



## Major clinical approaches of dental treatment in cancer patients: a systematic review

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### Abstract

**Introduction:** According to the National Cancer Institute, a total of 16,290 new cases of oral cancer were estimated in Brazil in 2017, with 12,370 new cases of oral cavity cancer in men and 4,010 in women corresponding to an estimated risk of 11.54 cases new for every 100 thousand men and 3.92 for each 100 thousand women. In this sense, oral cancer therapy is associated with a multitude of head and neck sequelae including hyposalivation, increased risk of tooth decay, osteoradionecrosis of the jaw, radiation fibrosis syndrome, mucositis, chemotherapy-induced neuropathy, dysgeusia, dysphagia, mucosal lesions, trismus, and infections. **Objective:** It was to present the main clinical approaches to dental treatment in cancer patients through a systematic review. **Methods:** The PRISMA Platform systematic review rules were followed. The search was carried out from November 2023 to February 2024 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 156 articles were found, 58 articles were evaluated in full and 29 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 32 studies with a high risk of bias and 20 studies that did not meet GRADE and AMSTAR-2. Most studies did not show homogeneity in their results, with  $X^2=61.8\%>50\%$ . It was concluded that preparing a

comprehensive treatment plan for cancer patients is essential to help minimize the risks of developing these oral and dental complications. Additionally, dentists should consider the patient's ongoing oncology therapy for those patients who see the dentist while receiving cancer treatment.

**Keywords:** Oral cancer. Cancer treatment. Dental treatment. Cancer therapy. Dental complications.

### Introduction

According to the National Cancer Institute, a total of 16,290 new cases of oral cancer were estimated in Brazil in 2017, with 12,370 new cases of oral cavity cancer in men and 4,010 in women corresponding to an estimated risk of 11.54 cases new for every 100 thousand men and 3.92 for each 100 thousand women [1,2]. Currently, it can be considered a public health problem in developing and developing countries like Brazil and has been responsible for 13.0% of all causes of death worldwide [3,4].

The number of cancer cases has increased significantly worldwide, especially since the last century, and is currently one of the most important public health problems in the world [5]. Of all malignancies that affect the oral region, 94.0% correspond to oral squamous cell carcinoma (OSCC). OSCC is an aggressive malignant epithelial neoplasm, which mainly affects ill. The scientific literature is unanimous regarding the language being the preferred location for the development of OSCC, followed by the floor of the mouth [6-9].

There is no consensus regarding the frequency of other anatomic sites. Cytopathology is a method based on the possibility of analyzing the cells collected from the lesions and interpreting, through light-field microscopy, the stained smear obtained from the collected material [10]. Several studies address the importance of dental surgeons in reducing oral cancer, with their participation in prevention, the anticipation of diagnosis, treatment orientation, and rehabilitation of patients. In this context, smoking is one of the main risk factors for oral cancer, becoming an important object for dentistry students and dental surgeons who are directly involved in the early diagnosis, treatment, and orientation of patients [11-13].

In this sense, oral cancer therapy is associated with a multitude of head and neck sequelae including hyposalivation, increased risk of tooth decay, osteoradionecrosis of the jaw, radiation fibrosis syndrome, mucositis, chemotherapy-induced neuropathy, dysgeusia, dysphagia, mucosal lesions, trismus and infections [14,15].

Therefore, the present study aims to present the main clinical approaches to dental treatment in cancer patients through a systematic review.

## Methods

### Study Design

The present study followed the international systematic review model, following the rules of PRISMA (preferred reporting items for systematic reviews and meta-analysis). Available at: <http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1>. Accessed on: 02/11/2024. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: <https://amstar.ca/>. Accessed on: 02/11/2024.

### Data Sources and Research Strategy

The literary search process was carried out from November 2023 to February 2024 and was developed based on Scopus, PubMed, Web of Science, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various to the present. The descriptors (MeSH Terms) were used: "Oral cancer. Cancer treatment. Dental treatment. Cancer therapy. Dental complications" and using the Boolean "and" between the MeSH terms and "or" between historical discoveries.

### Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low in terms of risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident

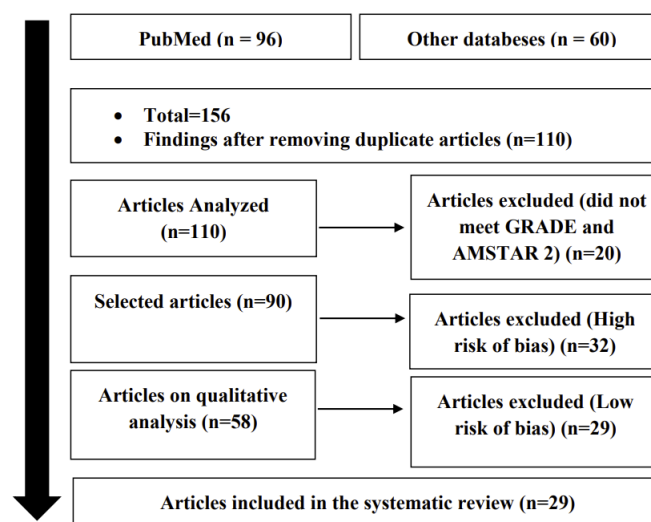
emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using the Cohen test (d).

## Results and Discussion

### Summary of Findings

A total of 156 articles were found that were subjected to eligibility analysis, with 29 final studies being selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. The biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with  $X^2=61.8\%>50\%$ . Considering the Cochrane tool for risk of bias, the overall assessment resulted in 32 studies with a high risk of bias and 20 studies that did not meet GRADE and AMSTAR-2.

Figure 1. The article selection process by the level of methodological and publication quality.

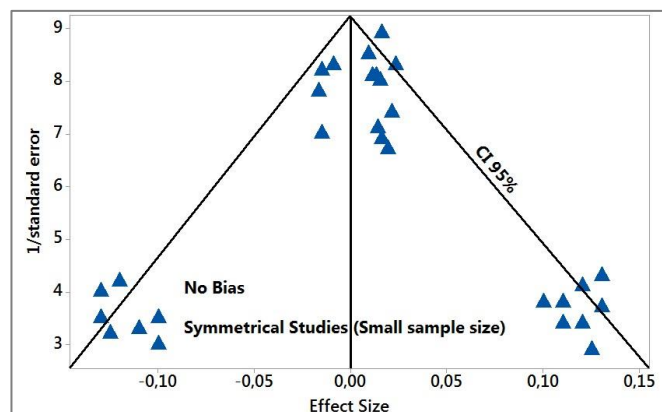


Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using the Cohen Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both between studies with a small sample size (lower precision) that are shown at the bottom of the

graph and in studies with a large sample size that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies that are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=29 studies).



Source: Own authorship.

### Major Clinical Outcomes

Oral cancer or oral carcinoma is a chronic, complex, multifactorial pathology resulting from the interaction of intrinsic and extrinsic factors that leads to an imbalance in the process of cell proliferation and growth control [1,2]. The main risk factors for the development of oral tumors are smoking, alcohol, ethnicity, age, gender, genetic predisposition, solar radiation, diet, chronic trauma, poor oral hygiene, low carotene consumption, family history of cancer, human papillomavirus, irritation caused by rough teeth, uneven surfaces in fillings, crowns or dentures against the tongue or cheekbones, microorganisms, and immune deficiency [3].

According to NCI, mouth cancer can develop in several places, with the tongue having the largest amount with 26.0% of all tumors followed by the lips with 23.0%, especially the lower floor of the mouth with 16.0%, and the glands Salivary with 11.0% [16-18]. Treatment with dental implants is considered contraindicated in cancer patients using high-dose antiresorptive medication (HDAR). Based on this, a prospective feasibility study evaluated implant treatment in HDAR cancer patients in terms of implant survival, implant success, and oral health-related quality of life (OHLQoL) after 2 years of loading. A total of 22 patients, 39 implants, completed the implant-based prosthetic treatment. A total of 13 patients (59%) with 23 implants (59%) completed 2 years of follow-up. The overall implant survival and success rate after 2 years of loading were 100% and 97.4%, respectively. OHLQoL for patients increased in all groups after treatment, a substantial increase was observed in group 3 [19].

In this context, a study evaluated the oral cancer patient population and the influence on the quality of life of two dental treatment protocols: unregulated hospital treatment versus regular hospital treatment. A quasi-experimental approach was used, justified for ethical reasons. A total of 41 patients were included in the control group (untreated outpatient health center) and 40 in the experimental group (inpatient treatment). A total of 14 questions for both groups were performed in three steps: before starting cancer treatment, during treatment, and after treatment. The proportions of positive responses in the different groups and times were compared by the chi-square test. Based on similar situations during cancer treatment, six questions were identified in favor of the experimental group difference. This number increased to nine after the end of cancer treatment. From our data, we can confirm that the planned dental treatment performed during oral cancer treatment produces an improvement in the quality of life of oral cancer patients [1-3].

Given the low prevalence of infections and the potential for complications after third molar extractions, partial protocols for dental evaluation/treatment before intensive chemotherapy are suggested, where minor caries, asymptomatic third molars, or asymptomatic teeth without excessive probing depth (<8 mm), mobility I or II or with periapical lesions <5 mm is a viable option when there is not enough time for complete dental assessment/treatment protocols. Chlorhexidine, fluoride mouthwashes, composite resin, resin-modified glass ionomer cement, and conventional resin amalgam restorations are recommended for patients with fluoride-compatible post-head and neck radiation [16].

A study with a total of 50 newly diagnosed head and neck carcinoma patients had saliva and plasma samples collected, along with periodontal clinical records. The nutritional status parameters consisted of body mass index, serum albumin, hemoglobin, and total lymphocyte count. Cystatin C and lysozyme were the antimicrobial proteins. A logistic regression model showed that periodontal parameters were inversely related to their nutritional status; However, antimicrobial protein levels were directly related to the periodontal condition. Therefore, there is an association between periodontal disease, nutritional status parameters, and antimicrobial protein levels [17].

Tumors found in the mouth and throat are Leukoplakia and Erythroplasia. Leukoplakia is characterized by a whitish area and erythroplasia by a slightly raised red area, usually asymptomatic, which does not go away when the lesion is scraped [18]. These whitish or reddish areas may present with dysplasia or neoplasia. Leukoplakia is a benign condition and rarely

develops into cancer. The finding may rule out the possibility of cancer [20-24]. Only 25.0 % of leukoplakias, when detected, involve precancerous changes that progress to cancer in 10 years if not treated properly [25]. However, in the case of erythroplakia, 70.0 % to 95.0 % of these lesions are cancerous at the time of initial biopsy or will progress to cancer [26-28].

More than 90.0 % of cancers of the mouth and throat are from squamous cells, known as squamous cell carcinomas or squamous cell carcinomas. Squamous cells are flattened, from the lining of the oral cavity and throat. Squamous cell carcinoma begins as a set of abnormal squamous cells known as carcinoma in situ, present only in the cells of the lining layer of the epithelium. In invasive squamous cell carcinoma, cancer cells have penetrated deeper layers of the oral cavity and oropharynx [29].

The main signs and symptoms are ulcers in the mouth that do not heal constant pain, persistent lump or thickening in the cheek, reddish or whitish area on the gums, tongue, tonsils or lining of the mouth, throat irritation or feeling of something stuck or pinched in the throat, difficulty in chewing and swallowing, paresis of the mandible or tongue, paresthesia of the tongue or other areas, jaw edema, loose or soft teeth in the gingiva, sialorrhea, trismus, bleeding, dysphonia, mandibular or teeth pain, persistent halitosis, nodules, Cervical lymphadenopathy, and weight loss in the late stages [3,18].

According to Cimardi et al. [20] the main reason that leads to a low rate of early diagnosis is the low adherence of the dentist to early diagnosis and referral of patients to the treatment of oral cancer in specialized units. Some conditions favor early diagnosis as knowledge of the groups at greater risk and the region of easy access to clinical examination, which does not require special equipment. Deficiencies in professional training or continuing education are pointed out as the main factors for the late diagnosis of oral cancer.

To better assist and assist patients in cancer treatment, the dental professional should be able to diagnose, prevent, control, and treat the oral complications that arise during the various stages of cancer treatment. "Simple clinical attitudes such as oral hygiene, control of oral biofilm, use of specific mouthwashes, can prevent or ameliorate secondary manifestations in the mouth caused by cancer treatment [16-20].

## Conclusion

It was concluded that preparing a comprehensive treatment plan for cancer patients is essential to help

minimize the risks of developing these oral and dental complications. Additionally, dentists should consider the patient's ongoing oncology therapy for those patients who see the dentist while receiving cancer treatment.

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## Ethical Approval

Not applicable.

## Informed consent

Not applicable.

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## Data sharing statement

No additional data are available.

## Conflict of interest

The authors declare no conflict of interest.

## Similarity check

It was applied by Ithenticate®.

## Peer Review Process

It was performed.

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