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Bariatric surgery and liver cancer in a consortium of academic medical centers

Baiyu Yang, PhD,

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-9774

Hannah P. Yang, PhD, ScM,

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-9774

Kristy K. Ward, MD, MAS,

Division of Gynecologic Oncology, University of Florida College of Medicine-Jacksonville, Jacksonville, FL, 32209

Vikrant V. Sahasrabudde, MBBS, DrPH, and

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-9774; Division of Cancer Prevention, National Cancer Institute, Bethesda, MD, 20892-9783

Katherine A. McGlynn, PhD, MPH

Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-9774

Baiyu Yang: baiyu.yang@nih.gov; Hannah P. Yang: yanghan@mail.nih.gov; Kristy K. Ward: kristy.kay.ward@gmail.com; Vikrant V. Sahasrabudde: vikrant.sahasrabudde@nih.gov; Katherine A. McGlynn: mcglynnk@mail.nih.gov

Abstract

Obesity is implicated as an important factor in the rising incidence of liver cancer in the United States. Bariatric surgery is increasingly used for treating morbid obesity and comorbidities. Using administrative data from UHC, a consortium of academic medical centers in the US, we compared the prevalence of liver cancer among admissions with and without a history of bariatric surgery within a 3-year period. Admissions with a history of bariatric surgery had a 61% lower prevalence of liver cancer compared to those without a history of bariatric surgery (prevalence ratio 0.39, 95% confidence interval 0.35 – 0.44), and these inverse associations persisted within strata of sex, race, and ethnicity. This hospital administrative records-based analysis suggests that bariatric surgery could play a role in liver cancer prevention.

Correspondence to: Baiyu Yang, PhD, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, 20892-9774 ; baiyu.yang@nih.gov.

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval: For this type of study formal consent is not required.

Informed Consent: Does not apply.

Keywords

bariatric surgery; liver cancer; administrative records; obesity; diabetes

INTRODUCTION

Liver cancer is the sixth most commonly occurring cancer in the world and the second leading cause of cancer death (1). Although relatively rare, the incidence of liver cancer has been rising rapidly in the United States since 1980 (2). Most common risk factors for liver cancer in high-rate areas (such as Asia and Africa) are hepatitis B virus (HBV) infection and exposure to aflatoxin, whereas common risk factors in low-rate areas (such as North America) include excessive alcohol consumption, hepatitis C virus (HCV) infection, obesity, diabetes, and nonalcoholic fatty liver disease (NAFLD) (3). In particular, obesity and diabetes are becoming increasingly important risk factors in the Western countries due to their high prevalence (3).

Bariatric surgery is increasingly used for treating morbid obesity and its comorbidities. It results in long-term weight loss and amelioration of metabolic disorders such as diabetes (4), and may also improve or completely resolve liver steatosis, steatohepatitis, and fibrosis (5). Thus, bariatric surgery may play a role in the prevention of liver cancer, particularly for morbidly obese individuals. Although several cohort studies have reported that bariatric surgery is associated with lower total cancer incidence and/or mortality (6), literature on its association with liver cancer is scarce (7). Herein, we report the association between bariatric surgery and the prevalence of liver cancer among admissions in academic medical centers in the United States.

MATERIALS AND METHODS

This analysis was based on administrative data from UHC's Clinical Data Base/Resource Manager (CDB/RM). UHC is an alliance of more than 110 academic medical centers and over 338 of their affiliated hospitals across the United States (8). As described previously, the UHC database contains discharge information on inpatient hospital stay such as patient characteristics, length of stay, 30-day readmission, postoperative morbidity, in-hospital mortality, and costs of inpatient care (9). Discharge summary data are collected from affiliated institutions and compiled into a secure, interactive, web-based database. Each hospital admission is considered a discrete event in the database, and patients are not followed longitudinally by design.

We evaluated records of inpatient admissions of patients from 18 to 99 years old included in the UHC dataset from October 2011 to April 2015. History of bariatric surgery was identified via International Classification of Diseases Ninth Revision [ICD-9] codes: 539.xx [complications of bariatric procedures], 649.2x [bariatric surgery status complicating pregnancy, childbirth, or the puerperium], or V45.86 [bariatric surgery status]. The outcome of interest for all analyses was the presence of liver cancer (ICD-9 155.0 [malignant neoplasm of liver primary] and 155.1 [malignant neoplasm of intrahepatic bile ducts]).

We calculated the prevalence of liver cancer per 100,000 hospital admissions among patients with and without a history of bariatric surgery, and calculated prevalence ratios (PRs) and 95% confidence intervals (CIs). We also conducted stratified analyses by sex, race, and ethnicity. PRs and 95% CIs were calculated using SAS software version 9.3 (SAS Institute, Cary, NC). All analyses were run in August 2015, but we did not include admission records after April 2015, to account for any delay in data reporting and to allow the more recent records to be completely cleaned.

RESULTS

During the study period, there were a total of 15,762,257 hospital admissions of which 74,738 (0.47%) recorded a diagnosis of liver cancer, and 178,192 (1.13%) recorded a history of bariatric surgery. As shown in Table 1, admissions with liver cancer were older and more likely to be male and Asian than were admissions without liver cancer. The mean age of admissions with liver cancer was 62.1 years compared to the mean age of admissions without liver cancer, which was 54.9 years.

As shown in Table 2, admissions with a history of bariatric surgery had a 61% lower prevalence of liver cancer compared to those without a history of bariatric surgery (PR=0.39, 95% CI=0.35 – 0.44). The inverse association persisted within strata of sex, race, and ethnicity.

DISCUSSION

In the current study, we observed an inverse association between a history of bariatric surgery and liver cancer, overall or within strata of sex, race, and ethnicity, based on hospital admissions data from a consortium of academic medical centers in the United States. This is the first study, to our knowledge, to report an inverse association of bariatric surgery with liver cancer.

Previous studies have investigated bariatric surgery in relation to overall cancer incidence/mortality, as well as some specific types of cancer. A recent meta-analysis of six observational studies reported a statistically significant 45% lower risk of total cancer incidence associated with bariatric surgery among obese individuals (6), and this benefit was most pronounced for obesity-related cancers (7). One cohort study examined liver cancer specifically, but the number of liver cancer cases was too small (N = 2) to allow meaningful interpretation of the results (7).

Our findings suggest a potential role of bariatric surgery in liver cancer prevention. There are several mechanisms by which bariatric surgery might reduce the risk of liver cancer. Obesity and diabetes are important risk factors for liver cancer (3). Bariatric surgery induces effective weight loss (4), and subsequently interrupt several obesity-associated carcinogenic pathways involving changes in sex steroids, oxidative stress, inflammation, and cellular energetics (10). Bariatric surgery may also improve or resolve diabetes and its related metabolic conditions (4); these effects may be partially mediated through the endocrine changes due to surgical modulation of the gastrointestinal tract, independent of weight loss and restricted caloric intake (11). Favorable regulation of body weight and/or metabolic

profiles by bariatric surgery may have implications in various cancer types, including liver, as these changes may subsequently improve several liver diseases including lobular steatosis, steatohepatitis, and fibrosis, and eventually lead to complete resolution of NAFLD and its most severe form, nonalcoholic steatohepatitis (NASH) (5). As NAFLD and NASH are present in a large proportion of morbidly obese patients and they may progress to liver cancer (12), it is biologically plausible that bariatric surgery could benefit morbidly obese individuals in the prevention of liver cancer.

The association between bariatric surgery and liver cancer risk appears to be modified by race, with the PR being substantially lower among blacks than whites. One possible explanation is confounding by socioeconomic status. Among eligible individuals, the likelihood of receiving bariatric surgery is related to socioeconomic variables such as income and insurance (13). Those who could afford the surgery may have better access to health care, and subsequently, lower likelihood of developing cancer. Not receiving the surgery may be more frequently due to socioeconomic disadvantages among blacks than whites, thus resulting in stronger inverse associations in blacks. Chance is also a possible explanation as the sample size was small for blacks with a history of both bariatric surgery and liver cancer (N = 19).

The strengths of this study include its large sample size and the geographical diversity of this nationally representative database. However, our results should be interpreted with caution due to several limitations, some of which are inherent in studies using administrative databases. By design, individual patients were not followed longitudinally, and both bariatric surgery history and liver cancer diagnosis were assessed at the time of hospital admission, with no detailed information on dates of surgery and cancer diagnosis. Consequently, we were unable to establish the temporality between bariatric surgery and liver cancer, although it is highly unlikely that bariatric surgery was performed after the diagnosis of liver cancer, considering most cases of liver cancer are detected late when prognosis is very poor (3). Due to the absence of individual-level data, we were unable to identify and exclude multiple admissions of the same patient during the 3-year study period, and the direction of bias due to multiple admissions is not clear. Also, we were unable to calculate the prevalence ratio with adjustment of potential confounders. For example, it is possible that several potential contraindications against bariatric surgery, such as alcohol dependency and cirrhosis with portal hypertension (14), may confound the association between bariatric surgery and liver cancer, as these factors may predispose individuals to higher liver cancer risk. However, information was not available on these variables.

Given the limitations of our administrative records-based study, the association of bariatric surgery with cancer outcomes should be better addressed using another study design, such as a prospective follow-up study. To our knowledge, the Swedish Obese Subjects cohort is the only prospective, controlled intervention study to assess the effect of bariatric surgery on health outcomes, although it was not possible to randomize the exposure; however, it was not sufficiently powered to evaluate specific types of cancer (15). Larger prospective studies are needed to compare specific cancer outcomes among morbidly obese patients who have undergone bariatric surgery vs. those receiving conventional treatment, with proper adjustment of potential confounders.

In conclusion, our study reports that a history of bariatric surgery may be associated with lower prevalence of liver cancer among admissions in academic medical centers. Although these findings should be interpreted cautiously with the aforementioned limitations, this study provides important data for future investigations of bariatric surgery in relation to liver cancer in epidemiological studies with individual level data.

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Table 1

Demographic characteristics among hospital admissions with and without diagnosis of liver cancer (UHC database, October 2011 to April 2015)

	<u>Diagnosis of liver cancer (N =74,738)</u>		<u>No diagnosis of liver cancer (N = 15,687,519)</u>	
	N	%	N	%
Sex				
Male	52,560	70.3	6,942,258	44.3
Female	22,177	29.7	8,745,012	55.7
Unknown	1	0	249	0
Race				
White	45,004	60.2	10,146,471	64.7
Black	12,477	16.7	3,215,703	20.5
Asian	5,466	7.3	358,361	2.3
Other	9,897	13.2	1,579,866	10.1
Missing ^a	1,894	2.5	387,118	2.5
Ethnicity				
Hispanic	7,320	9.8	1,169,017	7.5
Non-Hispanic	35,158	47.0	8,158,088	52.0
Missing ^b	32,260	43.2	6,360,414	40.5
Age				
18–29	795	1.1	2,098,904	13.4
30–39	1,387	1.9	2,006,136	12.8
40–49	4,930	6.6	1,912,755	12.2
50–59	23,134	31.0	2,802,229	17.9
60–69	27,199	36.4	2,832,477	18.1
70–79	12,667	16.9	2,138,423	13.6
80+	4,626	6.2	1,896,595	12.1

^aRace unknown, unavailable, or declined.

^bHispanic origin unknown, not reported, unavailable, or declined.

Table 2

Associations between hospital admissions for bariatric surgery and liver cancer diagnosis, overall and stratified by sex, race, and ethnicity (UHC database, October 2011 to April 2015)

	History of bariatric surgery	Diagnosis of liver cancer (N)	No diagnosis of liver cancer (N)	Total	Prevalence of liver cancer per 100,000 admissions	PR (95% CI)
All	No	74,402	15,509,663	15,584,065	477.42	1.0 (ref)
	Yes	336	177,856	178,192	188.56	0.39 (0.35–0.44)
Sex						
Male	No	52,430	6,905,471	6,957,901	753.53	1.0 (ref)
	Yes	130	36,787	36,917	352.14	0.47 (0.39–0.55)
Female	No	21,971	8,603,944	8,625,915	254.71	1.0 (ref)
	Yes	206	141,068	141,274	145.82	0.57 (0.50–0.66)
Race						
White	No	44,714	10,018,249	10,062,963	444.34	1.0 (ref)
	Yes	290	128,222	128,512	225.66	0.51 (0.45–0.57)
Black	No	12,458	3,182,359	3,194,817	389.94	1.0 (ref)
	Yes	19	33,344	33,363	56.95	0.15 (0.09–0.23)
Ethnicity						
Hispanic	No	7,306	1,160,231	1,167,537	625.76	1.0 (ref)
	Yes	14	8,786	8,800	159.09	0.25 (0.15–0.43)
Not Hispanic	No	34,968	8,059,478	8,094,446	432.00	1.0 (ref)
	Yes	190	98,610	98,800	192.31	0.45 (0.39–0.51)

Abbreviations: CI, confidence interval; PR, prevalence ratio.