Periodontal Disease as an Increased Risk Factor for Colorectal Cancer

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ABSTRACT

Periodontal disease (PD) is a combination of gingivitis and periodontitis caused by bacterial infection, affecting 42.2% of adults 30 years or old in the US, as of 2021. Colorectal cancer (CRC) is a common cancer that affects the colon and rectum by uncontrolled growth of malignant cells, ranked the third leading cause of death among men and second among women. While early research suggested that there was no link between PD and CRC, recent studies have shown that PD may be an increased risk factor for CRC. In order to further investigate whether PD is an increased risk factor for CRC, this literature review examines the epidemiology and biological mechanisms for each disease along with the clinical studies that investigated PD as a risk factor for CRC. Here, we analyzed multiple studies from numerous databases that discussed the relationship between periodontal disease and colorectal cancer. Our research revealed that individuals with PD are ~21% more likely to get CRC. Furthermore, it was found that the two conditions share common risk factors including smoking, genetics, and aging, as well as biological mechanisms that may explain their commonalities, such as chronic inflammation, bacterial pathogens, and a similar immune response. Further, several clinical studies have investigated the association between PD and CRC, one of which found that PD patients had 145% higher risk of developing CRC. However, to further investigate this relationship, there is a need for more observational, interventional, and clinical studies that examine the linkage between the two diseases.

METHODS

Analyzed primary and peer-reviewed scientific articles from multiple databases such as PubMed, NCBI, Springer Nature.

Primary Articles: 25
Peer Review Articles: 11

EPIDEMIOLOGICAL EVIDENCE

- Prevalence of PD is high and prevalent worldwide (Eke et al., 2012)
- CRC is the 3rd most common cancer in men & 2nd in women worldwide

Shared Risk Factors:

- Smoking: contributes to chronic inflammation & alterations in immune system (Momen-Heravi et al., 2016)
- Poor oral Hygiene & Diet high in processed foods and sugar: promotes microbial dysbiosis and chronic inflammation in mouth and gut (Momen-Heravi et al., 2016)

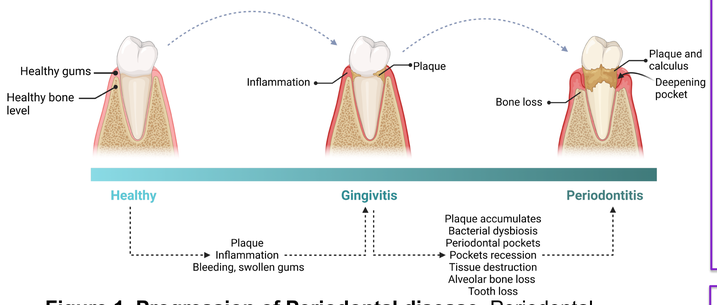

Figure 1. Progression of Periodontal disease. Periodontal disease begins with gingivitis where the patient has plaque which leads to inflammation and results in bleeding, swollen gums. If left untreated, it can progress to periodontitis which develops over time as dental plaque accumulates, bacterial dysbiosis, formation of periodontal pockets, pockets recession, tissue destruction, and alveolar bone loss, which leads to tooth loss.
(Image made on Biorender)

BIOLOGICAL MECANISMS

Chronic Inflammation:

- Chronic gum inflammation → increase systemic inflammation → risk factor for development of malignant tumors in the lower gastrointestinal tract (Sobocki et al., 2022)
- Chronic gum inflammation → release of proinflammatory cytokines and reactive oxygen species (ROS) → damage to genetic material → increase of cancer

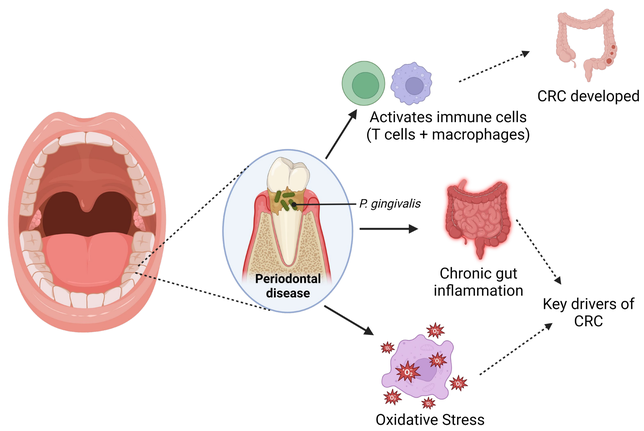

Figure 2. P. gingivalis contributing to CRC through multiple factors. P. gingivalis promotes chronic gut inflammation and oxidative stress which are key drivers for CRC. This pathogen also activates immune cells such as T cells and macrophages which contribute to the development of CRC.
(Image made on Biorender)

Immune Response:

- Immune mediators → systemic inflammation → development of CRC (Hajishengallis and Chavakis, 2021)
- PD → supports bacterial growth/ increase risk of bacterial infections → systemic inflammation → promotes chronic inflammation → increased risk of CRC (Di Spirito et al., 2020 ; Hajishengallis and Chavakis, 2021)

CLINICAL STUDIES

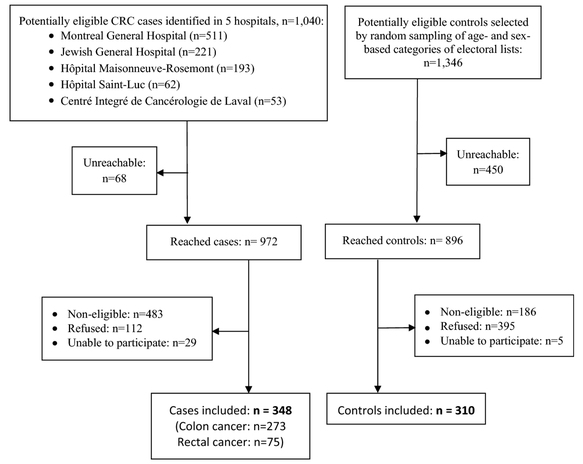

Figure 3. COLDENT Study recruitment flow chart. Rate of new diagnosis of CRC in patients w/ history of PD was **~ 1.45 times higher** than patients w/o history of PD (Idrissi Janati et al., 2022)

Nurses Health Study:

- Followed 77,443 women from 1992-2010
- Collected information on PD and # of natural teeth
- Used data to assess risk of CRC
- **Results**: Women w/ moderate to severe PD → higher risk of CRC (HR value = 1.22); Women w/ less than 17 teeth → 20% higher risk of CRC (Momen-Heravi et al., 2016)

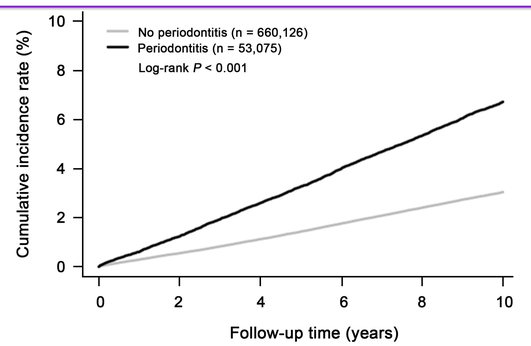

Figure 4. Population-based Cohort Study. Cumulative incidence of all cancers in periodontitis: **2.2 times higher** than control group + **aHR value for colon cancer = 1.129** (Kim et al., 2022)

LIMITATIONS & INCONSISTENCES

- Different definitions and diagnostic criteria
- Self-reported measures
- Clinical measures of PD (e.g. pocket depth or bleeding on probing)
- Establishing a temporal relationship
- Little research present on linkage between PD & CRC on a biological level

CONCLUSIONS + FUTURE DIRECTIONS

- **Conclusion:** All evidence provided points to PD being an increased risk factor for CRC.
- Increased research in this area such as conducting observational studies and interventional studies
- Need for more clinical studies with larger sample sizes, longer follow-up periods, and proper study designs
- Performing studies that bring together experts in the fields of periodontology, oncology, and epidemiology

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REFERENCES