Review

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Early-life obesity and adulthood colorectal cancer risk: a meta-analysis

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ABSTRACT

Objective. *This meta-analysis examines the relationship between early-life obesity and risk of colorectal cancer (CRC) in adulthood.*

Methods. *A systematic search of Google Scholar, PubMed, and reference data was conducted. Fifteen relevant studies were identified and meta-analyzed, for men and women separately. A random-effects model was used to compare the multivariable-adjusted relative risks (RR) of overall and subsite-specific CRC to the highest versus lowest categories of body mass index (BMI) in early life. Meta-regression was performed on factors that may have contributed to between-study heterogeneity.*

Results. *High early-life BMI was associated with a 39% increased risk of CRC in adult men (RR = 1.39, 95%CI = 1.20 – 1.62, P < 0.0001) and a 19% increased risk of CRC in adult women (RR = 1.19, 95%CI = 1.06 – 1.35, P = 0.004). No statistically significant heterogeneity was identified in meta-regression according to tumor subsite (RR = 1.06, 95%CI = 0.97 – 1.17, RR = 1.08, 95%CI = 0.99 – 1.18 for male and female proximal colon cancer; RR = 1.51, 95%CI = 1.22 – 1.87, RR = 1.08, 95%CI = 0.98 – 1.19 for male and female distal colon cancer; and RR = 1.39, 95%CI = 1.1 – 1.77, RR = 1.51, 95%CI = 0.94 – 2.03 for male and female rectal cancer) or other factors, including age of BMI assessment, self-reported or measured BMI, and adjustment for smoking.*

Conclusions. *The results suggest that high early-life BMI is associated with increased risk of CRC in adulthood. Further studies should investigate adult CRC risk in early-life obese individuals from non-Western countries and the underlying mechanisms by which early-life adiposity may influence CRC pathogenesis.*

Keywords Colorectal neoplasms; rectal neoplasms; obesity; body mass index; meta-analysis.

Colorectal cancer (CRC) causes the mortality of more than 50 000 people per year in the United States, with CRC risk in the Americas having increased throughout the past decade (1). Numerous studies have identified that a high adult body mass index (BMI) is associated with an increased risk of CRC in adulthood, referring to inflammatory cytokines, metabolic syndrome, and diet as potential causes of CRC pathogenesis (2 – 6). However, given the long induction period of carcinogenesis in the colon and rectum, early-life obesity has also been suggested to affect CRC development later in life (7).

Various narrative and systematic reviews have described the impact of early-life obesity on general causes of morbidity and mortality in adulthood, but none thoroughly addressed increased risks of CRC, only providing narrative review on studies concerning the risk of CRC mortality (8, 9). The small sample sizes of individual studies that investigated the relationship between high early-life BMI and adult CRC risk

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also produced underpowered results for subsite-specific CRC risk. This poses the following question: is obesity in early life associated with an increased risk of CRC in adulthood?

Tumor sublocation groups and effect sizes vary from studies that assessed the risk of CRC risk during adulthood in individuals obese in early-life, prompting the need for a meta-analysis. Although one meta-analysis has investigated the association between early-life obesity and CRC risk in adulthood, the authors did not conduct analyses on obese versus normal BMI categories and on tumor sublocations, leaving these associations unknown (10). This paper outlines the results of a meta-analysis that elucidates the relationship between obese early-life BMI and CRC risk in adulthood.

MATERIALS AND METHODS

Study selection

This meta-analysis was conducted in coherence with guidelines enumerated by the Meta-analysis of Observational Studies in Epidemiology checklist (11). Google Scholar (Google Inc., Mountain View, California, United States) and PubMed Central (U.S. National Library of Medicine, Bethesda, Maryland, United States) were used to search for studies published before 20 August 2017 using the following keywords: body mass index OR BMI OR overweight OR obese AND childhood OR adolescence OR youth AND risk OR morbidity OR mortality AND men OR males OR middle age AND cancer OR colorectal OR colorectal cancer OR colon. The option to use MeSH terms was also applied in PubMed and all languages were included in the language filter to adequately search for non-English studies. The titles and abstracts that did not mention the previous search terms were excluded. The references of included studies were assessed to identify more relevant literature. Any remaining study was included if it (a) had reported effect size in terms of relative risk (RR), odds ratio (OR), or hazard ratio (HR); (b) had a prospective cohort design; and (c) had only assessed BMI for participants 25 years of age or younger. Restrictions on publication date and language were not used.

Data extraction and analysis

Data from the following categories were extracted from the included studies: study name, year of publication, author, number of male and female participants, number of male and female cancer cases, age at BMI assessment, age at baseline, BMI comparison groups, methods of BMI collection (recall vs. measurements), effect sizes with 95% confidence intervals (95%CI), and adjusting confounding factors. All studies investigated the relationship between BMI (kilograms per meters squared) recorded or recalled before age 25 and risk of CRC above age 34. Variance between BMI comparison groups was concluded to be negligible. An analysis was conducted comparing overweight/obese and normal groups as all studies estimated risks by comparing CRC incidence in an obese group to that of a normal group. OR and HR were interpreted as RR in the final analysis.

Both contributors to this meta-analysis (HG and MS) individually searched for literature and identified extractable data while discussing study inclusion via voice calls and email. Study quality was determined using the 9-star Newcastle-Ottawa scale (12); scores per study are reported in Table 1. For studies that examined both cancer incidence and mortality, only the CRC incidence data were extracted. Growth charts provided by the United States Centers for Disease Control and Prevention (CDC) were used to derive the BMI comparison groups for studies that conducted analyses based on United States BMI percentiles (13).

Heterogeneity was assumed to be present as studies all analyzed different populations. The I^2 statistic also demonstrated moderate heterogeneity in men at 53.2% and low heterogeneity in women at 24.6% (< 25% low heterogeneity, 25 – 75% moderate heterogeneity, > 75% severe heterogeneity); therefore, a random effects model was used for data analysis. Evidence of publication bias was not identified after testing studies with Egger's regression intercept, Rosenthal's fail-safe n, and Begg's rank correlation. Men and women were analyzed separately because of the well established sex difference in the relationship between BMI and CRC (14, 15). Microsoft Excel™ (Microsoft Corp., Redmond, Washington, United States) and Comprehensive Meta-Analysis version 3 (Biostat, Englewood, New Jersey, United States) software programs were used to compile data and analyze statistical relationships (16). Confidence intervals were set at 95% and two-tailed *P*-values are presented in the results.

RESULTS

Following literature review, 15 studies (17 – 31) comprising more than 4.7 MM participants (around 3.2 MM men and 1.5 MM women) with 15 288 CRC cases were included in this meta-analysis (Figure 1, Table 1). The final analysis demonstrated a 39% increase in adulthood CRC risk for obese males in early-life (RR = 1.39; 95%CI = 1.20 – 1.62, $P < 0.0001$) and a 19% increase in adulthood CRC risk for obese females in early-life (RR = 1.19; 95%CI = 1.06 – 1.35; $P = 0.004$) when compared to controls (Table 2). Analysis of tumor sublocation (Table 3) also revealed that in men, an obese early-life BMI was more strongly associated with distal colon cancer (RR = 1.51; 95%CI = 1.22 – 1.87, $P < 0.0001$) and rectal cancer (RR = 1.39; 95%CI = 1.10 – 1.77; $P < 0.0001$) than proximal colon cancer (RR = 1.06; 95%CI = 0.97 – 1.17; $P < 0.0001$), whereas in women the association was stronger for rectal cancer (RR = 1.38; 95%CI = 0.94 – 2.03; $P = 0.009$) than proximal (RR = 1.08; 95%CI = 0.99 – 1.18, $P = 0.009$) and distal colon cancer (RR = 1.08; 95%CI = 0.98 – 1.19; $P = 0.009$) (P for heterogeneity = 0.22 and 0.22, respectively). Sensitivity analyses exhibited a relative risk range of 1.33 – 1.43 for males and 1.12 – 1.23 for females. Meta-regression was performed on all potential modifiers (Table 3).

DISCUSSION

Currently, this is the only meta-analysis investigating the association between early-life obesity and adulthood CRC incidence by comparing distinct groups of obese and non-obese individuals. This meta-analysis identified pooled, multivariable-adjusted relative risks of CRC and its subsites in men and women by comparing high versus low BMI categories in early-life, which were not identified by a previously published meta-analysis (10). Although all results regarding risk of CRC contain significant *P*-values, the confidence intervals for proximal colon cancer in men and all tumor sublocations in women include RRs at or

TABLE 1. Data extracted from studies included in a meta-analysis of early-life obesity and adulthood colorectal cancer risk

Author	Year	Age at BMI[a] assessment/ baseline age	No. of participants (men)	No. cases (men)	No. of participants (women)	No. cases (women)	BMI comparison groups	Study quality (out of 9)	Adjusted confounding factors
Jeffreys et al. (17)	2004	2 – 14 and 9 months / 58	2 347	38	0	0	Highest vs. lowest quartiles of BMI z-score	9	Age and sex
Bjørge et al. (18)	2008	14 – 19 / 51.9	114 977	97	111 701	108	> 25 to 18.5 – 23.5[b]	9	Age and birth year
Levi et al. (19)	2011	16 – 19 / 34.6	1 109 864	445	0	0	> 35 to < 18	9	Age at examination, year of birth, country of origin (grouped as Israel, Asia, Africa, Europe), urban or rural. place of residence, immigration status, years of schooling, socioeconomic status of the place of residence, and height
Kantor et al. (20)	2015	18 / 53.5	239 658	885	0	0	30 – < 55 to 15 – < 18.5	9	Erythrocyte volume fraction, age at conscription, erythrocyte volume fraction, household crowding, health status, systolic blood pressure, diastolic blood pressure, muscular strength, physical working capacity and cognitive function
Must et al. (21)	1992	13 – 18 / 53	508	6	0	0	> 25 to 18.5 – 23.5[b]	9	Body mass index and smoking status at the age of 53 years
Zhang et al. (22)	2015	m21,f18/m56,f55	34 533	808	75 238	1 180	27.5 – < 45 15 – < 19	8	Adult body mass index and other known colorectal cancer risk factors
Renehan et al. (23)	2011	18 / 62.8	168 294	2 070	105 381	962	> 30 to 18.5–21.9	8	Age, person years, race/ethnicity, educational level, physical activity level, smoking, alcohol consumption, family history of CRC, and among women, and menopausal hormone therapy use
Hughes et al. (24)	2011	20 / 36.5	58 279	1 211	62 573	1 106	23.7 – 31.8 to 11.8 – 19.8	8	Age, family history of CRC (yes/no), smoking status (never smoker, ex-smoker, or current smoker), socioeconomic status (educational level), total energy intake (kcal/day), alcohol intake (0, 0.1–4, 5–14, 15–29, or 30 g/day), recreational physical activity (90 minutes/day) for women, and occupational physical activity at the longest held job for men
Han et al. (25)	2014	25 / 54	6 332	151	7 569	147	> 30 to 18.5 – < 25	8	Race, age and height at baseline, education, cigarette smoking status at age 25, age at menarche, cigarette smoking, alcohol consumption and physical activity, menopause status and age at menopause, weight change from age 25 until baseline
Burton et al. (26)	2010	20 / 49	9 549	99	2 657	13	> 25 to 19 – 22.9	9	Smoking (none/any), father's social class (I, II/III, IV/V), height (continuous), age at menarche, and sex
Oxentenko et al. (27)	2010	18 / 55 – 69	0	0	36 941	1 464	> 40 to 18.5 – 24.9	8	Age at baseline, age at menopause, exogenous estrogen use, oral contraceptive use, smoking status, cigarette pack – years, physical activity level, self-reported diabetes mellitus, and intake of total energy, total fat, red meat, fruits and vegetables, calcium, folate, vitamin E, and alcohol
Kark et al. (28)	2017	16 – 19 / 40.6	1 087 358	1977	707 212	990	> 30 to 18.5 – 24.9	9	Birth year, sex, country of birth, and residential socioeconomic status
Jensen et al. (29)	2017	13 / 34	129 529	597	128 094	503	20.8 to 18.2[c]	7	None
Bassett et al. (30)	2010	20 / 40 – 69	221 606	189	332 977	211	> 25 to 18.5 – < 23	8	Education, processed and fresh meat consumption, fruit and vegetable consumption, fat intake, daily energy intake, smoking status, alcohol consumption, and county of birth
Win et al. (31)	2011	20 / 54	1 219	27	0	0	> 30 to 18.5 – < 25	8	Sex, country, cigarette smoking and alcohol drinking

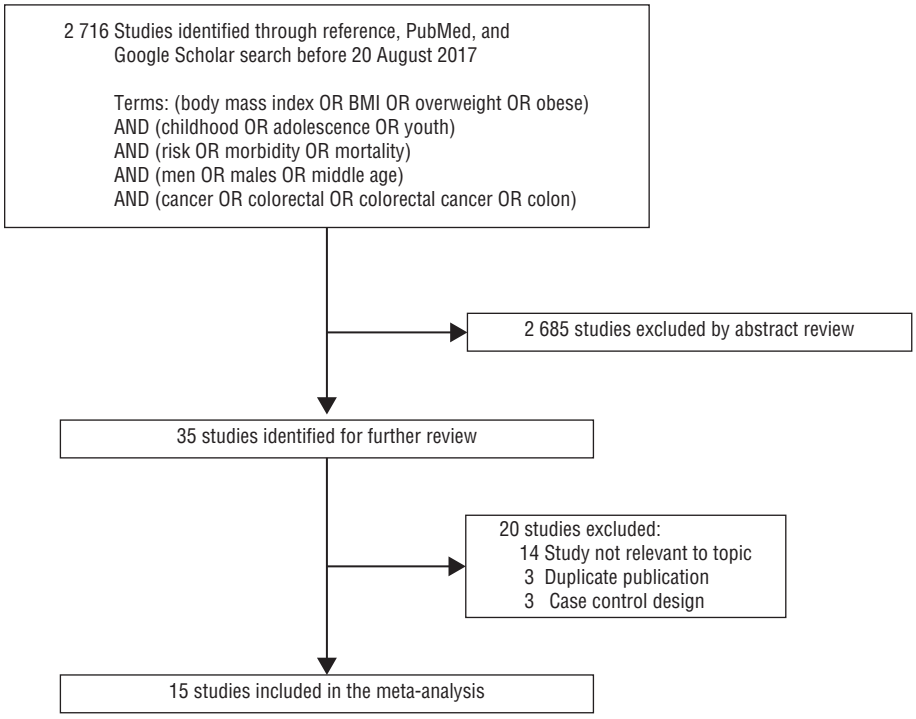
[a] Body Mass Index.

[b] BMI comparison groups derived from age at BMI assessment and CDC growth chart percentiles that were provided in the studies.

[c] BMI comparison groups derived from the median BMI and the BMI matched to 95th percentile using z-score equation.

Source: Prepared by the authors from study data and information extracted from previously published studies (17 – 31).

FIGURE 1. Section process for a meta-analyisis of studies on early-life obesity and adulthood colorectal cancer risk



Source: Prepared by the authors from study data.

below 1. Therefore, such results should be interpreted cautiously: despite the significant *P*-values created by the large total population included in the final analysis, the confidence interval suggests that there may not be increased risk for the aforementioned cancer sublocations in men and women.

Meta-regression also revealed that there were no significant differences between the ages at which participants were assessed for early-life BMI, the methods of early-life BMI assessment, and adjustment for smoking, demonstrating that none of these factors modifies the results of this meta-analysis (Table 3).

All studies included were conducted robustly according to the assessment using the 9-star Newcastle-Ottawa scale, suggesting that the quality of the individual studies should not confound the results of this review (12). Although around half of the studies did not attain perfect scores due to their methods of recalling early-life BMI, meta-regression demonstrated that there was no significant difference in CRC risk between studies that used recall methods and those that used pre-recorded data (P = 0.49 and 0.84 for men and women, respectively).

Increased risks for distal cancer and rectal cancer among obese individuals can be attributed to increased rates of such cancers among all individuals less than 55 years of age (32). Possibilities for the source of increased risk of CRC in obese individuals include insulin resistance and inflammatory cytokines (33 – 38). Obesity has been associated with hyperinsulinemia, an oversupply of insulin circulating in blood caused by insulin resistance (33, 34). It has been suggested that hyperinsulinemia is associated with decreased production of proteins that inhibit insulin-like growth factor-1 (IGF1), a protein that may induce carcinogenesis (33, 34). Analysis of CRC tumors has shown increased IGF1 expression in metastasized cells (34). Hyperinsulinemia is also related to diseases such as type II diabetes and metabolic syndrome, both of which are associated

TABLE 2. Relative risks (RR) of late life colorectal cancer (CRC) in early-life obese males and females

Authors of male studies	Study RR (95% Confidence Interval)	Study weight[a]	*P*-value	Authors of female studies	Study RR (95% Confidence Interval)	Study weight[a]	*P*-value
Jeffreys et al. (17)	1.36 (0.57 – 3.24)	2.62	0.49	Bjørge et al. (18)	2.00 (1.20 – 3.50)	4.64	0.73
Bjørge et al. (18)	2.10 (1.10 – 4.10)	4.11	0.03	Zhang et al. (22)	1.44 (1.06 – 1.95)	12.43	0.02
Levi et al. (19)	1.53 (1.17 – 2.00)	11.34	< 0.01	Renehan et al. (23)	1.44 (0.89 – 2.34)	5.60	0.14
Kantor et al. (20)	2.55 (1.44 – 4.61)	4.93	< 0.01	Hughes et al. (24)	1.12 (0.87 – 1.43)	17.02	0.37
Must et al. (21)	9.10 (1.08 – 76.38)	0.50	0.04	Han et al. (25)	1.10 (0.44 – 2.78)	1.64	0.84
Zhang et al. (22)	1.18 (0.84 – 1.65)	9.41	0.34	Burton et al. (26)	1.23 (0.15 – 10.07)	0.32	0.85
Renehan et al. (23)	1.48 (1.08 – 2.03)	9.99	0.02	Oxentenko et al. (27)	0.46 (0.07 – 3.23)	0.39	0.42
Hughes et al. (24)	1.21 (0.93 – 1.56)	11.62	0.15	Kark et al. (28)	1.52 (0.90 – 2.59)	4.75	0.12
Han et al. (25)	1.65 (0.87 – 3.11)	4.31	0.12	Jensen et al. 29)	1.08 (0.98 – 1.19)	44.85	0.12
Burton et al. (26)	1.25 (0.60 – 2.61)	3.45	0.56	Bassett et al. (30)	1.07 (0.73 – 1.58)	8.36	0.73
Kark et al. (28)	1.52 (1.13 – 2.04)	10.55	0.01	Overall RR	1.19 (1.06 – 1.35)	100	0.004
Jensen et al. (29)	1.06 (0.97 – 1.16)	16.47	0.20				
Bassett et al. (30)	1.21 (0.88 – 1.67)	9.86	0.24				
Win et al. (31)	3.00 (0.06 – 14.97)	0.85	0.18				
Overall RR	1.39 (1.20 – 1.62)	100	< 0.0001				

[a] Adjusted study weight as a percent of 100.

Source: Prepared by the authors from study data.

TABLE 3. Meta-regression analysis on potentially confounding factors in included studies on early-life obesity and adulthood colorectal cancer risk

Modifier	Subgroup	Men				Women			
		No. of participants	Relative risks	No. of studies	*P* value	No. of participants	Relative risks	No. of studies	*P* value
Age at assessment of body mass index (BMI)									
	Adolescence	2 887 030	1.49 (1.18 – 1.87)	8	0.56[a]	1 015 925	1.36 (1.08 – 1.28)	5	0.28[a]
	Early adulthood	229 332	1.26 (1.06 – 1.51)	6		442 717	1.11 (0.90 – 1.34)	5	
Methods of BMI assessment									
	Recalled adolescent/early adulthood BMI	490 263	1.29 (1.11 – 1.50)	6	0.49[a]	583 738	1.22 (1.04 – 1.44)	5	0.84[a]
	BMI measured in adolescence/ early adulthood	2 752 661	1.54 (1.17 – 2.02)	8		2 746 329	1.31 (0.94 – 1.83)	5	
Cancer location									
	Proximal colon	187 808	1.06 (0.97 – 1.17)	2	0.22[a]	227 608	1.08 (0.99 – 1.18)	3	0.22[a]
	Distal colon	1 168 143	1.51 (1.22 – 1.87)	2	< 0.001[b]	227 608	1.08 (0.98 – 1.19)	3	0.01[b]
	Rectum	2 263 453	1.39 (1.10 – 1.77)	8		875 116	1.38 (0.94 – 2.03)	3	
Adjustment for smoking									
	Yes	456 238	1.35 (1.12 – 1.63)	6	0.98[a]	568 154	1.14 (0.95 – 1.37)	5	0.47[a]
	No	2 727 815	1.42 (1.14 – 1.78)	8		1 002 189	1.35 (1.05 – 1.75)	5	

[a] P values from meta-regression analysis.
[b] P values from analysis of the three tumor sublocations.
Source: Prepared by the authors from study data.

with increased rates of CRC and have been increasing rapidly among obese youth (35). Early-life obesity can contribute to expression of IGF1 earlier in life than those with normal BMIs, leading to increased incidence of CRC among individuals who have been obese since childhood.

Excess adipose tissue may produce large amounts of tumor necrosis factor alpha, resistin, and interlukin-6; all of which have been found to induce inflammation and have been found in higher concentrations among individuals with CRC than in cancer free controls (36 – 38). Thus, individuals who have been obese as youth experience inflammation earlier than their non-obese counterparts, decreasing the time required for CRC pathogenesis in obese individuals (36 – 39). Excess adipose tissue may indicate a carcinogenic diet, as well as induce carcinogenesis itself because obese individuals typically consume large amounts of foods associated with CRC pathogenesis (40 – 44). High consumption of processed red meat, eggs, and refined sugar has been positively associated with increased rates of CRC (45 – 47). Such foods are typically consumed in larger amounts by obese individuals than by those with normal BMIs. Heterocyclic amines and nitrates found in processed meats have been shown to be associated with CRC pathogenesis in numerous studies (45, 48). Those who have obese early-life BMIs would thus consume a larger volume of such mutagens than people with normal early-life BMIs, which would lead to increased CRC rates.

Limitations. Studies that asked participants to recall their childhood BMI at baseline could have skewed results as this design is susceptible to recall bias, but this bias has been shown to be insignificant by meta-regression. All studies included in this analysis had checked hospital, national health service, and death certificate records, and followed up with participants to identify those who developed CRC in adulthood; therefore, the standardized methods of cancer screening programs in all studies should not have skewed the overall results.

Caution should be used when interpreting the outcomes of this analysis as diet may confound the association between the physical presence of excess adipose tissue and increased CRC rates. The participants in all studies resided in developed, Western countries, where diets differ significantly from those of other regions. Some studies also did not adjust for dietary factors, such as consumption of processed red meat and refined carbohydrates.

The authors believe the search strategy for English and non-English articles was adequate as all languages available in the filter section of PubMed and Google Scholar were included. However, since all the studies found through the search were in English, there may be other non-English publications analyzing non-Western populations that were not included in this review; therefore, the results of this analysis should only be applied to those living in Western countries.

Conclusions

A strong relationship exists between high early-life BMI and increased CRC incidence in adulthood. Similar relationships have also been identified between high early-life BMI and increased risk of distal and rectal cancer in men, and rectal cancer in women. Future research should adjust for diet and analyze non-Western populations to better and more comprehensively characterize the impacts of early-life adiposity on CRC risk in adulthood. The cellular and molecular mechanisms of CRC pathogenesis should also be identified to better understand how an accumulation of excess adipose tissue throughout life contributes to carcinogenesis.

Future studies should analyze other populations, identify the mechanisms of how adipose tissue induces carcinogenesis, and adjust for diet in order to limit factors that may confound the relationship between excess adipose tissue in early-life and CRC risk in adulthood.

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RESUMEN

Obesidad a edad temprana y riesgo de cáncer colorrectal en el adulto: metanálisis

Objetivo. En este metanálisis se examina la relación entre la obesidad a edad temprana y el riesgo de cáncer colorrectal en la edad adulta.

Métodos. Se llevó a cabo una búsqueda sistemática en Google Scholar, PubMed y datos de referencia. Se seleccionaron 15 estudios pertinentes y se realizó un metanálisis de esos estudios (hombres y mujeres por separado). Se usó un modelo de efectos aleatorios para comparar los riesgos relativos (RR) ajustados por multivariantes de tener cáncer colorrectal en las categorías de personas con mayor y menor índice de masa corporal (IMC) a edad temprana. Se realizó una metarregresión de los factores que pueden haber contribuido con la heterogeneidad entre estudios.

Resultados. Un IMC alto a edad temprana está asociado con un aumento de 39% del riesgo de cáncer colorrectal en los hombres adultos (RR = 1,39, IC de 95% 1,20 – 1,62, $P < 0{,}0001$) y un aumento de 19% del riesgo de cáncer colorrectal en las mujeres adultas (RR = 1,19, IC de 95% 1,06 – 1,35, $P = 0{,}004$). En la metarregresión no se encontró una heterogeneidad estadísticamente significativa por subsitio tumoral (RR = 1,06, IC de 95% 0,97 – 1,17, RR = 1,08, IC de 95% 0,99 – 1,18 para cáncer de colon proximal masculino y femenino; RR = 1,51, IC de 95% 1,22 – 1,87, RR = 1,08, IC de 95% 0,98 – 1,19 para cáncer de colon distal masculino y femenino; y RR = 1,39, IC de 95% 1,1 – 1,77, RR = 1,51, IC de 95% 0,94 – 2,03 para cáncer rectal masculino y femenino) u otros factores, incluidos edad de la evaluación del IMC, IMC notificado o medido por la propia persona y ajuste por tabaquismo.

Conclusiones. Los resultados indican que un IMC alto a edad temprana está asociado con un mayor riesgo de cáncer colorrectal en la edad adulta. Deben realizarse otros estudios para investigar el riesgo de cáncer colorrectal en el adulto en las personas obesas a edad temprana de países no occidentales, así como los mecanismos subyacentes por los cuales la adiposidad a edad temprana puede influir en la patogénesis del cáncer colorrectal.

Palabras clave Neoplasias colorrectales; neoplasias del recto; obesidad; índice de masa corporal; metaanálisis.

RESUMO

Obesidade no início da vida e risco de câncer colorretal na vida adulta: uma meta-análise

Objetivo. Examinar a relação entre a obesidade no início da vida e o risco de câncer colorretal na vida adulta.

Métodos. Foi realizada uma busca sistemática nas bases de dados do Google Scholar e PubMed e em dados de referência. Quinze estudos relevantes foram identificados e foi realizada uma meta-análise em separado para homens e mulheres. Um modelo de efeitos aleatórios foi usado para comparar os riscos relativos (RR) ajustados para multivariáveis de câncer colorretal de modo geral e específico ao subsítio às faixas superiores e inferiores de índice de massa corporal (IMC) no início da vida. Foi realizada uma análise de metarregressão dos fatores que possivelmente contribuíram para a heterogeneidade entre os estudos.

Resultados. IMC alto no início da vida foi associado a um aumento de 39% no risco de câncer colorretal em homens adultos (RR 1,39, IC 95% 1,20–1,62, $P < 0,0001$) e um aumento de 19% no risco de câncer colorretal em mulheres adultas (RR 1,19, IC 95% 1,06–1,35, $P = 0,004$). Heterogeneidade estatisticamente não significativa foi identificada na análise de metarregressão segundo subsítio tumoral (RR 1,06, IC 95% 0,97–1,17; RR 1,08, IC 95% 0,99–1,18 para o câncer de cólon proximal no sexo masculino e no sexo feminino; RR 1,51, IC 95% 1,22–1,87; RR 1,08, IC 95% 0,98–1,19 para o câncer de cólon distal no sexo masculino e no sexo feminino; e RR 1,39, IC 95% 1,1–1,77; RR 1,51, IC 95% 0,94–2,03 para o câncer retal no sexo masculino e no sexo feminino) e outros fatores, como idade na avaliação do IMC, IMC autorrelatado ou medido e ajuste para tabagismo.

Conclusões. Os resultados do estudo indicam que um IMC alto no início da vida está associado ao aumento do risco de câncer colorretal na vida adulta. Outros estudos devem ser realizados para investigar o risco de câncer colorretal na vida adulta em indivíduos obesos no início da vida em países não ocidentais assim como pesquisar os mecanismos subjacentes pelos quais a adiposidade no início da vida pode influir na patogênese do câncer colorretal.

Palavras-chave Neoplasias colorretais; neoplasias retais; obesidade; índice de massa corporal; metanálise.