

# Impact of Bariatric Surgery on the Incidence of Various Cancers. Narrative Review

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## Abstract

Obesity is a global epidemic. According to the World Health Organization (WHO), it is an abnormal or excessive accumulation of fat that can harm health. Its incidence is increasing alarmingly in developing countries. It is also a significant risk factor for developing chronic diseases such as type 2 diabetes *mellitus*, arterial hypertension, coronary disease, non-alcoholic fatty liver disease, and musculoskeletal disorders such as osteoarthritis. Furthermore, associations have been found between obesity and the development of prostate, liver, gallbladder, kidney, colon, endometrial, breast, and ovarian cancer. Bariatric and metabolic surgery is the most effective treatment for morbid obesity and its comorbidities. This surgery can reduce general mortality by 40% at ten years due to cardiovascular outcomes, diabetes, or cancer and improve metabolic diseases such as type 2 diabetes.

## Keywords

Obesity, cancer, bariatric surgery, metabolic surgery.

## INTRODUCTION

Obesity is a global epidemic representing the second cause of death in the United States<sup>(1)</sup>. It is defined by the World Health Organization (WHO) as an abnormal or excessive accumulation of fat that can be harmful to health, with a body mass index (BMI) greater than or equal to 30<sup>(1)</sup>. When the BMI is  $\geq 25$  and  $< 29.9$ , it indicates overweight<sup>(1)</sup>. Until recently, obesity was considered only a real problem in developed countries; however, its incidence also increases alarmingly in developing countries<sup>(2)</sup>. It is among the main factors that contribute worldwide to the general burden of morbidity due to its association with chronic diseases such as type 2 diabetes mellitus (T2DM), high blood pressure,

coronary heart disease, fatty liver, cirrhosis, musculoskeletal disorders such as osteoarthritis, and the development of various cancers, such as prostate, liver, gallbladder, kidney, colon, endometrium, breast, and ovarian cancer<sup>(2,3)</sup>. It has recently been found that childhood obesity increases the risk of cancers in adulthood<sup>(4)</sup>. It has also been documented that the fat deposition in the proximity of some cancers provides ideal environments that favor these tumors' growth, progression, and metastasis<sup>(5)</sup>. There is a proportional relationship between BMI and the prevalence and mortality of multiple types of cancer<sup>(6)</sup>.

The treatment of obesity is complex and requires multidisciplinary teams and various strategies that include low-calorie diets, medications (liraglutide, lorcaserin, nal-

trexone, bupropion, orlistat, phentermine/topiramate), endoscopic treatments, and bariatric surgeries<sup>(7)</sup>. In general, diets have low effectiveness in achieving weight loss, with a final success of 4-12 kg at 6 months, 4-10 kg at 1 year, and 3-4 kg at 2 years<sup>(7)</sup>. Adding medications to low-calorie diets can reduce weight by 5% in one year<sup>(8)</sup>. Bariatric surgery is considered the treatment of choice when the BMI is 35, and there is some comorbidity (T2DM, hypertension, dyslipidemia, sleep apnea) or when the BMI is  $\geq 40$  or more, regardless of whether there are comorbidities<sup>(9)</sup>.

Compared to diet, patients undergoing bariatric surgery can lose an average of 25 additional kg, reducing the risk of developing DM2 and other comorbidities and significantly improving quality of life<sup>(10)</sup>. Roux-en-Y gastric bypass (RYGB) and gastric sleeve are the most frequently used and popular procedures<sup>(11)</sup>. The average weight loss at 1 year with RYGB is 31.2%, while with a gastric sleeve, the weight loss is 25.2%<sup>(12)</sup>. The performance of this procedure has increased exponentially in recent decades and is currently one of the most popular and requested surgical procedures in gastroenterology<sup>(13)</sup>. In addition, it can reduce general mortality by 40% at ten years due to cardiovascular diseases, diabetes, or cancer and improve or “cure” diseases such as DM, hypertension, dyslipidemia, and sleep apnea<sup>(14)</sup>. Due to these effects, it has been considered a “metabolic surgery”<sup>(15)</sup>. Assessing the impact of bariatric surgery on obesity and its complications, we decided to conduct this study, focusing on its benefits on diverse types of cancer.

## MATERIALS AND METHODS

A literature search was conducted in the PubMed database using the following strategy: ((((((((((“Obesity”[Mesh])) OR (“Obesity/etiology”[Mesh] OR “Obesity/metabolism”[Mesh] OR “Obesity/physiopathology”[Mesh] OR “Obesity/statistics and numerical data”[Mesh])) AND “Neoplasms”[Mesh])) OR (“Endometrial Neoplasms/classification”[Mesh] OR “Endometrial Neoplasms/etiology”[Mesh] OR “Endometrial Neoplasms/physiopathology”[Mesh] OR “Endometrial Neoplasms/statistics and numerical data”[Mesh])) OR (“Breast Neoplasms/classification”[Mesh] OR “Breast Neoplasms/etiology”[Mesh] OR “Breast Neoplasms/physiopathology”[Mesh] OR “Breast Neoplasms/statistics and numerical data”[Mesh])) OR (“Prostatic Neoplasms/etiology”[Mesh] OR “Prostatic Neoplasms/physiopathology”[Mesh] OR “Prostatic Neoplasms/statistics and numerical data”[Mesh])) OR (“Colonic Neoplasms/etiology”[Mesh] OR “Colonic Neoplasms/physiopathology”[Mesh] OR “Colonic Neoplasms/etiology”[Mesh])) OR (“Liver Neoplasms/etiology”[Mesh] OR “Liver Neoplasms/physiopathology”[Mesh] OR

“Liver Neoplasms/statistics and numerical data”[Mesh])) OR (“Ovarian Neoplasms/physiopathology”[Mesh] OR “Ovarian Neoplasms/statistics and numerical data”[Mesh])) OR (“Pancreatic Neoplasms/etiology”[Mesh] OR “Pancreatic Neoplasms/physiopathology”[Mesh] OR “Pancreatic Neoplasms/statistics and numerical data”[Mesh])) OR (“Bariatric Surgery/epidemiology”[Mesh] OR “Bariatric Surgery/etiology”[Mesh] AND “Bariatric Surgery/statistics and numerical data”[Mesh] OR “Bariatric Surgery/therapeutic use”[Mesh])).

With the previous search, 38,266 results were returned. Subsequently, they were filtered by language (English and French), including texts from the last 10 years, full texts, and studies on humans, and by type of document (multicenter studies, clinical trials, meta-analyses, systematic reviews, literature reviews, and controlled randomized studies), which reduced the number to 3,132. The title and abstract were reviewed, and according to the authors’ criteria, those relevant to the topic of interest were selected. Articles with incomplete information or unrelated to the review’s objective were excluded.

This information was used to describe the epidemiology and etiology of the types of cancer and their relationship with obesity and, based on the clinical trials, meta-analyses, and systematic reviews found, the impact that bariatric surgery could have on the obese population concerning the incidence of various types of cancer, such as endometrial, breast, prostate, kidney, ovarian, liver, pancreatic, and colorectal.

## RESULTS

### Endometrial cancer and obesity

Endometrial cancer in the United States is the most common malignancy in gynecology<sup>(16)</sup>. Most women diagnosed with this type of cancer are in the early stages of the disease and have a good prognosis, with 5-year survival of up to 90%<sup>(16,17)</sup>. It was the first cancer to be associated with obesity<sup>(18)</sup>. In initial studies, a BMI between 30 and 35 kg/m<sup>2</sup> versus <25 kg/m<sup>2</sup> was associated with a 2.65-fold increased risk of endometrial cancer, and with a BMI >40 kg/m<sup>2</sup> versus <25 kg/m<sup>2</sup>, the risk increased to 4.84<sup>(19)</sup>.

Very few studies link diet to the risk of endometrial cancer. However, Bravi et al. in 2009, in a case-control study with 500 women with endometrial cancer compared to women without this cancer, identified a significant increase in the risk of tumors with the intake of red meat with an odds ratio (OR) of 2.07<sup>(18)</sup>. This same study found inverse associations for other foods such as coffee (OR: 0.83), cereals (OR: 0.92), and vegetables (OR: 0.83)<sup>(20,21)</sup>. Overweight and obese people have comorbidities such as

T2DM and insulin resistance, and there are some studies on the association between these conditions and endometrial cancer. However, the results are inconsistent, and there is controversy between studies<sup>(22-25)</sup>.

In 2020, a cohort analyzed by Tao et al. between 1980 and 2012<sup>(26)</sup> showed a decreased risk of this type of cancer in patients undergoing bariatric surgery compared to women diagnosed with obesity who did not have this surgery (hazard ratio [HR]: 0.69; 95% confidence interval [CI]: 0.56 to 0.84)<sup>(26)</sup>. A study by Zhang<sup>(27)</sup>, which included in the analysis 21 cohorts with a total population of 304,516 obese patients undergoing bariatric surgery, found a decreased risk of cancer (OR: 0.56; 95% CI: 0.46-0.68) and mortality from cancer (OR: 0.56; 95% CI: 0.41-0.75), and concerning endometrial cancer, a risk reduction was found when the patients underwent bariatric surgery (OR: 0.43; 95% CI: 0.26-0.71)<sup>(27)</sup>. Another meta-analysis of three studies with 890,110 patients found a 60% reduction in the risk of endometrial cancer (relative risk [RR]: 0.40; 95% CI: 0.20-0.79)<sup>(28)</sup>.

### Breast cancer and obesity

Breast cancer is a multifactorial entity in which genetic and environmental factors participate<sup>(29)</sup>. Worldwide, it is the most common cancer in women<sup>(30)</sup>. In the United States, it is estimated that 12% of women will have this type of cancer<sup>(31)</sup>. Globally, in developed countries, it is the second cause of death from cancer in women, with a 5-year survival rate of over 80%, thanks to prevention and screening strategies<sup>(32)</sup>. A meta-analysis that evaluated nine cohort and 22 case-control studies on the association between body weight, cancer, and menopause found that the risk of breast cancer is higher in postmenopausal women and that by a five-unit increase in BMI, the risk of this cancer increases 33% in postmenopausal women<sup>(33)</sup>.

A randomized clinical trial with 67,142 participants ages 50 to 79 who were followed for 13 years found that women with obesity grade 1 had a 52% higher risk of developing breast cancer than women with a normal BMI<sup>(34)</sup>. When their BMI was in the obese range, they had an 86% higher risk of breast cancer than those with average weight<sup>(34)</sup>. In the aforementioned European cohort study<sup>(26)</sup>, which included Denmark, Finland, Iceland, Norway, and Sweden, the objective was to study the impact of bariatric surgery on the risk of cancer and found a decreased risk of cancer in the female sex (HR: 0.86; 95% CI: 0.80-0.92), in contrast to the male sex, in which there was no statistically significant difference (HR: 0.98; 95% CI: 0.95-1.01). In the analysis of the 5-year incidence of specific types of cancer in women, a decrease in breast cancer was found (HR: 0.81; 95% CI: 0.69-0.95)<sup>(26)</sup>.

A 2018 meta-analysis<sup>(35)</sup>, which included eight population-based studies, concluded that bariatric surgery was associated with a significant reduction in the overall incidence of cancer (OR: 0.72; 95% CI: 0.59-0.87;  $p = 0.0007$ ) and incidence of cancer associated with obesity (OR: 0.55; 95% CI: 0.31-0.96;  $p = 0.04$ )<sup>(35)</sup>, and also protected against the development of cancer of breast (OR: 0.50; 95% CI: 0.25-0.99;  $p = 0.045$ )<sup>(35)</sup>. Another 2020 study, carried out by Zhang et al. (27), showed a reduction in the risk of breast cancer when obese patients underwent bariatric surgery (OR: 0.49; 95% CI: 0.33-0.72)<sup>(27)</sup>.

### Prostate cancer and obesity

Prostate cancer is one of the leading causes of morbidity and mortality in men and is estimated to cause 360 thousand deaths annually<sup>(36)</sup>. In a retrospective study that included 3,966 men with prostate-specific antigen (PSA) levels between 2.5 and 19.9 ng/mL undergoing prostate biopsy, Masuda et al.<sup>(37)</sup> revealed a significant positive association between BMI >27 and the risk of prostate cancer in men over 60 compared to non-obese controls (OR: 1.44; 95% CI: 1.13-1.84,  $p = 0.0319$ )<sup>(37)</sup>.

A cohort study carried out between 1980 and 2006<sup>(38)</sup>, whose objective was to study whether there was a reduction in the risk of cancer associated with obesity, included 13,123 subjects undergoing bariatric surgery and found a slight decrease in the risk of cancer; still, this difference was not significant ( $p = 0.34$ ) and in individuals with postoperative follow-up of more than ten years, the standardized incidence ratios were 0.71 (95% CI: 0.34-1.31)<sup>(38)</sup>.

### Kidney cancer and obesity

Renal cell carcinoma is the most common form of kidney cancer in men and women in the United States<sup>(39)</sup> and represents 85% of cancers of these organs<sup>(40)</sup>. The main risk factors identified for this tumor are smoking, obesity, and hypertension<sup>(41)</sup>. In one study, the association between obesity and kidney cancer was found with an RR of 1.8<sup>(42)</sup>. In another study, body weight was examined concerning kidney cancer. Obesity was evaluated as BMI, which revealed that the summary RR estimate was 1.07 (95% CI: 1.05-1.09) per unit increase in BMI and demonstrated that an increase in BMI is associated with an increased risk of kidney cancer in both men and women<sup>(43)</sup>. The cohort study in the Nordic countries mentioned previously showed an increased risk of kidney cancer in both sexes (HR:1.44; 95% CI: 1.13-1.84)<sup>(27)</sup>.

A recent retrospective study with 296,041 cases undergoing bariatric surgery and 2,004,804 controls with a mean age of 54 years and a BMI greater than 35 found that the

operated patients had a lower incidence of kidney cancer (OR: 1.10; CI 95 %: 1.02-1.22;  $p < 0.0224$ )<sup>(44)</sup>.

## Ovarian cancer and obesity

Every year, 240,000 women are diagnosed with ovarian cancer, an entity responsible for 150,000 deaths per year. It has become the eighth cause of death from cancer in women<sup>(45,46)</sup>. Incidence rates also vary by ethnicity; evidence was found that figures are 30% higher in non-Hispanic women than in African-American and Asian women and 12% higher than in Hispanic women<sup>(47)</sup>. There is vast epidemiological evidence that associates increased BMI with an increased risk of multiple types of cancer, including ovarian cancer<sup>(48)</sup>. The 5-year survival rate for this type of cancer is below 45%; still, evidence has been found that survival is lower in obese women than in their normal-weight counterparts<sup>(49)</sup>. A cohort study in the United Kingdom revealed that the RR of ovarian cancer due to a 5 kg/m<sup>2</sup> increase in BMI was 1.09 (99% CI 1.04-1.44)<sup>(50)</sup>.

A meta-analysis that included seven studies and 150,537 subjects sought to determine the risk of breast, ovarian, and endometrial cancer in obese women undergoing bariatric surgery and determined that the risk of ovarian cancer was reduced by 53% (RR: 0.47; 95% CI: 0.27-0.81)<sup>(51)</sup>.

## Gastric cancer and obesity

Gastric cancer is the fourth most common cancer worldwide in men after lung, prostate, and colorectal, and the fifth most common in women after breast, colorectal, cervical, and lung in 2011<sup>(52)</sup>. Approximately 8% of total cases and 10% of annual deaths from cancer worldwide are attributed to gastric cancer due to high mortality since most are detected in advanced stages<sup>(52)</sup>. Approximately two-thirds of gastric cancers worldwide come from developing countries, including East Asia, Central and Eastern Europe, and South America, compared to developed nations<sup>(52,53)</sup>. Demographic trends differ depending on tumor location and histology. Although there has been a marked decrease in distal intestinal-type gastric cancers, the incidence of cardia and proximal diffuse-type adenocarcinomas has been increasing, particularly in Western countries<sup>(53)</sup>. Incidence by tumor subsite also varies by geographic location, race, and socioeconomic status. Distal gastric cancer predominates in developing countries, among Black people, and in lower socioeconomic groups. Besides, proximal tumors are more common in developed countries, among White people, and at higher socioeconomic levels<sup>(53)</sup>.

The most important risk factors for proximal and distal cancer are chronic infection with *Helicobacter pylori* and Epstein-Barr virus, high diet intake of salt and nitrates,

smoking, and alcohol. However, according to the divergent trends depending on tumor location, it is suggested that they may represent two diseases with different etiologies. The main risk factors for distal gastric cancer are *H. pylori* infection and dietary factors, while proximal stomach cancer is more influenced by gastroesophageal reflux disease and obesity<sup>(53,54)</sup>. On the contrary, fruits and vegetables are considered protective factors, and some studies have shown that vitamin C reduces the risk<sup>(52-54)</sup>. Cases of gastric cancer have been described after bariatric surgery, and 83% of these have occurred in the stomach, excluding patients undergoing Roux-en-Y gastric bypass<sup>(55)</sup>, which probably reflects the impact of *H. pylori* infection not eradicated in that "hidden" stomach that is not susceptible to being routinely examined with the endoscope<sup>(56)</sup>. There is no evidence to suggest bariatric surgery as a risk factor for gastric cancer<sup>(55)</sup>.

## Liver cancer and obesity

Liver cancer is the fifth most common cancer worldwide, with a survival rate of 10% five years after diagnosis<sup>(57)</sup>. Hepatocellular carcinoma (HCC) accounts for 70% to 85% of liver cancers. It typically develops in the setting of advanced chronic liver disease, primarily related to hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol abuse<sup>(57,58)</sup>, and cirrhosis in general. Approximately 15-50% of HCC cases currently considered idiopathic are related to nonalcoholic fatty liver disease (NAFLD)<sup>(43,59)</sup>, characterized by excessive fat accumulation in the liver defined by steatosis in > 5% of hepatocytes<sup>(59)</sup>. It is estimated that NAFLD causes 13-38.2% of HCC cases in patients with cirrhosis unrelated to viruses or alcohol<sup>(43,59)</sup>. It is currently considered that the risk of HCC in patients with cirrhosis secondary to NAFLD is similar to the risk of cirrhosis of other etiologies<sup>(60)</sup>.

The most critical pathological mechanisms in hepatic steatosis involve increased secretion by visceral adipose tissue of proinflammatory cytokines and adipokines and the release of free fatty acids into the portal system and systemic circulation, causing dyslipidemia and resistance to systemic insulin<sup>(61)</sup>. From the above, it can be explained that NAFLD is strongly associated with metabolic syndrome, and the probability of developing NAFLD increases with the number of risk factors involved (obesity, DM2, hypertension, and dyslipidemia)<sup>(62,63)</sup>.

In several large-scale epidemiological studies, obesity has been described as making an enormous contribution to the overall burden of HCC, either alone or as a cofactor<sup>(64-66)</sup>. A recent meta-analysis (**Table 1**) that included more than seven million participants concluded that the RR of liver cancer was 17% for overweight subjects and 89% for obese subjects, with an average 24% increase in



**Table 1.** Associations between obesity and cancer

Study	Design	Population	Intervention	Control	Results
Bhaskaran et al., 2014 <sup>(49)</sup>	Meta-analysis	5.24 million	Increase of 5 kg/m <sup>2</sup>	Weight maintenance	- The RR of ovarian cancer per increase of 5 kg/m <sup>2</sup> was 1.09 (95% CI: 1.04-1.44).
Sohn et al., 2021 <sup>(67)</sup>	Meta-analysis of 28 cohorts	8,135,906	BMI ≥25 kg/m <sup>2</sup> , ≥30 kg/m <sup>2</sup> , and ≥35 kg/m <sup>2</sup>	BMI <25 kg/m <sup>2</sup>	- HR: 1.61 (95% CI: 1.14-2.27; I <sup>2</sup> = 80%) risk of mortality from primary liver cancer associated with obesity. - Risk of occurrence of primary liver cancer dependent on BMI: HR: 1.36 (95% CI: 1.02-1.81), HR: 1.77 (95% CI: 1.56-2.01), and HR: 3.08 (95% CI: 1.21-7.86) for a BMI >25 kg/m <sup>2</sup> , >30 kg/m <sup>2</sup> , and >35 kg/m <sup>2</sup> .
Matsuo et al., 2011 <sup>(60)</sup>	Meta-analysis of eight cohorts	300,000	BMI ≥25 kg/m <sup>2</sup>	BMI <25 kg/m <sup>2</sup>	- The association between colorectal cancer in individuals with a BMI >25 kg/m <sup>2</sup> was greater in men (3.62%; 95% CI: 1.91-5.30) than in women (2.62%; 95% CI: 0.74-4.47), for individuals with BMI >30 kg/m <sup>2</sup> (HR: 1.50; 95% CI: 1.15-1.96).

Table prepared by the authors.

risk per an increase of 5 kg/m<sup>2</sup> in BMI<sup>(67)</sup>. Another meta-analysis found an increased risk of primary HCC dependent on BMI, in which the HR values were 1.36 (95% CI: 1.02-1.81) for a BMI >25 kg/m<sup>2</sup>, 1.77 (95% CI: 1.56-2.01) for a BMI >30 kg/m<sup>2</sup>, and 3.08 (95% CI: 1.21-7.86) for a BMI >35 kg/m<sup>2</sup><sup>(68)</sup>.

Lastly, obesity is not only an independent risk factor for the development of HCC but also increased mortality regardless of whether the etiology of the tumor is different. A recent systematic review and meta-analysis found a pooled HR of 1.61 (95% CI: 1.14-2.27; inconsistency index [I<sup>2</sup>] = 80%) for mortality related to primary liver cancer<sup>(68)</sup>. Another recent meta-analysis<sup>(69)</sup> also demonstrated that a high BMI increases the incidence and mortality of primary HCC.

A retrospective cohort study evaluating the impact of bariatric surgery in obese patients with NAFLD for cancer development included 98,090 patients between 18 and 64 years old with a recent diagnosis of severe obesity (BMI >40) between 2007 and 2017, of which 33,435 underwent bariatric surgery<sup>(67)</sup>. It was found that this surgery reduced the risk of HCC with an adjusted HR of 0.48 (95% CI: 0.24-0.89)<sup>(70)</sup>.

### Pancreatic cancer and obesity

Pancreatic cancer is the most fatal and fastest-growing cancer with a poor prognosis, with a survival of 7% five years after diagnosis<sup>(71)</sup>. Pancreatic cancer incidence rates increase with age and are higher in men than women. Other risk factors that have been well-established are obesity, smoking, long-term diabetes, and chronic pancreatitis<sup>(72)</sup>. It

has been found that a high BMI is strongly associated with the future risk of pancreatic cancer, and in this association, abdominal obesity causes a higher independent risk<sup>(71,72)</sup>. Parkin et al.<sup>(73)</sup> found that around 12% of all pancreatic cancers could be attributed to a high BMI<sup>(73)</sup>. Other authors found that both overweight and obesity increase the risk of pancreatic cancer<sup>(74)</sup>. Overweight individuals (BMI of 25-29.9) aged between 14 and 39 years have a risk of pancreatic cancer with an OR of 1.67 (95% CI: 1.20-2.34), and obese individuals (BMI ≥ 30) with ages between 20 and 49 years have a higher risk with an OR of 2.58 (95% CI: 1.70-3.90)<sup>(74)</sup>. When obese patients undergo bariatric surgery, the risk of pancreatic cancer is reduced, although without a statistically significant difference (OR: 0.70; 95% CI: 0.24-2.01)<sup>(27)</sup>. However, a retrospective cohort study did find a decreased risk of pancreatic cancer with an HR of 0.46 (95% CI: 0.21-0.93)<sup>(69)</sup>.

### Colorectal cancer and obesity

Every year, 1-2 million patients are diagnosed with colorectal cancer (CRC), making it the third most common cancer in the Western Hemisphere<sup>(75,76)</sup>. Various genetic and environmental risk factors include lifestyle and socioeconomic factors<sup>(77)</sup>. It is the fourth most common cause of cancer globally; in 2015, there were 753,000 deaths from this disease<sup>(78)</sup>. The risk of developing this cancer is two times higher in men than in women<sup>(79)</sup>, and, likewise, it is higher in obese men with a RR of 1.24 (95% CI: 1.20-1.28)<sup>(80)</sup>.

A meta-analysis of eight cohort studies with nearly 300,000 subjects found an association between BMI and

CRC with an RR of 1.03 (95% CI: 1.02-1.04)<sup>(81)</sup>. The association between these two entities for individuals with a BMI >25 kg/m<sup>2</sup> was greater in men (3.62%; 95% CI: 1.91-5.30) than in women (2.62%; 95% CI: 0.74-4.47)<sup>(81)</sup>. Another systematic review and meta-analysis found that weight loss after bariatric surgery was associated with a significantly lower risk of CRC (RR: 0.73; 95% CI: 0.58-0.90; *p* = 0.004)<sup>(82)</sup>. Another meta-analysis did not find a statistically significant risk reduction (OR: 0.82; 95% CI: 0.41-1.64)<sup>(27)</sup>.

## CONCLUSIONS

Overweight and obesity are conditions closely related to several types of cancers. Research in recent decades has shown an increased risk of cancer proportional to BMI. Obesity is a state of chronic inflammation that facilitates the development and progression of various types of cancer and also increases the risk of other entities, such as diabetes, hypertension, and NAFLD, which further worsens the prognosis of cancer patients.

**Table 2.** Associations between bariatric surgery and cancer risk

Study	Design	Population	Intervention	Control	Results
Tao et al., 2020 <sup>(26)</sup>	Cohort Denmark, Finland, Iceland, Norway, and Sweden (follow-up 1980-2012)	483,572	49,096 patients with bariatric surgery, including gastric bypass, gastric band, and vertical banded gastroplasty	433,476 patients over 18 years of age with a diagnosis of obesity in the national patient registry	<ul style="list-style-type: none"> <li>- Decrease in the risk of cancer in females of 0.86 (95% CI: 0.80-0.92)</li> <li>- No decrease in the risk of cancer in men (HR: 0.98; 95% CI: 0.95-1.01)</li> <li>- Decreased risk for breast cancer (HR: 0.81; 95% CI: 0.69-0.95)</li> <li>- Reduced risk of endometrial cancer (HR: 0.69; 95% CI: 0.56-0.84)</li> <li>- Reduced risk of non-Hodgkin lymphoma (HR: 0.64; 95% CI: 0.42-0.97)</li> <li>- Increased risk of kidney cancer in both sexes (HR: 1.44; 95% CI: 1.13-1.84)</li> </ul>
Wiggins, 2018 <sup>(35)</sup>	Meta-analysis	635,642	114,020 patients with bariatric surgery (gastric bypass, gastric sleeve, gastric band, gastroplasty and undetermined)	521,622 obese patients not undergoing surgery	<ul style="list-style-type: none"> <li>- Reduction in the incidence of cancer associated with obesity with RR: 0.72 (95% CI 0.59-0.87; <i>p</i> = 0.0007) - POR: 0.55 (95% CI: 0.31-0.96; <i>p</i> = 0.04)</li> <li>- Protective factor for the development of breast cancer POR: 0.50 (95% CI: 0.25-0.99; <i>p</i> = 0.045)</li> </ul>
Ishihara, 2020 <sup>(50)</sup>	Meta-analysis, observational studies 6/7 retrospective cohorts	1,612,475	150,537 obese women undergoing bariatric surgery	1,461,938 obese women not undergoing bariatric surgery	<ul style="list-style-type: none"> <li>- The risk of ovarian cancer was reduced by 53% (RR: 0.47; 95% CI: 0.27-0.81)</li> <li>- The risk of endometrial cancer was reduced by 67% (RR: 0.33; 95% CI: 0.21-0.51)</li> </ul>
Zhang, 2020 <sup>(27)</sup>	Meta-analysis	8,796,924	304,516 obese patients with bariatric surgery	8,492,408 obese patients not undergoing bariatric surgery	<ul style="list-style-type: none"> <li>- Decreased risk of cancer (OR: 0.56; 95% CI: 0.46-0.68)</li> <li>- Reduction in cancer mortality (OR: 0.56; 95% CI: 0.41-0.75)</li> <li>- Decreased risk of breast cancer (OR: 0.49; 95% CI: 0.33-0.72)</li> <li>- Decreased risk of endometrial cancer (OR: 0.43; 95% CI: 0.26-0.71)</li> </ul>
Rustgi, 2021 <sup>(69)</sup>	Retrospective cohort	98,090	33,435 patients diagnosed with NAFLD and severe obesity with bariatric surgery	64,665 patients diagnosed with NAFLD and severe obesity not undergoing bariatric surgery	<ul style="list-style-type: none"> <li>- Decreased risk of pancreatic cancer in subjects undergoing bariatric surgery (HR: 0.46; 95% CI: 0.21-0.93)</li> </ul>

Table prepared by the authors.

Various observational studies and meta-analyses have shown that bariatric surgery is a protective factor for developing multiple types of cancer and that this protection is stronger in the female sex. Although some studies demonstrate its protective effect against certain types of cancer, it is noteworthy that its mechanism of action is not yet known with certainty, and individual factors may influence its effectiveness. For example, patients with greater weight loss after surgery may be better protected. However, there may also be other factors that influence the protection offered by bariatric surgery, such as duration of obesity, age of onset of obesity, other diseases, or the quality of the diet.

Still, the protection conferred by bariatric surgery is not similar in all studies. More rigorous and exhaustive prospective research is required to identify the initial risk and determine the consistency and reliability of the protection provided by bariatric surgery. Therefore, it is important to maintain a healthy lifestyle and a balanced diet to reduce the risk of developing cancer and other diseases related to overweight and obesity.

**Tabla 2** summarizes the primary studies that have examined the benefit of bariatric surgery in protecting against different cancers.

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