REVIEW ARTICLE

Periodontal Health and Cancer Risk: An Overview

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ABSTRACT

Periodontal disease, which includes gingivitis and periodontitis, is highly prevalent in adults and disease severity increases with age. The relationship between periodontal disease and oral cancer has been examined for several decades, but there is increasing interest in the link between periodontal disease and overall cancer risk, with systemic inflammation serving as the main focus for biological plausibility. Numerous case–control studies have addressed the role of oral health in head and neck cancer, and several cohort studies have examined associations with other types of cancers over the past decade. Existing data provide support for a positive association between periodontal disease and risk of oral, lung, and pancreatic cancers; however, additional prospective studies are needed to better inform on the strength of these associations and to determine whether other cancers are associated with periodontal disease. Future studies should include sufficiently large sample sizes, improved measurements for periodontal disease, and thorough adjustment for smoking and other risk factors.

Keywords: Cancer, Oral cancer, Periodontal disease, Periodontitis.

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INTRODUCTION

There has been a rapid increase in interest in understanding the relationship between periodontal disease and cancer risk; twice as many original observational studies were published with measures of periodontal disease. The reason for the large increase in publications on this topic is largely due to new interest generated by the research on the human microbiome and perhaps also due to the development of animal models of periodontal disease that has enabled researchers to measure the impact of periodontal pathogens on the local and systemic immune response.[1] Human studies have confirmed the impact of periodontal disease on the systemic immune response, demonstrating that levels of serum markers of inflammation, especially C-reactive protein, increase with advanced periodontal disease.[2,3] The link between systemic inflammation and cancer is well established and may contribute to the strong and consistent positive associations between obesity and cancer.[4] Interest in the role of inflammation on cancer, as well as the many parallels that exist between risk factors for heart disease and cancer (e.g., smoking, obesity, lack of physical activity, insulin resistance, and diabetes)[5] has motivated different lines of research to address the role of periodontal disease in cancer risk.

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PERIODONTAL DISEASE AND CANCER

Periodontal disease, also known as gum disease, encompasses gingivitis and periodontitis. Gingivitis, or inflammation of the gums which leads to bleeding gums, is considered an early form of periodontal disease. Periodontitis develops over time with accumulation of dental plaque, bacterial dysbiosis, formation of periodontal pockets, gum recession, tissue destruction, and alveolar bone loss, which can ultimately lead to tooth loss. Although periodontal treatment, such as rooting and scaling, can slow the progression of periodontal disease by removing plaque at the root of the teeth and reducing inflammation, once tissue and bone loss have occurred, it is permanent. Risk factors for periodontal disease include race, sex, income, education, and smoking. One of the biggest challenges in studying periodontitis and chronic diseases with observational studies resides in the measurement of periodontal disease.[6-11] Historically, tooth loss was used as a marker for periodontal disease, given that tooth loss that occurs in adults is largely due to periodontitis; however, the number of teeth lost is also a marker of oral health and can result from dental caries, accidents, or orthodontic treatment. Thus, tooth loss can represent a number of oral conditions, is often only a crude marker of periodontitis, and may vary dramatically depending on the population. In observational studies, periodontal disease has been measured using self-report of periodontitis (e.g., periodontal disease with bone loss) or using individual oral health assessments such as measurements of pocket depth, clinical attachment level, and alveolar

bone loss from panoramic radiographs. The large variation in methods and criteria used for the assessment and categorization of periodontitis may explain some of the discrepancies observed across observational studies. Recent studies including the third National Health and Nutrition Examination Survey[12] and the Buffalo OsteoPerio Study (an ancillary study of the Women's Health Initiative)[13] have examined the association between periodontitis and cancer risk using direct oral measurements and radiographs, respectively, to obtain more precise measures of periodontitis. Nevertheless, other limitations exist in observational studies on periodontal disease and cancer risk, which include small number of cases and potential confounding by smoking and other risk factors. Whether the impact of periodontal disease on cancer risk is a direct effect or a consequence of shared genetic and/or environmental factors is extremely difficult to untangle. These limitations have caused much controversy in the field of periodontitis and heart disease and will require interdisciplinary collaborations to address many remaining questions. Understanding the biological underpinnings of the associations and evaluating whether they are direct or indirect effects are critical to determine whether reductions in risk can be achieved through public health interventions. The largest number of observational studies examining oral conditions, including teeth number, and risk of cancer has been on head and neck cancers. At least historically, a link between oral disease and cancer in the oral cavity, or in the vicinity of the oral cavity, was more plausible than a link with more distant cancer sites given the visible and measurable local inflammation, known shifts in pathogenic oral bacteria, and physical injury caused by bone loss with advanced periodontitis. However, research conducted in the past decade has led to new studies examining the potential relationship between oral disease and the risk of orodigestive cancers, lung cancer and other smoking-related cancers (e.g., kidney, bladder), and even hormonal cancers such as breast, prostate, and ovarian cancers. The motivation behind these studies lies largely on new knowledge linking periodontitis and pathogenic bacteria to a systemic impact on the body, particularly on the immune response, providing plausibility for a role in carcinogenesis of distant tumors through those mechanisms.[14]

POTENTIAL ROLE OF CONFOUNDING BY GENETIC SUSCEPTIBILITY

It is possible that the positive associations observed between periodontal disease and cancer risk are driven by shared genetic susceptibility between these two diseases. On the basis of twin studies, it has been estimated that as much as 50% of periodontitis is heritable.[15] Large efforts and searches for genetic determinants of periodontitis, including several large genome-wide association studies, have failed to produce genetic associations for chronic periodontitis.[15] Genes that have been consistently associated with aggressive periodontitis include the glycosyltransferase 6 domain-containing 1 gene, the CDKN2B antisense RNA 1 gene (ANRIL), and the cyclooxygenase 2 gene (COX2).[15] Variants in the COX2 gene have also been associated with risk of digestive cancers,[16] and polymorphisms in the cyclin-dependent kinase inhibitor 2A and 2B genes (CDKN2A, CDKN2B) have been associated with nasopharyngeal cancer[17-19] and glioma. Therefore, although it is plausible that shared genetic susceptibility for periodontitis and cancer explains some of the associations observed, this would mostly be true if the associations observed were largely driven by aggressive periodontitis, given the lack of major susceptibility genes associated with chronic periodontitis. However, at this time, existing studies on cancer have not made the distinction between aggressive and chronic periodontitis, making it difficult to evaluate the potential role for confounding by underlying shared genetic factors.

CONCLUSION

Today, data provide support for positive associations between periodontal disease and risk of lung, pancreatic, and head and neck cancers. Despite the heterogeneity of measurements used to evaluate periodontal disease, consistency in findings for pancreatic and lung cancer risk is noteworthy and, at least for pancreatic cancer, observed associations across studies did not appear to be due to confounding by smoking. The literature on this field is still relatively sparse and prevented us from conducting quality meta-analysis on most cancer sites. Future studies with larger samples sizes improved measurements for periodontal disease, and more thorough adjustment for smoking and other risk factors should help to solidify the role of periodontal disease on cancer risk and assist with identification of individuals at higher risk. Moreover, clarification on the potential causal role of periodontal disease in cancer development is critical, as it may lead to new opportunities for cancer prevention and may warrant policy changes and recommendations for dental care access and coverage.

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