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Review Article

Pancreatic cancer: A critical review of dietary risk



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ABSTRACT

Pancreatic cancer is a deadly disease. It is estimated that about 90% of pancreatic cancer cases are due to environmental risk factors. Among these, approximately 50% of pancreatic cancer cases may be attributed to diet, which is largely modifiable. Given this large attribution to diet, there have been numerous epidemiological studies assessing the risk of various dietary factors on the incidence of pancreatic cancer. However, many of these studies present conflicting and/or inconclusive findings. The objective of this review is two-fold: (a) to summarize the current evidence on the association between various dietary factors and the risk of developing pancreatic cancer and (b) to discuss what additional studies are needed to better elucidate the role of diet as a potential risk factor for pancreatic cancer. We summarized the evidence by using data primarily from meta-analyses and pooled analysis when available, focusing on the most studied nutrients, foods, and dietary patterns. We observed that, while the association between individual nutrients and pancreatic cancer risk have been heavily studied, the evidence is mostly conflicting and inconclusive. In contrast, the evidence of certain associations among dietary patterns and pancreatic cancer risk is clearer, has more power, and is less conflicting. Therefore, we propose a shift in the focus of nutritional epidemiological research with regards to pancreatic cancer risk. We discourage further epidemiological research studies that focus on single nutrients, whereas we strongly encourage additional studies that investigate how a combination of diet and other lifestyle factors may promote or prevent pancreatic carcinogenesis.

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Article Outline

1. Introduction	2
2. Approach	2
3. Findings.	2
3.1. Nutrients and pancreatic cancer risk	2
3.1.1. Vitamin C	3
3.1.2. Folate (vitamin B9)	3
3.1.3. Vitamin E	4
3.1.4. Retinoids and carotenoids	4

Abbreviations: HCAs, Heterocyclic amines; AGE, Advanced glycation end products; NOCs, N-nitroso compounds; MD, Mediterranean diet.
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3.1.5. Vitamin D	5
3.1.6. Selenium	5
3.1.7. Lipids	5
3.1.8. Discussion: nutrients and pancreatic cancer risk	6
3.2. Foods and pancreatic cancer risk	6
3.2.1. Red and processed meat	6
3.2.2. Dairy products	7
3.2.3. Fruits and vegetables	7
3.2.4. Whole grains	7
3.2.5. High glycemic foods	7
3.2.6. Alcoholic beverages	8
3.2.7. Discussion: foods and pancreatic cancer risk	8
3.3. Dietary patterns and pancreatic cancer risk	8
3.3.1. Western-style dietary pattern	8
3.3.2. Prudent or healthy dietary pattern	8
3.3.3. Healthy Eating Index	8
3.3.4. Mediterranean Diet	9
3.3.5. Discussion: dietary patterns and pancreatic cancer risk	9
4. Conclusion	9
5. Knowledge gaps and future research directions	9
Acknowledgment	10
References	10

1. Introduction

Pancreatic cancer, currently the fourth leading cause of cancer death worldwide [1], is projected to become the 2nd by 2030 [2]. With a 5-year survival rate of approximately 8% [1] and an average survival time of 6 months for those with advanced metastasized disease [3], pancreatic cancer is one of the most fatal malignancies with an extremely dismal prognosis. This exceedingly short survival time, however, is counterbalanced with what research shows to be a very slow evolution lasting up to 18 years from the time of initiating mutations in pre-cancerous lesions to metastatic disease [4]. This dichotomy between a slow progression and rapid fatality strongly suggests that prevention should be a key emphasis in reducing pancreatic cancer burden.

Like many cancers, pancreatic cancer is considered to have a large environmental attributable risk [5]. It is estimated that only 5% to 10% of pancreatic cancer cases are hereditary, and the remaining 90% to 95% are due to environmental risk factors, which are largely modifiable [6]. Of those risk factors, smoking, alcohol, obesity, diet, and physical inactivity have been the most studied, and numerous studies have shown them to be associated with increased risk. Of these, smoking and obesity are the most well established to have a causal relationship, with estimates that these factors are significant triggers in approximately 33% and 16% percent of pancreatic cancer cases, respectively [7]. However, diet may have the largest attribution of cases; some have estimated that approximately 50% of pancreatic cancer cases may be attributed to diet [8,9].

Given this large attribution to diet, there have been numerous epidemiological studies assessing the risk of various dietary factors on the incidence of pancreatic cancer. However, many of these studies showed conflicting and/or inconclusive findings. The objective of this review is 2-fold: (a)

to summarize the current evidence on the association between various dietary factors and the risk of developing pancreatic cancer and (b) to discuss what additional studies are needed to better elucidate the role of diet as a potential risk factor for pancreatic cancer. Moreover, we point out some of the challenges and limitations of the research and emphasize the need for future research to include well-designed and carefully carried out clinical trials on dietary patterns to better guide us to elucidate how diet may influence the incidence of pancreatic cancer.

2. Approach

Using PubMed, we searched for meta-analyses or pooled analyses of epidemiological studies assessing the association between nutrients, diets, or dietary patterns and pancreatic cancer between 2010 and August 2017. When a large cohort study conducted after a meta-analysis was found, this was referenced as well. Search parameters used were “nutrients” or “vitamin” or “vitamin C” or “vitamin D” or “vitamin E” or “selenium” or “folate” or “cholesterol” or “fat” or “vitamin A” or “diet” or “dietary pattern” or “red meat” or “fruits and vegetables” or “whole grains” or “high glycemic” or “dairy” or “Mediterranean diet” or “alcohol” and “pancreatic cancer.”

3. Findings

3.1. Nutrients and pancreatic cancer risk

Multiple micro and macro nutrients have been assessed epidemiologically for their association with the incidence of pancreatic cancer (Table 1). Among the vitamins, those with a

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