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ORIGINAL ARTICLE

Impact of bariatric surgery on early-onset colorectal cancer risk: a systematic review and meta-analysis

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Abstract

The aim of this meta-analysis is to determine the impact of bariatric surgery on the risk of early-onset colorectal neoplasia. This systematic review was conducted according to PRISMA recommendations. It was registered in the PROSPERO international database. A comprehensive search was conducted in electronic databases (MEDLINE, EMBASE, and Web of Science) for completed studies until May 2022. The Search was made using a mixture of indexed terms and title, abstract and keywords. The search included terms: obese, surgical weight loss intervention, colorectal cancer, and colorectal adenomas. Studies that included bariatric intervention patient's vs non-surgical obese patients younger than 50 years were considered. Inclusion criteria were patients with BMI more than 35 kg/m^2 who underwent a colonoscopy. Studies with follow-up colonoscopy performed in less than 4 years after bariatric surgery and those that evaluated patients with a mean age difference of 5 or more years between groups were excluded. Outcomes analyzed in obese patients with surgical treatment vs control patients included colorectal cancer incidence. From 2008 to 2021, a total of 1536 records were identified. Five retrospective studies that included 48,916 patients were analyzed. Follow-up period ranged from 5 to 22.2 years. 20,663 (42.24%) patients underwent bariatric surgery and 28,253 (57.76%) were part of the control patients. Roux-en-Y gastric bypass was performed in 14,400 (69.7%) individuals. The intervention and control group were similar in age range, proportion of female participants and initial body mass index (35–48.3 vs 35–49.3, respectively). 126/20663 (0.61%) patients in the bariatric surgery group and 175/28253 (0.62%) individuals in the control group presented CRC. In this meta-analysis, we were unable to demonstrate a significant impact of the Bariatric Surgery on EOCRC risk. Prospective trials with longer follow-up periods should be done to prove the colorectal cancer risk reduction.

Keywords Bariatric surgery · Colorectal cancer · Systematic review · Meta-analysis · Early-onset colorectal cancer

Introduction

The incidence of colorectal cancer (CRC) is increasing at a rate of 4% per year in patients under the age of 50 [1, 2]. Early-onset colorectal cancer [1, 3] now accounts for 12% among all cases and 7% of all CRC deaths [4]. New research indicates a connection between increasing age and a higher risk of advanced stage colorectal cancer, with the largest increases among younger Hispanic and Afro-American patients [5].

Given the burden of EOCRC and the enormous costs associated with this, the United States Preventive Services Task Force [6] and the American Cancer Society had already dropped the recommended age for colorectal cancer screenings in average-risk adults to 45 years[1, 5–8]. This new guideline might well create more than 20 million Americans between ages of 45 and 50, newly eligible for CRC screening [9]. A better understanding of the disease may facilitate the ability to incorporate risk-based strategies for screening, diagnosis, and treatment of CRC in younger patients [1, 7].

An association between obesity and EOCRC has been demonstrated in previous studies [1, 4, 6, 7, 10, 11]. Obesity

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and sedentary lifestyle have been linked to metabolic dysregulation, which has been linked to EOCRC. Metabolic syndrome, defined as a collection of interconnected risk factors such as high blood pressure, dyslipidemia, and central obesity, has been linked to a 13% increased risk of CRC [12]. Furthermore, metabolic surgery has been shown to be the most effective long-term weight loss treatment, reducing the disease spectrum associated with metabolic syndrome. Bariatric surgery has also been shown to reduce mortality in the obese population, including cancer-related deaths [13].

A meta-analysis published in 2014 found that bariatric surgery was associated with a 27% lower risk of CRC in the general population [14]. However, the literature continues to produce contradictory findings, and several large series have presented data supporting a higher risk of CRC in patients who have undergone weight loss surgical interventions [15, 16].

To the best of our knowledge, data aiming to determine the impact of bariatric surgery on EOCRC is lacking.

The aim of this meta-analysis is to determine the impact of bariatric surgery on the risk of early-onset colorectal neoplasia.

Methods

This systematic review was conducted according to PRISMA recommendations [16]. It was registered in the PROSPERO international database (www.crd.york.ac.uk/prospero/).

Literature search

A comprehensive search was conducted in electronic databases (MEDLINE, EMBASE, and Web of Science) for completed studies until May 2022. The search was performed using a mixture of indexed terms and searches of title, abstract and keywords. The search included terms related to the obese population, all types of surgical weight loss intervention, colorectal cancer, colorectal adenomas and colorectal polyps. We restricted our study to human studies published in English. Two reviewers (L.B.L, M.S) performed the screening of titles and abstracts, whereas inconsistencies were solved by agreement and further evaluation by a senior author (J.RT.M).

Selection criteria

Studies that included bariatric intervention patient's vs non-surgical obese patients younger than 50 years were considered. Inclusion criteria were patients with BMI more than 35 kg/m^2 who underwent a colonoscopy. Studies with follow-up colonoscopy performed in less than 4 years after bariatric surgery and those that evaluated patients with a mean age difference of 5 or more years between groups were excluded. Outcomes analyzed in obese patients with surgical treatment vs control patients included colorectal cancer incidence and adenomas rate when available.

Data extraction and analysis

The following data were extracted using a standardized form: study design, country of origin, year of publication, type of bariatric surgery, follow-up period, baseline characteristics of population including initial body mass index, weight loss, CRC, polyps/adenomas in surgical intervened and control patients.

Results

From 2008 to 2021, a total of 1536 records were identified. Nine studies meet the inclusion criteria. Based on the difference in age between the groups, four studies reporting on CRC-related outcomes after bariatric surgery were excluded.

Five retrospective studies [15, 17–20] that included 48,916 patients were analyzed. Among these, two studies were from USA, and the other three were undertaken in Canada, England, and Sweden. Follow-up period ranged from 5 to 22.2 years (mean 10.5) (Table 1). 20,663 (42.24%) patients underwent bariatric surgery and 28,253 (57.76%) were part of the control patients. The bariatric surgery intervention most common used was Roux-en-Y gastric bypass, performed in 14,400 (69.7%) individuals. The intervention and control group were similar in age range (38.9 ± 10.3 to 47.2 ± 5.9 vs 39.1 ± 10.7 to 48.7 ± 6.3), higher proportion of female participants (16,667 (80.7%) vs 21,946 (77.7%)) and initial body mass index (BMI) ranging from 35 to 48.3 ± 8 vs 35 ± 49.3 respectively (Tables 1, 2).

Pooled results

126/20,663 (0.61%) patients in the bariatric surgery group and 175/28,253 (0.62%) individuals in the control group presented CRC (Fig. 1).

Discussion

In EOCRC, this meta-analysis shows comparable risk of CRC in the bariatric surgery and control group for morbidity obese patients. To the best of our knowledge, our study is the first systematic review and meta-analysis studying the impact of bariatric surgery in EOCRC.

An increased incidence of EOCRC was shown in the control group (Adams, Christou, Taube), whereas Kwak demonstrated a comparable incidence. On the other hand,

Table 1 Characteristics of included studies

	Country	Study design	Type of bariatric surgery *n* [13]	Follow-up (*n* years)
Adams et al. [19]	USA	Retrospective	RYGB: 6596 (100)	12.5
Christou et al. [20]	Canada	Retrospective	RYGB: 841 (81.3) Vertical banded gastroplasty: 194 (18.7)	5
Kwak et al. [21]	USA	Retrospective	RYGB: 1719 (77.1) Gastric banding: 303 (13.6) Sleeve gastrectomy: 165 (7.4) Other surgeries: 44 (2)	7.8
Mackenzie et al. [17]	England	Retrospective	RYGB: 4978 (56.6) Gastric banding: 2957 (33.6) Sleeve gastrectomy: 859 (9.8)	4.58
Taube et al. [22]	Sweden	Retrospective	Vertical banded gastroplasty: 1365 (68) Gastric banding: 376 (18.7) RYGB: 266 (13.3)	22.2

Mackenzie et al. [16] show a doubled incidence of CRC in the bariatric surgery group.

The relationship between body weight and diverse cancers is now well understood. Obesity is a well-known risk factor for CRC, which remains a major health care problem in the United States. Obesity increases the risk of CRC by five times for every 5 kg/m^2 increase in BMI (Body Mass Index). Obesity is also related to an increased risk of colorectal adenoma. Weight loss in this population might be expected to result in a lower risk of CRC. Although bariatric surgery has been shown to reduce the risk of obesity-related cancer in general, the effect on colorectal cancer risk in obese patients is uncertain.

Given the latency period in colorectal carcinogenesis, the effects of bariatric surgery on the risk of CRC and adenomas may be variable and take years to express. Based on the only meta-analysis of observational studies, bariatric surgery is associated with a 27% lower risk of CRC.

Gender's impact

Premenopausal women show a minor CRC risk than the same-age men of all races and ethnicities [5, 22]. Taking into consideration that 80% of the intervened and matched controlled subjects in this study were female, we cannot conclusively determine whether the results of this study were influenced by the effect of sex on CRC risk. Furthermore, CRC incidence in the current cohorts was not reported by sex, limiting an objective analysis of the sex effect on these results.

Years of obesity/sedentarism and follow-up periods

This is especially important given the recent rise in the prevalence of overweight and obesity among kids and teenagers in many countries [23, 24].

The association between decreasing age and increased risk of advanced stage colorectal cancer among younger Hispanic and Afro-American patients is notable, possibly due to the low rate of screening colonoscopy in this group of patients. Other research suggests that biological tumors are more aggressive.

Obesity and CRC outcome studies have produced contradictory results [2, 12, 16, 25]. Meyerhardt et al. [26] were not considerably related with increased risks of colon cancer recurrence or death. The increased risk of mortality includes tumor aggressive, late diagnosis, and reduced treatment response.

The association between obesity and CRC still is unclear. The complex health problem that obesity caused could be the association between the higher adiposity and greater CRC.

The consequence of the bariatric treatment reduces inflammatory markers, genomic damage, and could boost antineoplastic responses, and with all these mechanics, a decrease in CRC after surgery could be expected; however, an independent effect of surgery on the progression of early lesions has yet to be established.

Strengths and limitations

The strengths of this systematic review are that we focused on studies with control groups and had more than 4 years after the surgery in order to find some difference in the colonoscopy.

Nonetheless, the consequence of the bariatric surgery in the carcinogenesis of CRC may take decades to become obvious and we did not know the actual timeframe for this analysis.

The insufficient data in the primary studies had as consequences many different lengths of follow-up.

Table 2 Outcomes of included studies

	Patients *n*		Mean age Years (SD)		Gender Female *n* (%)		Body mass index kg/m^2 (SD)		Weight loss		CRC cases		Colorectal polyps N New polyps/n adenomas, serrated lesions	
	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control
Adams et al. [19]	6596 (database: 1984–2002)	9442 BMI > 35	38.9 (10.3)	39.1 (10.7)	5654 (85.72)	7872 (83.37)	44.9 (7.6)	47.4 (6.5)	n/a	n/a	25	52	n/a	n/a
Christou et al. [20]	1035 (database: 1986–2002)	5746	45.1 (11.6)	46.7 (13.1)	679 (65.6)	3678 (64)	≥ 35	≥ 35	Excess weight loss: 62.1% SD 26.8 BMI reduction: 31.9% SD 13.2	n/a	2	35	n/a	n/a
Kwak et al. [21]	2231	2231	42.6 (10.3)	42.8 (13.4)	1846 (82.7)	1882 (84.4)	48.3 (8)	49.3 (11.4)	Excess weight loss: 55.5%	1.4%	6	5	101/41	49/71
Mackenzie et al. [17]	8794 (database: 1997–2012)	8794	42 (8)	42 (8)	7069 (80.4%)	7069 (80.4%)	n/a	n/a	n/a	n/a	35	16	n/a	n/a

Table 2 (continued)

	Patients *n*		Mean age Years (SD)		Gender Female *n* (%)		Body mass index kg/m^2 (SD)		Weight loss		CRC cases		Colorectal polyps N New polyps/n adenomas, serrated lesions	
	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control	Surgery	Control
Taube et al. [22]	2007	2040	47.2 5.9	48.7 6.3	1419 (70.7)	1445 (70.9)	42.4 (4.5)	40.1 (4.7)	Mean weight losses (SD): 28.7 (14.3) kg at 2 years, 21.1 (15.1) kg at 10 years, 21.6 (16.6) kg at 15 years and 22.1 (16.5) kg at 20-year follow-up visits	Weight loss ≤ 3 kg	58 19 rectal cancers	67 31 rectal cancers	n/a	n/a

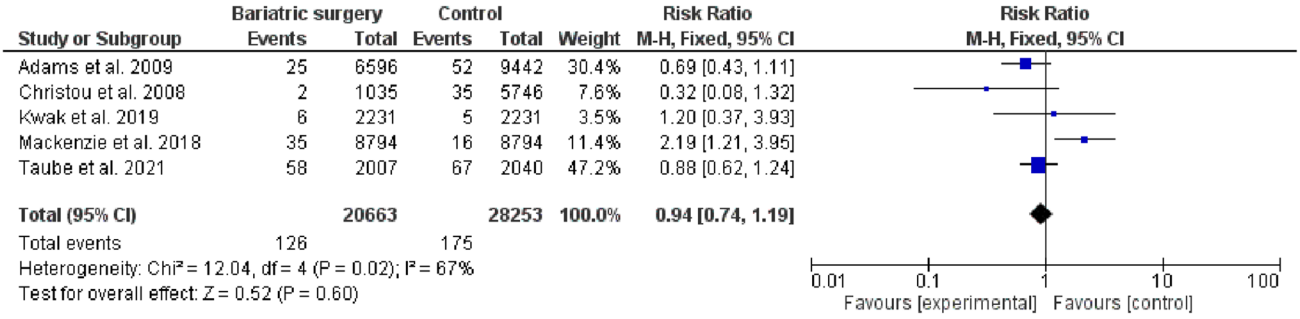

Fig. 1 Plot with meta-analysis between bariatric surgery and control group

Selection bias

Lifestyle and environmental aspects impact the risk of CRC, obesity is only one of them and weight loss could be a protective factor, but not the only one. Others lifetime risk as sedentary life needs to be addressed in these group of patients in order to remove other factors for CRC. The increase of physical activity after bariatric surgery is well documented and is an important step for these patients.

The biggest limitation in this endeavor remains the lack of high-quality studies about CRC and the impact of bariatric surgery.

A major limitation is the few number of studies that could meet the inclusion criteria.

The retrospective nature of all the papers is another potential limitation.

Conclusion

In this meta-analysis, we were unable to demonstrate a significant impact of the bariatric surgery on EOCRC risk. Prospective trials, with longer follow-up periods and more balanced sex distribution population should be undertaken to further evaluate the effect of weight loss surgical interventions on EOCRC risk.

Data Availability Not Applicable.

Declarations

Conflict of interest The authors had no conflict of interest.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent It does not apply.

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