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Associations of body mass index with cancer incidence among populations, genders, and menopausal status: A systematic review and meta-analysis

Jun Wang*, Dong-Lin Yang, Zhong-Zhu Chen, Ben-Fu Gou*

International Academy of Targeted Therapeutics and Innovation, Chongqing University of Arts and Sciences, 319 Honghe Avenue, Yongchuan District, Chongqing 402160, China

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ABSTRACT

In order to further reveal the differences of association between body mass index (BMI) and cancer incidence across populations, genders, and menopausal status, we performed comprehensive meta-analysis with eligible citations. The risk ratio (RR) of incidence at 10 different cancer sites (per 5 kg/m^2 increase in BMI) were quantified separately by employing generalized least-squares to estimate trends, and combined by meta-analyses. We observed significantly stronger association between increased BMI and breast cancer incidence in the Asia–Pacific group (RR 1.18:1.11–1.26) than in European–Australian (1.05:1.00–1.09) and North-American group (1.06:1.03–1.08) (meta-regression $p < 0.05$). No association between increased BMI and pancreatic cancer incidence (0.94:0.71–1.24) was shown in the Asia–Pacific group (meta-regression $p < 0.05$), whereas positive associations were found in other two groups. A significantly higher RR in men was found for colorectal cancer in comparison with women (meta-regression $p < 0.05$). Compared with postmenopausal women, premenopausal women displayed significantly higher RR for ovarian cancer (pre- vs. post- = 1.10 vs. 1.01, meta-regression $p < 0.05$), but lower RR for breast cancer (pre- vs. post- = 0.99 vs. 1.11, meta-regression $p < 0.0001$). Our results indicate that overweight or obesity is a strong risk factor of cancer incidence at several cancer sites. Genders, populations, and menopausal status are important factors effecting the association between obesity and cancer incidence for certain cancer types.

Contents

* Corresponding authors.
E-mail addresses: minxian.student@sina.com (J. Wang), benfugou@163.com (B.-F. Gou).

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1. Introduction

Overweight [body mass index (BMI): 25.0–29.9 kg/m^2] and obesity (BMI >30.0 kg/m^2) are defined by the World Health Organization (WHO) as abnormal and excessive fat accumulation. Approximately 2.3 billion adults are overweight and more than 700 million are obese globally. Obesity and overweight have become a global problem, and have numerous harmful consequences for an individual's health. Overweight and obesity are major risks factors of many chronic diseases, including diabetes [1] and cardiovascular diseases [2,3]. The medical costs associated with overweight and obesity have become great burdens to society [4].

The association between body weight and cancer has been extensively studied during the past several decades [5]. Numerous epidemiologic studies suggested that overweight and obesity are risk factors for several types of cancer [6–14]. Epidemiological studies showed that men often suffer from upper body obesity, while women are prone to leg fatness [15]. Different BMI distributions were also observed across regions and populations [16]. For instance, highest BMIs were observed in some Oceania countries and lower BMIs were found in a few countries in East, South, and Southeast Asia. USA had the highest BMI among developed countries. The above facts pose the existence of heterogeneity between sexes and cross populations regarding to association of BMI and cancer incidence. In 2008, Renehan et al. published a landmark meta-analysis [17], which systematically reported the association between cancer incidence and increased BMI for many cancer types in males and females, respectively, and simultaneously compared the estimates among different populations. They observed significantly stronger association between increased BMI and colon cancer incidence in men than in women, and recorded stronger associations in Asia–Pacific populations between increased BMI and breast cancer risk. But comparisons across populations and genders for many other cancer types were not reported in Renehan's work due to limited datasets. Since 2007, large number of high-quality epidemiological studies have been published. Here, to update associations of BMI–cancer incidence and further reveal the differences among populations, genders, and menopausal status, we performed a standardized and comprehensive meta-analysis with the most updated databank to quantify the risk ratio (RR) (per 5 kg/m^2 BMI increase) for the incidence of 10 common cancer types.

2. Methods

2.1. Literature searching strategy

An extensive literature search with no language restriction was performed in PubMed, Medline, and Emabase (from Jan 1985 to Jan 2015) for studies focusing on the association between BMI and cancer incidence by three independent investigators (JW, DLY, and BFG). The reference lists of the selected studies were also reviewed for additional relevant studies. The bodyweight-related terms ("obesity", "BMI", "adiposity", and "body size") in combination with specific terms for the cancer site (breast, colon, lung, liver, pancreas, thyroid, prostate, ovarian, renal, or esophagus and gastric cancer) were used as keywords in the searches.

2.2. Inclusion criteria

The following inclusion criteria were used to identify the eligibility of each retrieved study: a full-published cohort study or case-control study on cancer incidence, not mortality; reported gender-specific risk estimates (relative risks, odds ratios, or hazard ratios) with a 95% confidence interval (CI); at least three BMI categories; contained information about the number of cases and person years for cohort studies or cases and controls for case-control studies, or it at least provided sufficient information to calculate these values; and self-reported or directly measured height and weight for BMI calculation. The inclusion analysis was performed independently by three investigators (JW, DLY, and ZZC).

2.3. Data extraction

Data extraction was conducted by JW followed by two rounds of quality assessments by DLY and BFG. The following information was extracted: author and publication year, study design (cohort or case-control studies), gender, population (North-American, Asia–Pacific, and European–Australian), most adjusted risk estimates and their 95% CIs with the corresponding BMI categories, cases and person years or controls plus cases, years of follow-up (>10 or <10 years), and assessment of anthropometry (measured or self-reported). The values assigned to the closed BMI and left-bound opened BMI category were the mid-point and median (assuming a normal BMI distribution), respectively. For the right-bound opened BMI category, we took the mid-point and predicted that it has the same span as its most adjacent BMI category [18].

2.4. Statistical analysis

Based on the assumption of a linear correlation between the natural logarithm of RR and increasing BMI, estimates of the RR (per 5 kg/m^2 increase) in BMI were obtained using the generalized least-squares method for trend estimation [19]. The meta-analysis was performed to combine the RRs (per 5 kg/m^2 increase) in random effect [20]. Besides 95% confidence intervals(CIs), 95% predictive intervals (PIs) were also calculated to give the true variation of RRs. We compared the results between the random-effects and fixed-effects model to analyze the sensitivity. I-squared statistic was used to indicate the proportion of heterogeneity between studies in total variation; the cut-off points for low, moderate, and high degrees of heterogeneity were 25%, 50%, and 75%, respectively. For each cancer site, subgroup analysis and meta-regression analysis were conducted to identify the influential factors affecting the association of BMI increase and cancer incidence that contributed to heterogeneity between the studies [21]. Adjusted R-squared was shown to explain