

# Bariatric surgery as a factor of colorectal cancer prevention – an integrative review

## *A cirurgia bariátrica como um fator de prevenção ao câncer colorretal – uma revisão integrativa*

Jorge Daher Scander Sielski<sup>1</sup>, Juliany Bendas Beiro<sup>1</sup>, Mirella Mantovani<sup>1</sup>, Marcos Fabiano Sigwalt<sup>1</sup>

### ABSTRACT

**Introduction:** The increasing levels of obesity around the world and its intimate relation with colorectal neoplasms invite introspection to a protective effect of bariatric surgery.

**Objective:** To review articles that clarify the protective effect of bariatric surgery in the development of colorectal neoplasms.

**Method:** Integrative review based on PubMed and BVS databases, with the following keywords according to the platform Decs: "bariatric surgery and colorectal neoplasms". The subsequent process applied filters including publications from the last 5 five years, in English and Portuguese, that were complete. After critical analysis studies were selected based on their relevance and correlation with the theme.

**Results:** 16 articles were compared based on the effects of bariatric surgery in the prevention of colorectal cancer, which included different techniques and the relation between the pathophysiology of metabolic syndrome and carcinogenesis of the cancer studied.

**Conclusion:** It was observed that bariatric surgery, despite the used technique, has protective effect in the development of colorectal cancer.

**KEYWORDS:** Bariatric surgery. Colorectal neoplasms. Obesity.

### Central Message

In recent years, there has been an exponential increase in the incidence of obese people in the world, considering it one of the great challenges of public health. Obesity is associated with several diseases, including colorectal cancer, which represents the third most common cancer in the world. Bariatric surgery, in turn, is an alternative that helps in weighted weight loss and, in the long term, has proven benefits in reducing the risk of cancer.

### Perspective

Bariatric surgery presents a protective factor in colorectal cancer; this is justified by the understanding of the pathophysiological relationship between metabolic syndrome and obesity, since after the surgical procedure, there is a reduction in tissue inflammation, epigenetic changes and other biochemical factors, which hinder the carcinogenic process. In addition, when comparing the sleeve and bypass techniques, both were similar in terms of their protective effect against cancer.

### RESUMO

**Introdução:** O aumento dos índices de obesidade no mundo e a sua íntima relação com o câncer colorretal faz refletir se procedimentos bariátricos poderiam ter algum efeito protetor no desenvolvimento dessa neoplasia.

**Objetivo:** Realizar revisão que esclareça o efeito protetor da cirurgia bariátrica no desenvolvimento de câncer de colorretal.

**Método:** Revisão integrativa de acordo com a base de dados PubMed e BVS, com os seguintes descritores, de acordo com a plataforma Decs: "bariatric surgery and colorectal neoplasms" com filtros que incluíssem artigos dos últimos 5 anos em inglês e português, e que estivessem completos. A partir da leitura dos textos filtrados foram selecionados os estudos de acordo com relevância e maior relação com o tema.

**Resultados:** Dezesesseis artigos foram selecionados, comparando-se os efeitos da cirurgia bariátrica na prevenção do câncer de colorretal, incluindo as diferenças técnicas das operações e a relação da fisiopatologia da síndrome metabólica com a carcinogênese do tipo de câncer estudado.

**Conclusão:** A cirurgia bariátrica, independente da técnica utilizada, tem efeito protetor no desenvolvimento de câncer de colorretal.

**PALAVRAS-CHAVE:** Cirurgia bariátrica. Câncer colorretal. Obesidade.

<sup>1</sup> Universidade Positivo, Curitiba, PR, Brazil

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## INTRODUCTION

The prevalence of obesity continues to increase worldwide, being one of the biggest problems for public health today<sup>1</sup>. In 2016, approximately 40% of adults over 18 years of age were overweight and 13% of the world's population was obese. In addition, compared to previous years, the preponderance of obesity practically tripled between 1975 and 2016. The consequences of this metabolic disorder are diverse, such as hypertension, type 2 diabetes, dyslipidemia, cardiovascular diseases, kidney injury, osteoarthritis and various cancers.<sup>2</sup>

Among the possible malignant diseases that can affect the obese population is colorectal cancer (CRC). This is the third most frequent cancer in the world and the second leading cause of cancer-related death, with approximately 1.8 million new cases and 881,000 deaths in 2018, with an expected increase in its incidence of up to 60% by 2030. In cases of CRC, studies have suggested that obesity is associated with an increased risk of up to 70% in men, in which it was perceived that for every 5 kg/m<sup>2</sup> increase<sup>1,3</sup> in BMI there was a 24% increase in risk.<sup>3</sup>

Because of this, the various recommendations for cancer prevention include weight loss. However, for those who cannot reach their target weight with diet and exercise alone, bariatric surgery is a way to achieve rapid weight loss. Currently, it is considered for patients with a body mass index (BMI) equal to or greater than 40 kg/m<sup>2</sup> or for those with a BMI equal to or greater than 35 kg/m<sup>2</sup> with comorbidities related to obesity<sup>4</sup>. Studies have shown a strong association between weight loss, achieved after bariatric surgery, and a decrease in the risk of solid organ cancer. However, studies on the effect of bariatric surgery on CRC risk are still conflicting.<sup>5</sup>

The objective of this study was to review the effect of bariatric surgery on CRC, analyzing whether there was really any difference in those patients undergoing this procedure and whether different bariatric surgery techniques have divergent impacts.

## METHOD

This is an integrative review, carried out according to the 6 stages foreseen for its development. The filters used to select the sample included works published in the last 5 years, in English and Portuguese and full texts. The first was to define the guiding question: "Is bariatric surgery a factor for preventing colorectal cancer?". In the second, the search or sampling in the literature in the PubMed and VHL databases was determined, with the descriptors Decs: "Bariatric surgery and colorectal neoplasms". In the third, the inclusion and exclusion criteria were defined, which included studies that addressed the guiding question, adult patients who underwent bariatric surgery, along with the keywords; texts that addressed only the relationship between obesity and colorectal cancer and that brought purely clinical treatments, without

weight loss operations. The fourth stage, in turn, was the critical analysis of the included studies, which after applying the filter resulted in 8 articles; in PubMed, there were also 8 articles. Thus, joining the VHL and PubMed platforms, a total of 16 articles were selected (Figure). Finally, the fifth and sixth stages were the interpretation and synthesis of the results, comparing the data collected.

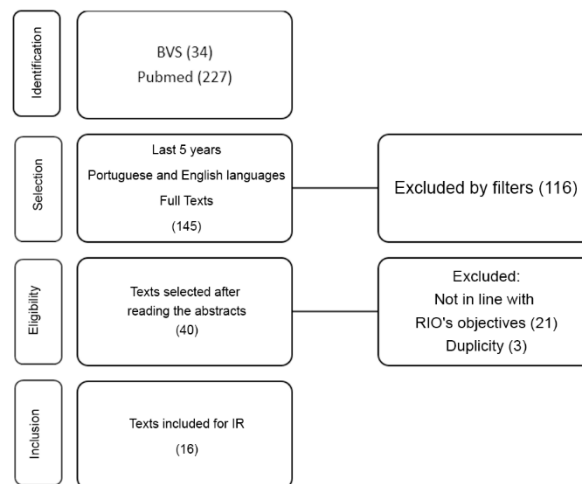


FIGURE – Summary of the methodology

## RESULT

The Table shows the synthesis of the analysis of the articles focused on the theme in question.

## DISCUSSION

The increase in the rates of obese and overweight patients is a public health concern. The high intake of industrialized and hypercaloric food leads to the accumulation of lipids, weight gain and consequently dysregulation of several biochemical reactions. Obesity is characterized by a state of low-grade systemic inflammation, which plays a significant role in the development of metabolic morbidity and, demonstrably, in the genesis of cancer.<sup>2</sup>

Excess adipose tissue in the body results in a state of inflammation due to oxidative stress, the spread of inflammatory cytokines, and increased DNA damage and repairs. The immune system is also impaired, as it results in dysbiosis, leading to even greater inflammation, contributing to cell mutation and consequently to the development of neoplastic cells.<sup>3</sup>

By 2016, almost 2 billion adults were obese and 650 million were overweight. In addition, about 481,000 new cases of cancer were diagnosed in adults aged 30 and older in 2012, presumably caused by increased body mass index (BMI).<sup>2,6</sup>

These obesity-related neoplasms mainly encompass colorectal cancer and other hormone-sensitive types, such as endometrial, breast, and prostate cancers. As for CRC, the magnitude of the risk associated with BMI is remarkable, being present in about 11.9% of obese men and 13.1% of obese women, and for each 5 kg/m<sup>2</sup> increase in BMI, the risk of this cancer increases by 24% in

**TABLE** – Compilation of results based on their objectives

Number Reference	Title	Authors	Kind	Goals	Periodic
11	The protective effect of bariatric surgery on the development of colorectal cancer: A systematic review and meta-analysis	Nikolaos Pararas; Anastasia Pikouli; Dionysios Dellaportas; Constantinos Nastos; Anestis Charalampopoulos; Mohamad Ayham Muqresh; George Bagias; Emmanouil Pikoulis; Dimitrios Papaconstantinou	Meta-analysis	To investigate whether bariatric surgery reduces the risk of developing colorectal cancer in morbidly obese patients	International Journal of Environmental Research and Public Health Doi: 10.3390/ijerph20053981
22	Systematic review and meta-analysis of the impact of bariatric surgery on future cancer risk	Robert B. Wilson; Dhruvi Lathigara; Devesh Kaushal	Systematic review	To analyze whether bariatric surgery reduces cancer incidence and mortality, especially in types associated with obesity	International Journal of Molecular Sciences DOI: 10.3390/ijms24010447
33	Does bariatric surgery reduce the risk of colorectal cancer in individuals with morbid obesity? A systematic review and meta-analysis	Andrea Chierici; Paolo Amoretti; Céline Drai; Serena De Fatico; Jérôme Barriere; Luigi Schiavo; Antonio Iannelli	Systematic review	To investigate whether bariatric surgery reduces the incidence of colorectal cancer in patients with obesity by analyzing meta-analysis of 18 studies	MDPI DOI: 10.3390/nu15010087
44	Incidence of polyp formation following bariatric surgery	Andrew C. Droney; William Sellers; Anjali Gupta; Kelly Rose Johnson; Marcus Fluck; Anthony Petrick; Joseph Bannon; Thomas Erchinger; Bogdan Protyniak	Integrative review	To investigate patients undergoing weight reduction surgery and their potential for developing precancerous lesions or polyps with carcinogenic potential, aiming to clarify any risk factors or relationships between bariatric surgery and colorectal cancer.	Surgery for Obesity and Related Diseases doi: 10.1016/j.soard.2021.06.020
55	Long-term incidence of colorectal cancer after bariatric surgery or usual care in the Swedish obese subjects	Magdalena Taube; Markku Peltonen; Kajsa Sjöholm; Richard Palmqvist; Johanna C. Andersson-Assarsson; Peter Jacobson; Per-Arne Svensson; Lena M. S. Carlsson	Original	To examine long-term incidence of colorectal cancer after bariatric surgery and usual care, based on intervention study of Swedish obese subjects (SOS)	Plos One DOI: 10.1371/journal.pone.0248559
66	Colorectal cancer risk following bariatric surgery in a nationwide study of french individuals with obesity	Laurent Bailly; Roxane Fabre; Christian Pradier; Antonio Iannelli	Cohort	To investigate whether bariatric surgery affects the risk of developing colorectal cancer in people who are overweight	JAMA Surgery Doi: 10.1001/jamasurg.2020.0082
77	Obesity surgery and risk of colorectal and other obesity-related cancers: an English population-based cohort study	Ariadni Aravani; Amy Downing; James D. Thomas; Jesper Lagergren; Eva J.A. Morris; Mark A. Hull	Cohort	To investigate whether bariatric surgery is associated with changes in cancer risk, including colorectal, breast, endometrial, kidney, and lung cancers, compared to obese patients without operations.	Cancer Epidemiology doi: 10.1016/j.cane.2018.01.010
88	Biomarkers of colorectal cancer risk decrease 6 months after Roux-en-Y gastric bypass surgery	Sorena Afshar; Fiona Malcoms; Seamus B. Kelly; Keith Seymour; Sean Woodcock; John C. Mathers	Cohort	To assess the impact of weight loss and bariatric surgery in relation to colorectal cancer	Obes Surg DOI: 10.1007/s11695-017-2972-3
99	The long-term impact of roux-en-y gastric bypass on colorectal polyp formation and relation to weight loss outcomes	Hisham Hussain; Alyssa Drosdak; Melissa Le Roux; Kishan Patel; Kyle Porter; Steven K. Clinton; Brian Focht; Sabrena Norio9	Integrative review	To assess the long-term impact of Roux-en-Y gastric bypass on precancerous colon polyps and to identify risk factors associated with this increased risk.	Obes Surg DOI: 10.1007/s11695-019-04196-3
1010	Colorectal cancer after bariatric surgery (Cric-Abs 2020): Sicob (Italian Society of Obesity Surgery) endorsed national survey	Maria Chiara Ciccioriccio; Angelo Iossa; Cristian Eugeniu Boru; Francesco De Angelis; Pietro Termini; Mary Giuffrè; Gianfranco Silecchia	Cohort	To analyze the incidence of colorectal cancer after bariatric surgery in Italy, comparing techniques to determine whether it is associated with the development of this type of cancer.	International Journal of Obesity DOI: 10.1038/s41366-021-00891-7
1111	Evaluating the correlation of bariatric surgery and the prevalence of cancers in obese patients: a study of the national inpatient sample (NIS) database	Devashish Desai; Sachi Singhal; Jean Koka	Cohort	To understand whether bariatric surgery can reduce the prevalence of certain cancers in morbidly obese patients.	Cureus Doi: 10.7759/cureus.23987
1212	Bariatric surgery is independently associated with a decrease in the development of colorectal lesions?	Minyoung Kwak; J. Hunter Mehaffey; Robert B. Hawkins; Traci L. Hedrick; Craig L. Slingluff Jr; Bruce Schirmer; Peter T. Hallowell; Charles M. Friel	Case-control	To review patients undergoing bariatric surgery, comparing with non-operated patients for demographics, comorbidities, body mass index, and socioeconomic factors	Surgery doi: 10.1016/j.surg.2019.04.015
1313	The impact of surgical weight loss procedures on the risk of metachronous colorectal neoplasia: the differential effect of surgery type, sex, and anatomic location	Hisham Hussain; Mohamed R. Ali; Shehnaz K. Hussain; Victoria Lyo; Eric McLaughli; ChienWei Chiang; Henry J. Thompson,	Cohort	To evaluate the impact of bariatric operations (sleeve gastrectomy and Roux-en-Y gastric bypass) on the risk of colorectal polyp recurrence in patients with a prior history of polyps, comparing them with controls without bariatric surgery	Journal of the National Cancer Institute Monographs DOI: 10.1093/jncimonographs/lgad009
1414	The impact of bariatric surgery on colorectal cancer risk	Sara D'Amato; Maria Sofia; Marcello Agosta; Giorgia Litrico; Iacopo Sarva; Gaetano La Greca; Saverio Latteri	Integrative review	Understanding whether bariatric surgery, especially Roux-en-Y gastric bypass, increases the risk of colorectal cancer and the mechanisms involved	Surgery for Obesity and Related Diseases doi: 10.1016/j.soard.2022.10.015
1515	Colon and rectal cancer risk after bariatric surgery in a multicountry Nordic cohort study	Wenjing Tao; Miia Artama; My von Euler-Chelpin; Mark Hull; Rickard Ljung; Elsebeth Lyngø; Guðrún H. Ólafsdóttir; Eero Pukkala; Pål Romundstad; Mats Talbäck; Laufey Tryggvadóttir; Jesper Lagergren	Cohort	To investigate whether bariatric surgery increases the risk of colorectal cancer in obese patients by looking at a group of adults over several decades in the Nordic countries.	International Journal of Cancer DOI: 10.1002/IJC.32803
1616	Bariatric surgery is associated with a recent temporal increase in colorectal cancer resections, most pronounced in adults below 50 years of age	Hisham Hussain; Arsheya Patel; Samuel Akinyeye; Kyle Porter; Dennis Ahnen; David Lieberman	Cohort	To investigate the incidence of colorectal cancer in relation to other obesity-related gastrointestinal cancers, among morbidly obese individuals who have undergone bariatric surgery and those who have not.	Obes Surg DOI: 10.1007/s11695-020-04921-y

men and 9% in women<sup>7</sup>. This important relationship is not only observed in malignant lesions, but also in premalignant lesions, such as colorectal adenoma.<sup>8</sup>

The pathophysiology involving the relationship between obesity and CRC can be explained by biochemical markers, with changes in the mechanisms that drive cancer, such as increased insulin sensitivity, decreased insulin-like growth factor-1 (IGF-1), decreased adiponectin, increased inflammation

of adipose and systemic tissue, increased leptin, epigenetic changes, among others.<sup>9,10</sup>

Through these significant associations between obesity and colorectal cancer, it becomes crucial to promote healthy lifestyle habits. For the reduction of obesity, lifestyle changes are only responsible for the loss of 5-10% of the body mass of the obese individual. In addition, it is a method that is difficult to adhere to and sustain in the long term, mainly due to

the various complications that obesity brings, such as depression, nutritional deficiency, a state of constant inflammation, osteoarthritis and sarcopenia.<sup>2</sup>

Bariatric surgery, in turn, promotes consistent weight loss, resulting in a greater reduction of excessive adipose tissue and consequently of the hyperinflammatory state. With the performance of the operation, there is significant weight loss, associated with the improvement of comorbidities.<sup>2,11</sup> Because of this, the hypothesis of bariatric surgery as a possible protective action in cases of CRC has been raised.

In this scenario, the literature is controversial, some studies have shown that there is a significant decrease in CRC cases, however, others consider bariatric surgery as a risk factor. There are also studies that show differences between the techniques, with Roux-en-Y bypass being associated with the worst prognosis.

A review was carried out encompassing more than 6.2 million patients who underwent bariatric surgery and underwent a 5-year follow-up.<sup>1</sup> In the analysis of this study, a 44% reduction in the incidence of RCC was observed in the 2 main surgical procedures, gastric sleeve (GS) and Roux-en-Y bypass (RYGB).<sup>1</sup> Reinforcing this relationship, the 2023 Chierici study showed a significant reduction of 54% comparing a sample of 12.5 million patients followed over the period of 3 to 20 years.<sup>3</sup> In addition, smaller studies followed this same trend, showing a reduction of up to 38% and an incidence of CRC of 0.10% after a 10-year follow-up of bariatric surgery.<sup>10,12</sup>

There were articles that failed to conclude this same relationship; however, they showed that obese patients without bariatric surgery had a risk of CRC of more than 34% compared to the general population. Concomitant with these findings, a significant decrease in polyp recurrence was also evidenced by 30% after the operation.<sup>13</sup>

Regarding the type of bariatric procedure, OS and RYGB were the most common surgeries, in which most studies indicated no significant difference in the risk of developing CRC.<sup>3,10</sup> However, in a small number of studies, there was a more protective effect with the use of GS.<sup>1,14</sup>

Another important variable is the gender of the participants. In women, the operation seems to be more beneficial, with a significant reduction in cases of CRC; for men, the data are more heterogeneous, some articles suggest that there are no differences when compared to women, and others suggest less protection after the procedure, resulting in higher incidences of CRC in this group.<sup>3,10,12</sup>

On the other hand, some studies have shown an increased risk of CRC after surgery for obesity, and the mechanisms underlying this are still uncertain. One of the hypotheses would be regarding the cellular and molecular changes in the gastrointestinal tract after it, mainly using samples obtained from the rectum to justify this relationship.<sup>15</sup> There are also authors

who indicate only RYGB as a risk factor for CRC, stating that there would be hyperproliferation and inflammation associated with changes in the intestinal microbiota that would be related to carcinogenesis in these cases.<sup>14</sup>

In view of this heterogeneity, the meta-analysis by Chierici et al.<sup>3</sup> of 2023, suggested follow-up time as a possible influencer on the results obtained - the longer the follow-up time, the higher the incidence of cancer. In addition, in the studies analyzed, odds ratios and risk ratios were used to measure the risk of colorectal cancer, this represents an important limitation, as studies that report time-dependent risk estimates cannot be effectively compared when the follow-up interval is different. For this, this article used the hazard ratio as a risk measure, which is independent of time and allows the identification of the risk of CRC after bariatric surgery. From this, with a more in-depth observation of the studies used and using this other indicator, a 19% reduction in the risk of CRC was found after bariatric surgery.<sup>3</sup>

However, it is also important to highlight the influence of multifactorial factors and the lifestyle of bariatric patients, since, despite weight reduction and some inflammatory factors, there are genetic and behavioral issues, such as smoking, alcoholism, diabetes, which interfere with and increase the incidence of CRC.<sup>5</sup> In addition, there is evidence of recurrence in 20% of patients with a BMI  $\geq$  35 kg/m<sup>2</sup> after 10 years, so bariatric surgery alone does not completely exclude risk factors.<sup>16</sup> In addition, most studies that showed it as a risk factor used only the information collected in databases, which can lead to bias if not correctly considered.

## CONCLUSION

The association of CRC carcinogenesis with obesity and metabolic syndrome is increasingly elucidated and described as an important modifiable risk factor. Knowing the great difficulties and limitations that the population encounters in weight loss, bariatric surgery has positive results both in weight loss and in reducing the incidence of related cancers. Even with a certain discrepancy in the results in the literature, it is perceived that in the most recent studies it is possible to conclude that there is a protective factor of the bariatric procedure, regardless of the technique (SG and RYGB), in the development of colorectal cancer, mainly due to the consequent biochemical changes, making them more physiological and less carcinogenic. It is necessary to note, however, that performing the procedure, without the proper criteria, does not have a strong impact on the prevention of colorectal cancer.

### Authors' contributions

Jorge Daher Scander Sielski: Conceptualization

Juliany Bendas Beiro: Methodology

Mirella Mantovani: Writing (original draft)

Marcos Fabiano Sigwalt: Writing (review and editing)

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