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Review Article

Increased total iron and zinc intake and lower heme iron intake reduce the risk of esophageal cancer: A dose–response meta-analysis

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ABSTRACT

Several epidemiological studies investigated the relationship between dietary intake of essential trace elements and the risk of esophageal cancer (EC), yielding inconsistent results. We therefore conducted a systematic meta-analysis to investigate and quantify the putative association between the intake of various essential trace elements and the risk of EC. We searched Embase, PubMed, and Web of Science for eligible articles published through April 2018 reporting the odds ratio (OR) with 95% confidence interval (95% CI). Pooled results were then calculated using fixed and random effect models. A total of 20 articles containing 4855 cases from 1 387 482 participants were included in our analysis. We found a significant inverse correlation between total iron intake and the risk of EC (OR = 0.81, 95% CI: 0.70–0.94), particularly in Asian populations. A dose–response analysis revealed that each 5 mg/day increase in total iron intake was associated with a 15% reduction in EC risk (OR = 0.85, 95% CI: 0.79–0.92). In contrast, each 1 mg/day increase in heme iron intake was associated with a 21% increase in EC risk (OR = 1.21, 95% CI: 1.02–1.45). Lastly, a pooled risk estimate revealed that each 5 mg/day increase in zinc intake was associated with a 15% reduction in EC risk (OR = 0.85, 95% CI: 0.77–0.93). Taken together, our analysis indicates that increased dietary intake of total iron and zinc, as well as decreased heme iron intake, may be associated with a lower risk of developing esophageal cancer. These findings have important public health implications with respect to preventing this relatively common form of cancer.

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Abbreviations: BMI, body mass index; CI, confidence interval; DHQ, Dietary History Questionnaire; EAC, esophageal adenocarcinoma; ESCC, esophageal squamous cell cancer; FFQ, Food Frequency Questionnaire; HBCC, hospital-based case–control; HR, hazard ratio; N/A, not available; NOS, Newcastle-Ottawa Scale; NSAID, nonsteroidal anti-inflammatory drug; OR, odds ratio; PBCC, population-based case–control; RR, relative risk.

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Article Outline

1. Introduction

Cancer is the second leading cause of death. Cancer currently accounts for approximately 24% of all deaths worldwide and is expected to surpass heart disease as the leading cause of death within the next several years [1]. Currently, esophageal cancer (EC) is the eighth most common form of cancer worldwide and the sixth leading cause of cancer-related death [2], contributing to significant burden associated with global mortality. Unfortunately, this burden is estimated to rise significantly in the coming decades [3]. Fortunately, however, recent evidence suggests that cancer is largely a preventable disease and that the risk of cancer can be substantially reduced by changes in diet [4]. Therefore, many studies now focus on the role of diet in the cause, prevention, and control of EC; moreover, the putative association between the risk of EC and several dietary factors such as the intake of vitamins, minerals, fruits, vegetables, meats, fats, and salted foods has been thoroughly evaluated [5-8].

Iron, zinc, copper, and selenium are essential trace elements that play important roles in a wide range of key physiological functions, including nucleic acid synthesis, protein synthesis, oxygen transport, cellular respiration, enzyme production and function, and other biological processes [9-12]. Thus, an imbalance in any of these micronutrients can cause a variety of diseases states, including oxidative stress, metabolic disease, and even cancer [11-13].

In recent years, a growing number of epidemiological studies investigated the association between dietary intake of trace elements and the risk of EC, yielding inconsistent results. A recent meta-analysis revealed a correlation between zinc intake and the risk of digestive tract cancers [14]; however, other trace minerals, including iron, copper, and selenium, were not included in this analysis. Moreover, to the best of our knowledge, no meta-analysis has examined the putative association between the intake of various trace elements and the risk of EC. Therefore, we conducted a systematic meta-analysis in order to investigate this association. In addition, we conducted a systematic review of other essential trace elements, including manganese, chromium, cobalt, fluorine, and bromine; however, an insufficient number of epidemiological studies have been published, precluding such an analysis regarding these elements. Thus, we focused this meta-analysis on examining the association between dietary intake of iron, zinc, selenium, and copper and the risk of EC.

2. Approach

2.1. *Search strategy*

This meta-analysis was designed, implemented, and analyzed in accordance with the Meta-analysis of Observational Studies in the Epidemiology (MOOSE) protocol [15] and is reported in accordance with PRISMA guidelines [16].

We systematically searched PubMed, Embase, and Web of Science for relevant epidemiological studies published through April 2018. The search strategy included the following MeSH terms and relevant keywords: (Iron[MeSH] OR Fe[tx] OR Zinc[MeSH] OR Zn[tx] OR Selenium[MeSH] OR Se[tx] OR Copper[MeSH] OR Cu[tx]) AND (Esophagus[MeSH] OR

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