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Adult weight change and risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition ☆

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Abstract ***Aim:*** Weight change during adult life may reflect metabolic changes and influence colorectal cancer (CRC) development, but such role is not well established. We aimed to explore the association between adult weight change (from age 20 to 50) and CRC risk. In particular, we investigated differences according to colon and rectal cancer, sex and measures of attained adiposity.
Methods: We included 201,696 participants from six participating countries in the European Prospective Investigation into Cancer and Nutrition (1992–2010). During a mean follow-up of 11.2 years 2384 (1194 in men and 1190 in women) incident CRC cases occurred. Cox proportional hazard models adjusted for body mass index at age 20 and lifestyle factors at study recruitment were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs).
Results: After multivariable adjustment, each kg of weight gained annually from age 20 to 50 was associated with a 60% higher risk of colon cancer (95% CI 1.20–2.09), but not rectal cancer (HR 1.13, 95% CI 0.79–1.62, $P_{\text{interaction}} = 0.04$). The higher risk of colon cancer was restricted to people with high attained waist circumference at age 50 (HR 1.82, 95%CI 1.14–2.91, $P_{\text{interaction}} = 0.02$). Results were not different in men and women ($P_{\text{interaction}} = 0.81$).
Conclusion(s): Adult weight gain, as reflected by attained abdominal obesity at age 50, increases colon cancer risk in both men and women. These data underline the importance of weight management and metabolic health maintenance in early adult life years for colon cancer prevention.

1. Introduction

Colorectal cancer (CRC) is the third most common cancer in men (663,000 cases, 10.0% of the total) and the second in women (570,000 cases, 9.4% of the total) worldwide and prevention strategies for reducing cancer-associated burden are highly demanded.[1] Excess body weight has been identified as one of the modifiable lifestyle factors convincingly related to CRC risk.[2] However, an important question still to be answered is whether fluctuations in weight over time may also contribute to CRC risk. Weight change in different life periods can be regarded as a dynamic measure reflecting different health outcomes. History of weight gain in middle life may be indicative of the formation of metabolic processes or diet-lifestyle characteristics that are not reflected adequately by a static measure of body fatness like body mass index (BMI).[3] Middle life weight gain, even among those with initially healthy weight, has been related to a higher chronic disease risk and a reduced probability of healthy survival in older ages.[4] Since the year 2000, when the International Agency for Research on Cancer judged that evidence in support of the association between weight change and risk of CRC is limited,[5] a number of prospective cohort[6–9] and case-control studies[10–13] have explored these associations. However, the evidence remains inconclusive about whether associations may be different by colon and rectal cancer, sex and measures of attained adiposity. Current research indicates that the relation between obesity and CRC incidence is stronger for cancer of the colon than cancer of the rectum[14]; but it is not clear if this is true also with regard to weight change, as most of the studies to date have been of small sample size and did not report results by cancer site. Also, studies observed these associations to be present either in men only[18,22,25] or in women[15,16]; while the few studies combining data for men and women did not evaluate whether differences by sex were statistically significant. Finally, the potential influence of body size at young and late adult age on the association between weight change in middle life and CRC risk has not been sufficiently evaluated. Some studies have questioned whether weight change may be associated with disease incidence beyond its effect on attained adiposity.[17] In particular, it is of interest to explore whether the associations may be modified by attained abdominal obesity as measured by waist circumference (WC) which is more closely related to metabolic changes compared to general obesity as determined by BMI.[18] To help clarify this evidence, we prospectively investigated the association between adult weight change (from age 20 to 50) and CRC risk in a large prospective study within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort.

2. Methods

2.1. Study population and collection of data

EPIC is a large prospective cohort study with approximately 520,000 participants enrolled between 1992 and 1998 from 23 centres in 10 European countries. The present analysis is based on participant data from study centres in Denmark, Germany (Potsdam), Greece, Italy (Naples,Varese), Sweden (Malmö) and the United Kingdom, with available information on recalled body