration between several skilled scholars, representing each country, has provided a very useful network for further cancer research that hopefully will benefit many future patients.

List the publications resulting from the NCU research grant

Author(s), title, journal and edition	PMID (8 digits, only if possible)
1. Tao W, Plecka-Östlund M, Lu Y, Mattsson F, Lagergren J. Causes and risk factors for mortality within 1 year after obesity surgery in a population-based cohort study. <i>Surg Obes Relat Dis</i> 2015;11:399-405.	25604834
2. Sverdén E, Mattsson F, Sondén A, Leinsköld T, Tao W, Lu Y, Lagergren J. Risk Factors for marginal ulcer after gastric bypass surgery for obesity: A population-based cohort study. <i>Ann Surg</i> 2016;263:733-7.	26106845
3. Maret-Ouda J, Tao W, Mattsson F, Brusselaers N, El-Serag HB, Lagergren J. Esophageal adenocarcinoma after obesity surgery in a population-based cohort study. <i>Surg Obes Relat Dis</i> 2017;13:28-34.	26723560
4. Tao W, Konings P, Hull MA, Adami HO, Mattsson F, Lagergren J. Colorectal cancer prognosis following obesity surgery in a population-based cohort study. <i>Obes Surg</i> 2016 Nov 7. [Epub ahead of print]	27822767
5. Tao W, Holmberg D, Näslund E, Näslund I, Mattsson F, Lagergren J, Ljung R. Validation of obesity surgery data in the Swedish National Patient Registry and Scandinavian Obesity Registry (SOReg). <i>Obes Surg</i> 2016;26:1750-6.	26667162
6. Tao W, Artama M, von Euler-Chelpin M, Konings P, Ljung R, Lyng E, Mattsson F, Ólafsdóttir GH, Pukkala E, Romundstad P, Tryggvadóttir L, Wahlin K, Lagergren J. Cohort Profile: The Nordic Obesity Surgery Cohort (NordOSCo). Submitted manuscript.	
7. Tao W, Wahlin K, von Euler-Chelpin M, Lyng E, Ólafsdóttir GH, Artama M, Pukkala E, Romundstad P, Tryggvadóttir L, Hull M, Lagergren J. Risk of colorectal cancer following obesity surgery in a Nordic cohort study. Manuscript writing.	
8. Tao W, Wahlin K, Lyng E, Ólafsdóttir GH, Pukkala E, Artama M, Romundstad P, Tryggvadóttir L, von Euler-Chelpin M, Lagergren J. Cancer risk after obesity surgery in a Nordic population-based cohort study. Manuscript writing.	

Brief overview of expenditures for last year 1 vedlegg (Brief overview expenditures_Jesper Lagergren.doc)