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Cancer Incidence and Mortality After Gastric Bypass Surgery

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Abstract

Despite weight loss recommendations to prevent cancer, cancer outcome studies after intentional weight loss are limited. Recently, reduced cancer mortality following bariatric surgery has been reported. This study tested whether reduced cancer mortality following gastric bypass was due to decreased incidence. Cancer incidence and mortality data through 2007 from the Utah Cancer Registry (UCR) were compared between 6,596 Utah patients who had gastric bypass (1984–2002) and 9,442 severely obese persons who had applied for Utah Driver's Licenses (1984–2002). Study outcomes included incidence, case-fatality, and mortality for cancer by site and stage at diagnosis of all gastric bypass patients, compared to nonoperated severely obese controls. Follow-up was over a 24-year period (mean 12.5 years). Total cancer incidence was significantly lower in the surgical group compared to controls (hazard ratio (HR) = 0.76; confidence interval (CI) 95%, 0.65–0.89; $P = 0.0006$). Lower incidence in surgery patients vs. controls was primarily due to decreased incidence of cancer diagnosed at regional or distant stages. Cancer mortality was 46% lower in the surgery group compared to controls (HR = 0.54; CI 95%, 0.37–0.78; $P = 0.001$). Although the apparent protective effect of surgery on risk of developing cancer was limited to cancers likely known to be obesity related, the inverse association for mortality was seen for all cancers. Significant reduction in total cancer mortality in gastric bypass patients compared with severely obese controls was associated with decreased incidence, primarily among subjects with advanced cancers. These findings suggest gastric bypass results in lower cancer risk, presumably related to weight loss, supporting recommendations for reducing weight to lower cancer risk.

INTRODUCTION

Greater body fatness and obesity have been associated with increased risk for cancer (1–7). National cancer prevention guidelines include recommendations to lose weight (8), but

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/oby

DISCLOSURE

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whether or not intentional weight loss reduces risk for cancer is unclear. Although voluntary weight loss and cancer incidence studies have shown probable reduction in specific cancers following sustained weight reduction, little research has been conducted (9–12), in large part because long-term weight loss maintenance in large population studies is very difficult to achieve (13,14).

Postbariatric surgery patients experience significant and sustained weight loss (15,16) and as a result, represent a unique population to explore the effects of long-term voluntary weight loss on cancer (17,18). Building upon our group's recent report of reduced total and cancer-specific mortality following gastric bypass surgery when compared to severely obese controls (18), this study was undertaken to determine possible explanations for the observed reduced cancer mortality. This study compared incidence, case-fatality, and mortality of total and stage-specific cancer in a large number of postgastric bypass patients in Utah, and a group of severely obese controls recruited from the general Utah population.

METHODS AND PROCEDURES

Study groups

We previously described a retrospective cohort mortality study of 9,949 post-Roux-en-Y gastric bypass patients whose surgery was performed between the years 1984 and 2002 by a single practice of Utah bariatric surgeons in Utah, and 9,628 severely obese adult controls with a self-reported BMI of ≥35 who were chosen from Utah driver's license or identification card (ID) applicants between the years of 1984 and 2002 (ref. 18). Self-reported height and weight are required data at the time of application for a driver's license or ID. Controls were group matched to represent the gender, age, and BMI distribution of the surgical patients. This included the use of 5-year age categories, exact year at the time of surgery or license application categories, and three BMI intervals (35–44, 45–54, and ≥55) (ref. 18). Presurgical BMI measurement was used for the surgery group and corrected self-reported BMI at the time of the license application for the control group. For this cancer-specific study, these same subjects, excluding non-Utah residents, were linked to the Utah Cancer Registry (UCR) using names, date of birth, gender, and social security number if available for years 1984 through 2007. After exclusion of non-Utah residents, there remained 6,709 Utah resident surgical patients and 9,609 Utah driver's license and ID card controls for linking to the cancer registry. Cancer record linking through 2007 extended the length of mean follow-up of our previous study by 5 years to a total 12.5 years. Because the UCR only reports persons who resided in Utah at the time of cancer diagnosis, only reported residents of the state of Utah from each original group were evaluated. The gastric bypass surgical practice is a multi-state referral center with a large out-of-state referral base.

The UCR is a population-based cancer registry in operation since 1966 and has been a member of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program since 1973. Patient and cancer information are provided to the UCR on behalf of the Utah Department of Health for state-wide cancer surveillance activities and research. In addition, the UCR periodically links National Death Index data to identify Utah residents whose deaths have occurred outside the state of Utah. For gastric bypass patients and controls who linked to UCR, data identifying site (type), stage of cancer, date of diagnosis, vital status, and date of death were obtained according to SEER standards. The SEER staging system codes are defined as follows: 0 = *in situ*; 1 = localized; 2 = regional, direct extension only; 3 = regional, regional lymph nodes only; 4 = regional, direct extension and regional lymph nodes; 5 = regional, not otherwise specified (NOS); 7 = distant metastasis; and 9 = unstaged (19).

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The study was reviewed and approved by the Institutional Review Board at the University of Utah School of Medicine. The Institutional Review Board granted a waiver of consent because no subjects were contacted for this study. The UCR created a de-identified data set for analysis. Confidentiality measures established by federal and state government were adhered to throughout the study period.

Statistical analysis

The primary outcomes included cancer incidence and mortality in both the surgical and control groups, and case-fatality among those subjects with incident cancer for both groups. Incident cancer cases were those diagnosed following gastric bypass surgery or driver's license or ID card application in subjects who were cancer-free at the time of the surgery or application. Mortality was defined as any death from cancer occurring after surgery or license application among people who were cancer-free at the time of the surgery or application. Case-fatality was defined as death from cancer after the diagnosis of cancer following gastric bypass surgery or driver's license application. Where multiple incident cancers occurred, analyses were restricted to the first diagnosed primary cancer site.

Any surgical or control subject identified as having been diagnosed with cancer prior to the date of gastric bypass surgery or the date of application for driver's license or ID card was considered a prevalent case. Prevalent cases were statistically compared between groups using χ^2 analysis. All prevalent cases (1.9% in surgical subjects and 2.0% in controls, $P = 0.55$) were excluded from analyses of incidence, case-fatality and mortality leaving 6,596 surgical patients and 9,442 controls for analysis (Table 1).

Following the recommendations of an international consensus report and other reports identifying greater body fatness as a likely cause for specific subsets of cancers (2,7,8,11), obesity-related cancers were defined as esophagus (adenocarcinoma only), colorectal, pancreas, postmenopausal breast, corpus and uterus, kidney, non-Hodgkin's lymphoma, leukemia, myeloma, liver, and gallbladder. Incidence and mortality of obesity-related cancers were determined separately from incidence and mortality due to cancers not defined as obesity-related cancers.

Cox proportional hazards regression analysis was used to compare the risk of overall and site-specific cancer incidence, case-fatality and mortality in the two study groups. To analyze cancer incidence, subjects were followed from baseline (defined as date of gastric bypass surgery or application for a Utah Driver's License) to date of incident cancer diagnosis. To analyze case-fatality, subjects with newly diagnosed cancer were followed from date of diagnosis to date of death from cancer. Because stage is an important confounder of survival following cancer diagnosis, a proportional hazards analysis adjusting for cancer stage as a covariate was also performed. In the analysis of cancer mortality, all subjects were followed from baseline to death from cancer. In these analyses, subjects were censored either at time of death for causes other than cancer, or 1 January 2008, whichever occurred first. Sex and mean BMI differences, though small, were significantly different between study groups ($P < 0.001$; Table 1). Therefore, all Cox regression models were adjusted for sex (unless stratified by sex), baseline age and baseline BMI to correct for these differences. The proportional hazards assumption was met for all analyses.

Measured baseline BMI was obtained from the surgeons' medical records for the surgical subjects. For controls, the self-reported BMI was obtained from the driver's license and then adjusted to correct for misreporting by gender-specific regression equations developed in our earlier study (18). Data used to produce these regression equations were obtained from the actual height and weight data obtained from 592 patients just prior to their surgery compared to their height and weight self-reported when making application for a driver's

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license within a 5-year period prior to their gastric bypass surgery. Cancer incidence analyses were repeated adjusting for uncorrected, self-reported driver's license BMI to further establish the robustness of the results. Unfortunately, BMI at follow-up was not available for either group. The expected number of cancers in the gastric bypass group was determined by multiplying the incidence rate in controls by the number of total surgeries. The observed number of cancers was subtracted from the expected number in the gastric bypass group to obtain the number of cancers prevented. The same method was used for cancer deaths.

Analyses were completed with the use of SAS software (version 9.1; SAS, Cary, NC). *P* values and 95% confidence intervals (CIs) are two-sided. Because three primary hypotheses were tested for all combined cancers (incidence, case-fatality, and mortality), we used the Bonferroni test (0.05/3) to adjust the *P* value threshold that we would declare a result significant. We declared the results from each test significant only if $P < 0.017$. In the tables, *P* values are unadjusted for multiple comparisons.

RESULTS

Table 1 includes characteristics of all subjects who were linked to the UCR from 1984 to 2007, and the numbers of incident cancers and deaths. There were 148 total deaths in subjects with incident cancer. The percent of recorded deaths outside Utah was the same for both groups (surgical patients, 11.3%; controls, 11.5%).

During the total follow-up over a 24-year period, there were 254 (3.1/1,000 person years) and 477 (4.3/1,000 person years) incident cancers in the gastric bypass and population control groups, respectively, (Table 1). Incident cancers by site are detailed in Table 2. As shown in Table 2, incidence of cancer was 24% lower in the gastric bypass group compared with severely obese controls (hazard ratio (HR), 0.76; 95% CI, 0.65–0.89; $P = 0.0006$). The decreased incidence was only apparent in women (HR, 0.73; 95% CI, 0.62–0.87; $P = 0.0004$), whereas no difference was seen in men (HR, 1.02; 95% CI, 0.69–1.52; $P = 0.91$). There was a significant decrease in uterine cancer incidence for gastric bypass surgery subjects compared to controls (HR, 0.22; 95% CI, 0.13–0.40; $P < 0.0001$). Cancers likely to be obesity-related showed a 38% reduction in incidence (HR, 0.62; 95% CI, 0.49–0.78; $P < 0.0001$). No significant reduction was observed in incident cancer for nonobesity-related cancers. Total cancer incidence was reduced by 27% (HR, 0.73; 95% CI, 0.63–0.86; $P = 0.0002$) adjusting for uncorrected, self-reported BMI instead of the 24% reduction when adjusting for corrected BMI of the controls. Neither self-reported BMI nor adjusted BMI were significant covariates in the incidence models. Finally, to prevent one incident cancer, ~71 gastric bypass surgeries would be required.

To identify which stages of cancer may be responsible for the overall reduced cancer incidence, HRs by stage are reported in Table 3. Regional cancers were significantly reduced in gastric bypass patients compared to control subjects. The HR for distant cancers was also reduced similar to the regional cancers. However, if one uses $P < 0.01$ as the significance level to account for the five multiple comparison tests in this table, the distant cancers were no longer significant. Finally, as shown in Table 3, there was no significant difference in incidence between groups for *in situ* or localized cancers. The mean time from baseline to diagnosis was not significantly different between the two groups for any stage (Table 3). There were no significant differences in case-fatality cancer rates for any individual cancer stage (results not shown), but the total number of site-specific cancer deaths in the case-fatality analyses was not large. For all stages combined, adjusting for stages, case-fatality was also not significant (Table 4).

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The overall cancer mortality was reduced by 46% in the postgastric bypass surgical patients when compared to the nonoperated controls (HR, 0.54; 95% CI, 0.37–0.78; $P = 0.001$; Table 5). Grouping cancers likely to be obesity-related together, the gastric bypass patients had a 46% reduction in cancer mortality (HR, 0.54; 95% CI, 0.32–0.90; $P = 0.02$). Mortality for nonobesity-related cancers was also significantly lower among the surgical group when compared to controls (HR, 0.53; 95% CI, 0.31–0.91; $P = 0.02$). Finally, mortality comparisons between gastric bypass surgery patients and driver's license controls by gender (Table 5) showed a significant reduction for female patients compared to female controls (HR, 0.38; 95% CI, 0.23–0.64; $P = 0.0003$), but not for males (HR, 0.70; 95% CI, 0.34–1.48; $P = 0.35$). HRs for mortality according to cancer site are detailed in Supplementary Table S1 online.

In the gastric bypass patients, cancer mortality was 0.50 deaths/1,000 person-years compared to 0.94 deaths/1,000 person-years in the severely obese controls (Table 1). These estimates predict that after 12.5 years of mean follow-up in 6,596 surgical patients, 37 cancer deaths were prevented. These numbers translate to 5.6 cancer deaths prevented per 1,000 gastric bypass surgical patients or for approximately every 179 gastric bypass surgeries performed one cancer death was prevented.

DISCUSSION

The surprising lower total cancer mortality result previously reported for gastric bypass surgery (18) served as motivation for the subsequent incidence and site-specific cancer mortality analyses contained in this paper. By linking the study subjects to more recent data in the UCR, we extended cancer mortality follow-up five additional years compared with the previous study. Total reduction in cancer mortality after mean follow-up of 12.5 years was 46% in the gastric bypass subjects compared to severely obese controls. The reduction in cancer mortality appeared to be due to a reduced cancer incidence and not cancer survival. In addition, although cancer incidence between the two groups appeared similar for *in situ* and local staged cancers, incidence rates of regional and distant staged cancers were lower for the surgical group compared to the control group. Further, the reduction in incidence appeared to be greatest for cancers likely associated with obesity, whereas the mortality reduction was equally great for obesity-related cancers and cancers with less evidence for an association with obesity. These findings suggest that the weight loss associated with gastric bypass surgery may reduce the development of new cancers likely related to obesity. Although cancers were not diagnosed earlier in time for the surgical group, we suspect that cancers were diagnosed earlier in stage. Therefore, we surmise the regional and distant cancers that would have resulted without the surgery were detected in the *in situ* and local stages and that *in situ* and local stage cancers that would have occurred without surgery were prevented or delayed beyond the end of the follow-up period. The lack of significant reduction in cancer mortality seen in men may have been due to the low number of male subjects. Generally, <20% of gastric bypass patients are men (20).

Convincing evidence from large prospective observational studies has shown significant association of obesity with risk for several cancers (7,8,13,21,22). Because choosing cancers related to obesity varies as more literature is reported, this report attempted to include cancers where sufficient evidence exists for these cancers to be at least "likely" related to obesity. Evidence for biological mechanisms relating increased cancer risk with obesity has primarily focused on chronic inflammation, increased release of steroid hormones, and promotion of tumor growth stimulated by hyperinsulinemia in the face of insulin resistance (8,11). Because few individuals maintain voluntary weight loss without surgical intervention (11,14,23), analyzing cancer outcomes in large population groups maintaining long-term weight loss has been limited (9–12,14,17,18,24–26). Our group reported a significant 60%

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reduction in cancer mortality when comparing postgastric bypass patients to severely obese controls (18). With five additional follow-up years that more than doubled cancer deaths compared to the previous study, there was a 46% reduction in cancer mortality. This smaller risk reduction may relate to some degree of weight regain after surgery, or perhaps due to better mortality estimates resulting from the larger number of cancer deaths. Trentham-Dietz *et al*. reported 30% reduction in risk for endometrial cancer for women who reported sustained weight loss (12).

Several possibilities may have contributed to the 24% reduction in incident cancers and the 46% reduction in cancer mortality in the surgery group compared with controls. The severely obese controls had only self-reported height and weight from their driver's licenses. Although each control had a reported BMI >35 kg/m^2, high BMI is known to be under-reported. Therefore, regression equations were derived from a subset of study subjects who had both measured and self-reported BMI, as has been previously discussed (18). This report shows that using either reported or a regression-corrected BMI in the controls as a covariate had very little effect on the relative risk estimates for cancer mortality. In addition, BMI was not a significant covariate in the incidence or mortality proportional hazards model, suggesting that the findings are robust to this possible source of error.

Possible unknown health status differences between groups at study entry could also have affected the results. Because patients previously diagnosed with major cancer (within 5 years) are generally denied gastric bypass surgery, this restriction could result in a healthier surgical group at study entry. However, there were no differences in cancer prevalence between groups at study entry, suggesting that if there were underlying differences in risk factors for cancer, they were not manifest by increasing baseline cancer prevalence. The possibility exists that gastric bypass patients may have sought surgery because they were experiencing greater obesity-related illness or decreased quality of life compared to controls. On the other hand, prior to seeking gastric bypass surgery, the patients may have been healthier than controls due to socioeconomic or educational reasons, with subsequent increased access to health care. In terms of selection bias, however, the severely obese controls, randomly selected from the entire Utah population, were not contacted for study inclusion, eliminating self-selection for participation. Likewise, the surgical patients included all consecutive patients undergoing surgery over an 18-year period. Without detailed baseline data, one must rely on the observations that baseline age and a history of cancer are two of the strongest risk factors for cancer mortality. Because patients and controls were similar in age and all prevalent cancers at baseline were removed, additional underlying biases related to risk factors for cancer development should be minimized. For example, if smoking rates were different in the two groups, an increased prevalence of cancer would be expected at baseline, but was not seen. Utah has one of the lowest smoking rates in the United States, further minimizing the likelihood that smoking played an important role in the reported results. In addition, results from a prospective study of the health of similarly recruited Utah gastric bypass patients and severely obese controls in which several clinical variables were measured, demonstrated no differences in baseline blood pressure, lipids, glucose, smoking, weight, or sleep apnea assessment (data not shown). On the other hand, quality of life measures were significantly greater among the control group when compared to the surgical group prior to their gastric bypass procedure. These data, when applied to the current study, suggest equal or slightly better health in the controls than the patients at baseline, increasing confidence that the reported results are unbiased or perhaps even conservative.

At study entry and the years following study entry, additional group dynamics may have contributed to the cancer-related outcomes. Surgical patients may have been more likely to participate in preventive cancer screening or have increased medical surveillance than the

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control subjects. In addition to increased screening participation, a reduction in body weight and body fatness may have led to earlier self-detection of cancer by the postsurgery patients and/or improved screening accuracy. Heavier women have been shown less likely to undergo mammography screening (27), and cancers self-detected by women with a high BMI are more likely to be at an advanced stage (11,28). We note that cancer diagnosis and treatment were not performed at the bariatric surgeon's clinic. Rather, cancer diagnosis and subsequent treatment for both study groups would have been conducted using general Utah cancer resources, independent of surgical status. Within the limitations of our retrospective cohort design, there was no significant difference in incidence of early stage cancers (*in situ* and local) between the two study groups and no difference in time to first diagnosis of cancer comparing surgical and control groups at any stage. Furthermore, case-fatality after controlling for stage at diagnosis was not different in the two groups, suggesting little evidence of differential treatment of cancer. These findings suggest that new cancers, regardless of stage, were not likely to be diagnosed earlier in surgical patients than controls, implying that the potential for greater surveillance, improved detection, or earlier and more effective treatment were not likely major contributors toward reduced cancer mortality and incidence rates. Despite the very large sample sizes used in this study, giving good representation of the Utah severely obese population who do or do not choose surgery, the possibility remains that subtle differences between the two groups at baseline or during follow-up contributed to the significant results. To investigate whether the reduction in incident cancers or cancer deaths after gastric bypass surgery differed over the follow-up interval, the sample was split by median follow-up and reanalyzed. The results suggested similar protection in both subgroups, suggesting that gastric bypass surgery protects against cancer onset and death near- and long-term.

Further limitations to this study include the absence of follow-up BMI, preventing analysis of long-term weight loss to cancer incidence, lack of follow-up medical history, and small numbers of incident cancers and deaths for some cancer sites. We also recognize that information such as family history, smoking history, prior use of postmenopausal hormones, and whether or not postgastric bypass patients adhered to recommended dietary (including vitamin supplementation) and physical activity regimens are not available for analyses. These lifestyle practices may have been factors accounting for the cancer-related differences observed between the surgical and control groups.

In summary, our findings suggest that gastric bypass surgery may result in lower cancer incidence and mortality. We emphasize, however, that bariatric surgery is not an accepted therapy for cancer and in fact, history of an internal malignancy within a 5-year period is often considered a contraindication for obesity surgery. The cancer-related benefits of gastric bypass surgery were strongest in females. Because severe obesity is more prevalent in women than men (20) and 80% of patients who undergo gastric bypass surgery are women, the results of our study have important medical and population implications. Although the benefit of reduced incidence was limited to cancers likely related to obesity, reduction of cancer mortality was seen for both obesity-related and nonobesity-related cancers. We conclude that recent national guidelines recommending weight loss to reduce future cancer risk are supported by results from this study.

Supplementary Material

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Table 1

Characteristics of subjects in the study groups linked to the Utah Cancer Registry

Characteristics	Surgery group	Control group
No. of subjects including prevalent cancer cases	6,709	9,609
No. of subjects not including prevalent cancer cases	6,596	9,442
Male, *N* (%)	942 (14)[a]	1,570 (17)
Female, *N* (%)	5,654 (86)[a]	7,872 (83)
Age, years (s.d.)	38.9 (10.3)	39.1 (10.7)
BMI, kg/m^2 (s.d.)	44.9 (7.6)[a]	47.4 (6.5)[b]
Follow-up		
Mean, years (s.d.) for incidence	12.3 (5.7)	11.8 (5.6)
Person-years for incidence[c]	81,203	111,430
Mean, years (s.d.) for mortality	12.5 (5.7)	12.0 (5.6)
Person-years for mortality[d]	82,611	113,667
All incident cancers, *N*	254	477
Year of incident cancer diagnosis, *N*		
1984–1989	7	14
1990–1994	27	54
1995–1999	54	91
2000–2004	92	173
2005–2007	74	145
Cancer deaths, *N*	41	107
Cancer deaths/1,000 person years[e]	0.50	0.94

[a] $P < 0.001$ for the comparison with the control group.

[b] Corrected BMI. See Methods and Procedures section.

[c] Person-years are from baseline to the end of 2007, unless censored. Observations are censored for first diagnosis of cancer or death, whichever is earlier.

[d] Person-years are from baseline to the end of 2007, unless censored. Observations are censored at time of death.

[e] Crude mortality rate.

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Table 2

Cancer incidence[a] and hazard ratios in the study groups (1984–2002) for common cancer sites, cancers by sex, obesity-related cancers, and nonobesity-related cancers

	Surgery *N* = 6,596		Control *N* = 9,442			
Cancer site[b]	**Number of cases**	**Rates/1,000 person years**	**Number of cases**	**Rates/1,000 person years**	**Hazard ratio[c] (95% CI)**	***P* value**
All cancers	254	3.13	477	4.28	0.76 (0.65–0.89)	0.0006
All cancers, male	39	3.73	65	3.83	1.02 (0.69–1.52)	0.91
All cancers, female	215	3.04	412	4.36	0.73 (0.62–0.87)	0.0004
Obesity-related cancers[d]	104	1.28	253	2.27	0.62 (0.49–0.78)	<0.0001
Nonobesity-related cancers[e]	150	1.85	224	2.01	0.91 (0.73–1.12)	0.37
Oral cavity and pharynx (20010–20100)	3	0.04	9	0.08	0.46 (0.12–1.75)	0.25
Esophagus (21010)	3	0.04	4	0.04	0.98 (0.21–4.66)	0.98
Stomach (21020)	2	0.02	2	0.02	1.70 (0.24–12.2)	0.59
Small intestine (21030)	1	0.01	4	0.04	0.38 (0.04–3.47)	0.39
Colorectal (21041–51052)	25	0.31	52	0.47	0.70 (0.43–1.15)	0.15
Liver (21071)	1	0.01	1	0.01	1.69 (0.10–27.80)	0.71
Gallbladder (21080)	0	0	2	0.02	—	—
Pancreas (21100)	9	0.11	8	0.07	1.75 (0.66–4.63)	0.26
Other digestive (21130)	0	0	1	0.01	—	—
Larynx (22020)	1	0.01	2	0.02	0.81 (0.07–9.03)	0.87
Lung and bronchus (22030)	5	0.06	11	0.10	0.71 (0.25–2.08)	0.53
Other respiratory (22010, 22020, 22050)	1	0.01	3	0.03	0.51 (0.05–4.97)	0.56
Trachea (22060)	0	0	2	0.02	—	—
Soft tissue including heart (24000)	4	0.05	4	0.04	1.13 (0.26–5.00)	0.87
Melanoma of skin (25010)	17	0.21	29	0.26	0.71 (0.38–1.34)	0.30
Other nonepithelial skin (25020)	4	0.05	2	0.02	2.37 (0.40–14.0)	0.34
Breast (26000)	73	0.90	107	0.96	0.91 (0.67–1.24)	0.54
Premenopausal female breast	49	0.60	65	0.58	0.93 (0.63–1.37)	0.69
Postmenopausal female breast	24	0.30	40	0.36	0.96 (0.57–1.63)	0.89
Cervix uteri (27010)	9	0.11	14	0.13	0.88 (0.37–2.08)	0.78
Corpus and uterus NOS (27020–27030)	14	0.17	98	0.88	0.22 (0.13–0.40)	<0.0001

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	Surgery *N* = 6,596		Control *N* = 9,442			
Cancer site[b]	**Number of cases**	**Rates/1,000 person years**	**Number of cases**	**Rates/1,000 person years**	**Hazard ratio[c] (95% CI)**	***P* value**
Ovary (27040)	7	0.09	19	0.17	0.19 (0.23–1.34)	0.19
Vulva (27060)	9	0.11	2	0.02	6.15 (1.30–29.2)	0.02
Prostate (28010)	17	0.21	17	0.15	1.71 (0.87–3.36)	0.12
Urinary bladder (29010)	4	0.05	3	0.03	1.98 (0.43–9.06)	0.38
Kidney and renal pelvis (29020)	11	0.14	13	0.12	1.22 (0.54–2.78)	0.63
Brain and CNS (31010–31040)	6	0.07	10	0.09	0.69 (0.24–2.02)	0.50
Thyroid (32010)	10	0.12	20	0.18	0.64 (0.29–1.41)	0.27
Hodgkin’s lymphoma (33011–33012)	1	0.01	2	0.02	0.73 (0.06–8.78)	0.80
Non-Hodgkin’s lymphoma (33041–33042)	7	0.09	17	0.15	0.54 (0.22–1.37)	0.20
Myeloma (34000)	2	0.02	4	0.04	0.46 (0.06–3.28)	0.44
Leukemia (35011–35043)	4	0.05	7	0.06	0.37 (0.08–1.64)	0.19
Other	4	0.05	8	0.07	—	—

CI, 95% confidence interval; CNS, central nervous system; NOS, not otherwise specified.

[a] Incidence is defined as cancers diagnosed after gastric bypass surgery for the surgical group and following application for driver’s license or identification card for the severely obese controls.

[b] The SEER (Surveillance Epidemiology and End Results) site-specific coding is included within the parentheses. Menopause assumed to occur at age 50 for breast cancer analysis.

[c] Analyses are adjusted for sex, age, and BMI. For gender-specific sites, analyses are adjusted for age and BMI.

[d] Obesity-related cancers included esophageal adenocarcinomas, colorectal, pancreas, postmenopausal breast, corpus and uterus, kidney, non-Hodgkin lymphoma, leukemia, multiple myeloma, liver and gallbaldder.

[e] All cancers that are not included as obesity-related cancers.

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Table 3

Hazard ratios for incident cancer and mean time to diagnosis by cancer stage

	Incident cancers				Mean time to cancer diagnosis, years ± s.d.	
Cancer stage	**Surgery *N***	**Control *N***	**Hazard ratio[a] (95% CI)**	***P* value[*]**	**Surgery**	**Control**
0 (*In situ*)	44	73	0.86 (0.59–1.26)	0.44	9.2 ± 6.5	9.1 ± 5.2
1 (Local)	128	219	0.86 (0.69–1.07)	0.17	8.4 ± 5.2	9.0 ± 5.5
2–5 (Regional)	49	98	0.61 (0.43–0.89)	0.009	9.3 ± 5.2	8.9 ± 5.3
7 (Distant)	28	68	0.61 (0.39–0.96)	0.03	9.5 ± 6.3	9.0 ± 5.6
9 (Unstaged)	5	19	0.40 (0.15–1.09)	0.07	6.2 ± 7.3	8.9 ± 5.1

CI, 95% confidence interval.

[a] Analyses are adjusted for age, sex, BMI.

[*] *P* values are unadjusted for multiple comparisons.

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Table 4

Case-fatality number and hazard ratio for incident cancer cases by obesity- and nonobesity-related cancers and combined obesity- and nonobesity cancers

	Adjusted for cancer stage		
Case-fatality	**Obesity-related, *N***	**Nonobesity related, *N***	**Combined obesity and nonobesity, *N***
Surgery deaths after cancer, *N*	20	21	41
Control deaths after cancer, *N*	55	52	107
HR (95% CI)[a]	1.04 (0.56–1.93)	0.80 (0.47–1.37)	0.80 (0.55–1.16)
P[*]	0.89	0.42	0.24

CI, 95% confidence interval; HR, hazard ratio.

[a] Surgery group relative to the severely obese control group after diagnosis of cancer and adjusted for sex, age, and BMI.

[*] *P* values are unadjusted for multiple comparisons.

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Table 5

Hazard ratios for mortality according to cancer groups

	Deaths		Hazard ratios for cancer deaths[a]	
	Surgery group *N* = 6,596	Control group *N* = 9,442	Surgery vs. control groups	
Cancer site	***N* (rates/1,000 person years)**	***N* (rates/1,000 person years)**	**Hazard ratio (95% CI)**	***P* value***
All cancers: males and females combined	41 (0.50)	107 (0.94)	0.54 (0.37–0.78)	0.001
All cancers: males only	10 (0.12)	24 (0.21)	0.70 (0.34–1.48)	0.35
All cancers: females only	31 (0.38)	83 (0.73)	0.38 (0.23–0.64)	0.0003
Obesity-related cancers[b]	20 (0.24)	55 (0.48)	0.54 (0.32–0.90)	0.02
Nonobesity-related cancers[c]	21 (0.25)	52 (0.46)	0.53 (0.31–0.91)	0.02

CI, 95% confidence interval.

[a] Hazard ratios adjusted for age, sex and BMI. Prevalent cancers at baseline were excluded.

[b] Obesity-related cancers included esophageal adenocarcinomas, colorectal, pancreas, postmenopausal breast, corpus and uterus, kidney, non-Hodgkin lymphoma, leukemia, multiple myeloma, liver, and gallbaldder.

[c] All cancers that are not included as obesity-related cancers.

* *P* values are unadjusted for multiple comparisons.