

Review Article

Periodontitis and malignancy: a growing concern

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ABSTRACT

Periodontitis is an inflammatory disease affecting the supporting structures of the tooth resulting in tooth mobility and tooth loss. Periodontitis has been consistently associated with a higher risk for head and neck cancer. Possible mechanisms include the chronic inflammatory nature of the disease, epigenetic damage to the epithelial cells by periodontal pathogens and dysbiosis. The present review focuses on various pathways of spread of head and neck cancers and the role of various periodontal pathogens in initiating this carcinogenesis.

Keywords: Periodontitis, Microorganisms, Risk, Cancer

INTRODUCTION

Periodontitis is an inflammatory disease of the periodontium caused by micro-organisms resulting in low grade systemic inflammation.¹ This inflammatory nature of periodontal disease explains the epidemiological association between periodontitis and non-communicable disease.² Periodontitis is influenced by presence of many risk factors such as smoking, diabetes and contributing factors like overhanging restoration, open interproximal contact, occlusal trauma, mucogingival deformity, and several anatomical factors. Cancer has defined as a genetic disease and in some point, cancer can be changed to unmodifiable intrinsic factors, that cause accumulation of mutation in dividing cell population.³ Periodontitis and exposure to oral pathogens are also linked to increased risk of cancer incidence and mortality in epidemiological studies.^{4,5}

This review article focuses on the relation between periodontitis and risk of cancer.

MICROORGANISMS ASSOCIATED WITH CANCER

The oral cavity harbors a remarkably intricate microbial ecosystem comprising up to 2000 species of bacteria,

viruses and fungi with a higher proportion of non-cultivable organisms.⁶

While most oral microorganisms coexist as commensals, certain opportunistic pathobionts with oncogenic potential can emerge, causing harm. Beyond their local effects on teeth and gums, members of the oral microbiome can translocate to various body sites, particularly in cases of periodontitis, where the compromised mucosal barrier and increased microbial load in pockets and saliva facilitate their spread.⁷ Periodontal pathogens that translocate and the pro-inflammatory mediators released into the bloodstream from the subgingival environment can interact and will make a way for initiation of carcinogenesis (Figure 1).

PERIODONTITIS AND ITS LINK WITH HEAD AND NECK CANCER

Periodontitis linked to head and neck cancer. It can be explained in five mechanisms.

Altered microbiomes can contribute to cancer development through toxins and metabolites that damage epithelial cell DNA. For example, *Aggregatibacter actinomycetemcomitans*' toxins and byproducts (ROS, and sulfides) have oncogenic potential, causing DNA damage

and mutations.^{8,9} Second pathway involves specific oral pathogens that can trigger epigenetic changes by regulating gene expression.¹⁰ A third pathway involves periodontitis-related microbiome promoting tumor growth through inflammation, increasing cell proliferation and inhibiting apoptosis, mediated by toll-like receptors (TLRs) and NF- κ B activation.¹¹ The fourth pathway involves microbial impairment of epithelial barrier function through pathogen associated molecular patterns (PAMPs) and metabolites (e.g: lactic acid), enhancing carcinogenesis.¹² Examples include *P. gingivalis* and *T. denticola* disrupting junction proteins.¹³ Lastly, periodontal pathogens can promote immune evasion by upregulating immune checkpoints like programmed death receptor (PD-L1), allowing tumor cells to evade T-cell responses and immunity.¹⁴

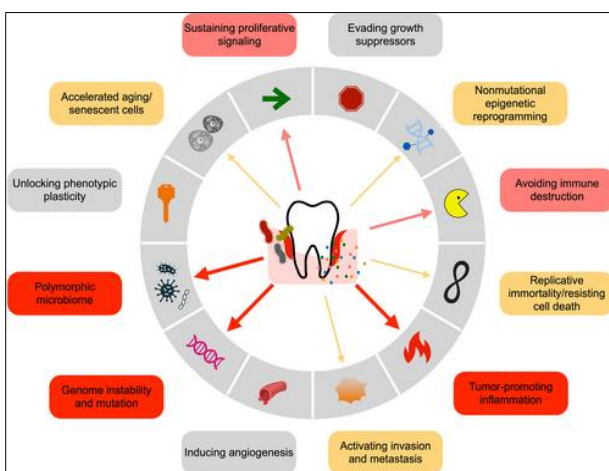


Figure 1: Proposed route for periodontitis leading to risk for cancer.

Association of periodontitis pathogens with likelihood of developing various cancer is inconclusive.

Lung cancer

Evidence suggests the role of *Acinetobacter*, *Pseudomonas*, *Prevotella*, *Veillonella* and *Streptococcus* in the tumor involved tissues.¹⁵ Oral microbes can migrate to lungs through micro-aspiration, potentially causing lung diseases like COPD, pneumonia, and worsening COVID-19.¹⁶

Breast cancer

Oral bacteria, such as *F. nucleatum*, have been found in cancerous breast tissues.¹⁷ Parhi et al studied the presence of *F. nucleatum* in breast tumors in mice, and found that binding to tumor expressed Gal-GalNAc was 100 times more than normal tissue.¹⁸

Prostate cancer

Periodontal pathogens (*P. intermedia*, *P. gingivalis*, *T. denticola*) were found in prostate secretions of patients

with chronic prostatitis and periodontitis.¹⁹ Colonized periodontal bacteria in the prostate may trigger chronic inflammation, potentially accelerating prostate cancer development and progression.²⁰

Esophageal and gastric cancer

Periodontal pockets may harbor *H. pylori*, a known carcinogenic bacterium. Periodontitis is linked to higher gastrointestinal cancer mortality in people with *H. pylori* infection.²¹

Pancreatic cancer

Microbial imbalance, along with smoking, pancreatitis and obesity is a potential risk factor.²² Studies found oral presence of *P. gingivalis* and *A. actinomycetemcomitans* and a high antibody levels against these periodontal pathogens are linked to higher risk for pancreatic cancer risk.^{23,24}

Colorectal cancer (CRC)

Recent studies show that bacteria present in oral cavity may be linked to cancers in the lower digestive tract. Specifically, *Fusobacterium nucleatum* (*F. nucleatum*) is commonly found in colorectal cancer tissues.²⁵

CONCLUSION

Periodontitis and its linked microbial imbalance may contribute to tooth decay and cancer development, particularly in head and neck cancers. Key mechanisms include inflammation, immune system disruption, and microbial imbalance, with specific microbiomes found in tumors often featuring periodontal pathogens.

While there's strong evidence linking periodontitis to some cancers, more research is needed to understand its role in others, like breast and prostate cancer. Future studies should explore the complex interactions between periodontal inflammation and cancer development, including the role of non-traditional pathogens. Advanced technologies and large-scale studies can help uncover new therapeutic targets and diagnostic markers, ultimately informing cancer prevention strategies.

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