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Obesity indices as risk factor for colorectal cancer in patients at a national police hospital in Peru

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ABSTRACT

Introduction: Colorectal cancer (CRC) represents the third most diagnosed form of cancer around the world, accounting for 11% of all cancer diagnoses. It has been seen that obesity is closely linked to this disease.

Materials and methods: This study is a non-paired case-control study. To measure obesity, the body mass index (BMI), new body mass index (NBMI), and the triponderal index (TPI) were used. Logistic regression was used to obtain the adjusted odds ratio (aOR) by age and sex, confidence interval (95%CI).

Results: The sample was 246 patients. The prevalence of obesity according to BMI was 12.20%. The multivariable analysis found statistically significant association between CRC and obesity according to BMI (aOR: 3.23; 95% CI 1.26-8.30) compared to normal weight; NBMI tertile 3 (aOR: 4.02; 95% CI 1.95-8.30), compared to tertile 1; and TPI tertile 3 (aOR: 4.55; 95% CI 2.21-9.35) versus tertile 1.

Conclusions: Obesity, is a risk factor for CRC. Future studies might consider useful different ways to measure obesity to define population strata with a higher-risk of CRC.

Keywords: colorectal cancer, overweight, obesity, aging, case-control (mesh terms)

INTRODUCTION

Cancer is a global public health problem, due to the burden of disease and because it causes a high rate of mortality and disability [1]. In 2018, approximately 18.1 million new cases of cancer were diagnosed globally [2]. Furthermore, this number is estimated to increase to 21.3 million cases each year by 2030 [1].

According to data from the Global Cancer Observatory (GLOBOCAN) of 2018, colon cancer is the fourth cancer in incidence worldwide, while rectal cancer is the eighth in incidence; both types of cancer make up colorectal cancer (CRC), representing the third most diagnosed form of cancer around the world, accounting for 11% of all cancer diagnoses [2]. In 2018 alone, around 881,000 deaths were reported from CRC [3].

Obesity has been associated with more than 13 types of cancer [4]. Obese men have been found to have a 50% increased risk of colon cancer and a 20% increased risk of rectal cancer (these figures are 20% and 10% for women, respectively). In addition, this not only predisposes to higher incidence rates but also decreases the probability of survival [5].

To our knowledge, no prospective study in Peru has investigated the association of CRC with obesity, considering the different ways of identifying it through weight and height indices. The identification of which indicators are associated with this neoplasm may be useful for risk stratification and a better understanding of the pathophysiological mechanisms underlying the obesity-cancer relationship. Therefore, this study aimed to determine the association between obesity rates and CRC in patients from a hospital in Lima, Peru.

MATERIAL AND METHODS

Study Design and Population

An unpaired case-control study. It was carried out during the period from 2017 to 2019.

Population and Sample

The population was the patients treated in the oncology service of the Hospital Policía Nacional del Perú (PNP). From the list obtained from this, the cases were selected through the selection criteria. The controls were selected from the same oncology department during the same period, who presented other types of oncological diseases.

Exclusion criteria were preoperative neoadjuvant chemotherapy/radiotherapy, a history of colonic diseases like CRC, inflammatory bowel disease, and a family history of CRC.

Table 1. Descriptive characteristics of the patient sample

Characteristic	n (%)
Sex	
Male	122 (49.80)
Female	123 (50.20)
Categorized age	
18 to 49 years old	32 (13.01)
50 to 59 years old	56 (22.76)
60 to 69 years old	53 (21.54)
70 year old or more	105 (42.68)
Categorized BMI	
Normal weight	108 (43.90)
Overweight	108 (43.90)
Obesity	30 (12.20)
NBMI	
Tertile 1	83 (33.74)
Tertile 2	81 (32.93)
Tertile 3	82 (33.33)
TPI	
Tertile 1	84 (34.15)
Tertile 2	81 (32.93)
Tertile 3	81 (32.93)

Note. *Mean & standard deviation

The sample size was calculated through the Epidat program. The number of cases and controls was calculated based on an exposure ratio among cases of 0.5, a predicted odds ratio for obesity of 2.2 [6], with a confidence level of 95%, a statistical power of 0.80, and a number of controls per case of 1. This resulted in a final sample size of 224 patients, 114 cases, and 114 controls. Consecutive non-probabilistic sampling was used.

The sample of patients in the case group had a diagnosis determined by colonoscopy and confirmed by pathology. The control group was taken from individuals who underwent colonoscopy screening for CRC that was negative for polyps and CRC throughout the colon and rectum.

Variable Definition

The dependent variable was the diagnosis of CRC. This was detected through the diagnosis registered in the patients' medical records of the oncology service. The independent variables were overweight/obesity, which were evaluated according to three obesity indices that use weight and height:

Body mass index (BMI)=Weight (kg)/Height^2 (meters),

Triponderal index (TPI)=Weight (kg)/Height^3(m) [7], and

New BMI (NBMI)=1.3×(weight (kg)/height (m)) [8].

BMI was divided according to the WHO reference points: normal weight (18.5 to 24.99 kg/m^2), overweight (25 to 29.99 kg/m^2), and obesity (≥30 kg/m^2).

The TPI was divided into tertiles (tertile 1: 8.87 to 14.24; tertile 2: 14.26 to 16.47; and tertile 3: 16.47 to 25.60). The NBMI was divided into tertiles (tertile 1: 14.50 to 23.80; tertile 2: 23.80 to 27.30; and tertile 3: 27.34 to 40.94).

The covariates studied were age (18 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years and over) and sex (male vs. female), tumor grade (grade I to IV), and the tumor location [9].

Procedures and Statistical Analysis

To collect the data, it was through medical records, a data collection sheet with the required information was used as an instrument. Then, the data was filled in the Microsoft Excel program. Data were analyzed with STATA version 17 program.

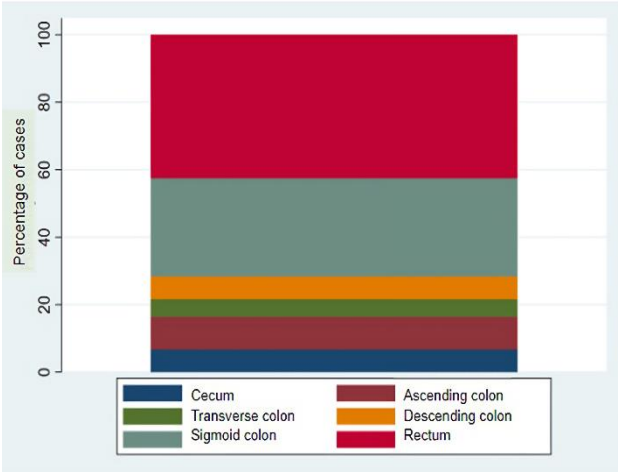

Figure 1. Tumor location (Source: Authors' own elaboration)

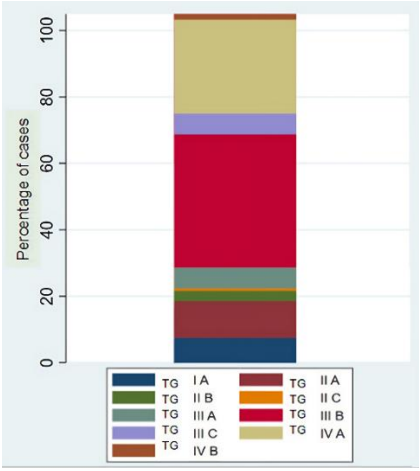

Figure 2. Tumor grade (Source: Authors' own elaboration)

In descriptive statistics, categorical variables were described using absolute and relative frequencies. For the bivariate analysis, the chi-square of independence was used.

Finally, the crude and adjusted OR (for age and sex) performed with simple and multivariable logistic regression analysis for each type of obesity was used as a measure of association. These were presented with their corresponding 95% confidence intervals (95% CI) with a statistical significance level of 5% ($p<0.05$).

Ethical Aspects

All procedures performed in this study preserved the integrity and fundamental rights of the patients under investigation. The data recorded was anonymous, so the confidentiality of the data obtained was guaranteed at all times.

RESULTS

The male sex was 49.80%. The prevalence of obesity according to BMI was 12.20%. The majority of the sample was 70 years of age or older (42.68%) (**Table 1**).

Additionally, the location of the CRC cases in the rectum, where 42.54% (**Figure 1**).

While half of the cases (50%) had CRC grade III (**Figure 2**).

Table 2. Bivariate characteristics of the factors associated with CRC

Characteristic	CRC		p*
	Cases	Controls	
	n (%)	n (%)	
Sex			
Male	45 (40.54)	77 (57.46)	0.008
Female	66 (59.46)	57 (42.54)	
Categorized age			
18 to 49 years old	22 (19.64)	10 (7.46)	<0.001
50 to 59 years old	36 (32.14)	20 (14.93)	
60 to 69 years old	26 (23.21)	27 (20.15)	
70 year old or more	28 (25.00)	77 (57.46)	
Categorized BMI			
Normal weight	56 (50.00)	52 (38.81)	0.089
Overweight	47 (41.96)	61 (45.52)	
Obesity	9 (8.04)	21 (15.67)	
NBMI			
Tertile 1	49 (43.75)	34 (25.37)	0.003
Tertile 2	36 (32.14)	45 (33.58)	
Tertile 3	27 (24.11)	55 (42.04)	
TPI			
Tertile 1	51 (54.54)	33 (24.63)	<0.001
Tertile 2	38 (33.93)	43 (32.09)	
Tertile 3	23 (20.54)	58 (43.28)	

Note. *Analysis performed with Chi-square of independence

The bivariate analysis, a statistically significant association was found between sex (p=0.008), categorized age (p<0.001), NBMI in fertile (p=0.003), and TPI in fertile (p<0.001). No association with BMI was found (p=0.089) (**Table 2**).

In the multivariable regression analysis, a statistically significant association was found between CRC and obesity according to BMI (aOR: 3.23; 95% CI 1.26-8.30) compared to normal weight; NBMI tertile 3 (aOR: 4.02; 95% CI 1.95-8.30) compared to tertile 1; and TPI tertile 3 (aOR: 4.55; 95% CI 2.21 - 9.35) versus tertile 1 (**Table 3**).

Table 3. Simple & adjusted multivariate regression analysis of the association between satisfaction & obesity rates & CRC

Characteristic	Crude analysis			Adjusted analysis*		
	cOR	CI 95%	p	aOR	CI 95%	p
Categorized BMI						
Normopeso	Ref.			Ref.		
Sobrepeso	1.39	0.81-2.38	0.221	1.47	0.82-2.66	0.198
Obesidad	2.51	1.05-5.98	0.037	3.23	1.26-8.30	0.014
NBMI						
Tertile 1	Ref.			Ref.		
Tertile 2	1.74	0.94-3.24	0.076	1.76	0.88-3.49	0.105
Tertile 3	3.89	2.03-7.47	<0.001	4.02	1.95-8.30	<0.001
TPI						
Tertile 1	Ref.			Ref.		
Tertile 2	1.80	0.96-3.34	0.062	1.75	0.88-3.44	0.105
Tertile 3	2.93	1.55-5.54	0.001	4.55	2.21-9.35	<0.001

Note. *Adjusted for sex & age; significant p-value<0.05; OR: Odds ratio; & CI 95%: Confidence interval at 95%

DISCUSSION

Main Findings

The aim of this study applied to 246 patients was to determine the association between obesity rates and CRC in patients at the PNP hospital. The study found that, regardless of the obesity index used with weight or height, it is associated with the indicated event. Three indicators studied worldwide were chosen, due to the practical way of measuring weight and height at different levels of health care. Hence the importance of this for all types of diseases, even more in cancer. To the best of our knowledge, this is the first study in Peru that makes this type of evaluation.

Comparison With Other Studies

Obesity could be evaluated through several different anthropometric indices. Although BMI has been used classically, it has been questioned for some time, since it can overestimate fat accumulation in tall people and underestimate it in short people [10], so the use of other markers was considered, like the IMCN. Although some studies have not found significant differences between NBMI and CRC [11], in this manuscript there was a greater strength of association with it, followed by TPI. Therefore, everything seems to indicate that obesity is closely related to this disease.

It has been previously shown that approximately 50% of cancer patients had an abnormally high BMI [12]. Furthermore, many authors [13-16] have reported the relationship between obesity and colorectal polyps. The article [17] states that the time for this sequence to occur is approximately 10 years, so the removal of adenomatous polyps is important to reduce the incidence of CRC. In addition, it also points out that among the factors that have increased the incidence of CRC in young patients, it may be due to the progressive increase in BMI, which increases the probability of forming colorectal polyps, which can trigger carcinogenesis [17].

A cohort study with a 23-year follow-up by Levi et al found that adolescents who were overweight or obese were at increased risk of developing CRC. It was suggested that the increased incidence of CRC in young adults might be related to obesity as an important etiologic factor [18, 19]. It was shown that in a group of 257,623 children, childhood BMI and height were significantly associated with CRC [20]. In other words, the tallest and heaviest children had a higher risk of developing CRC compared to those who were within the normal range. It was found that the relationship between BMI and CRC risk varied significantly depending on the presence or absence of poorly differentiated foci [21]. When there were no poorly differentiated foci, a high BMI was associated with an increased risk of CRC. In a study [22], a high BMI was found to be associated with increased long-term mortality from CRC, while a low BMI may reduce the risk of cancer mortality. A meta-analysis on 12,837 cases of CRC found that abdominal obesity was related to CRC [23].

Although the present study did not find an association with overweight, this contrasts with other works such as that of [24], who conclude that there is an unfavorable trend of risk factors, including overweight, which leads to an increase in the incidence of CRC. It was shown that subjects who were overweight at the age of 21 years had a higher risk of CRC than individuals with a normal BMI [25]. These differences found may be due to the different populations evaluated.

Results Analysis

The process behind the development of cancer is still being investigated. Fatty tissue produces different hormones and inflammatory substances, such as IL-6, TNF-α, leptin, and adiponectin, which can create a favorable inflammatory environment for cancer cells [26, 27].

In addition, the increase in the size of fat cells and the excessive accumulation of fat tissue (mainly in the abdominal region) can lead to the formation of abnormal fat cells and diseases related to fat tissue. Fat cells play a central role in this inflammatory response in obese people, as they secrete hormones, growth-stimulating substances, and inflammatory cytokines. These molecules are especially important in the formation of tumors in the large intestine. Among the hormones secreted by fat cells, the most relevant for the development of tumors in the large intestine are adiponectin, leptin, resistin and ghrelin. All of these substances are involved in cell growth and multiplication, as well as in the formation of new blood vessels in the tumor, and their presence has been shown to change the colonic mucosa from normal to adenoma to adenocarcinoma, suggesting They play a role in various stages of tumor formation in the large intestine. The formation of fatty tissue and the formation of new blood vessels directly influence the formation of tumors [28].

Furthermore, elevated levels of IL-23 and IL-10 in serum [29] and of IL-8 and IL-6 in the microenvironment were shown to be associated with CRC progression [30]. Recent research has highlighted the role of IGF in CRC. IGF1 and IGF2 have been associated with numerous gastrointestinal cancers [31]. Several studies have clarified that serum level and loss of IGF2 imprinting were associated with advanced colorectal adenoma and poor prognosis in advanced stages of CRC, respectively [32].

Study Limitations

Limitations of this study are related to its observational, retrospective, and single-institution design; however, it is representative of the study population of police officers and direct family members. Other variables that could have been used for adjustment were not always available in the clinical records, such as family history of CRC, history of colon polyps, inflammatory colonic disease, clinical and laboratory indicators of obesity such as waist circumference and waist-hip ratio. New oncological and molecular markers should be evaluated in future studies.

Weaknesses of this written paper include the possibility of sample selection error, the absence of waist circumference measurements, and the ratio of waist-hip circumference to BMI. For future research, it would be advisable to record these measurements and follow up the patients, which would also be informative. In addition, multicenter studies could be conducted to increase study capacity and improve its scientific quality. The results of these studies could be used to inform policy and healthcare decision-making for CRC screening programs.

CONCLUSIONS

Obesity, regardless of the anthropometric measurement used, is a risk factor for CRC. If these results are confirmed in the future, the use of different ways to measure obesity may be useful to define population strata with a higher risk of CRC.

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Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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