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Oral health in older adults with cancer

Saúde oral em pessoas idosas com câncer

Ana Patricia Navarrete-Reyes^a , Juan Pablo Negrete-Najar^a , Gabriel Cojuc-Konigsberg^b ,
Jimena Gómez-Camacho^a , Yoselin Juárez-Carrillo^a , Luis Gerardo López-Mosqueda^c ,
Rodrigo Rangel-Tapia^d , Juan Alberto Ríos-Nava^d , Carlos Alberto Ruiz-Manríquez^a ,
Darío Alejandro Sandoval-Valdez^a , Ana Cristina Torres-Pérez^a ,
Juan Miguel Antonio García-Lara^a , Enrique Soto-Perez-de-Celis^a , Yanin Chavarri-Guerra^c 

^a Department of Geriatric Medicine, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán – Mexico City, Mexico.

^b Faculty of Health Sciences, Universidad Anáhuac – Estado de México, Mexico.

^c School of Medicine, Universidad Olmeca – Villahermosa, Mexico.

^d Faculty of Medicine, Universidad Autónoma Metropolitana – Mexico City, Mexico.

^e Department of Hemato-Oncology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán – Mexico City, Mexico.

Correspondence data

Ana Patricia Navarrete-Reyes – Vasco de Quiroga 15, Belisario Domínguez sección 16 – CP 14080 – Alcaldía Tlalpan – Mexico City, Mexico. E-mail: apnavarrete09@gmail.com

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Abstract

Cancer is a disease of older adults, with 60% of cancer diagnoses and 70% of cancer deaths occurring in individuals ≥ 65 years. Normal oral aging may transition to disease in the presence of one or more potential modifiers, such as a new oncological diagnosis or a new treatment. Oral conditions in patients with cancer cause significant morbidity. Previous work suggests that oral conditions are neither elicited/assessed/reassessed nor well-managed or investigated in older patients. However, frequently reported oral conditions in patients undergoing cancer therapy include xerostomia, dysgeusia, candidiasis, mucositis, and dental caries. Some oncological treatments such as hematopoietic stem cell transplant or chemotherapy/radiotherapy for head and neck cancers entail higher risks of oral complications. No specific recommendations in the case of older adults with cancer-associated oral conditions are available. Treatment recommendations are based on low levels of evidence and/or evidence extrapolated from younger patients with cancer.

Keywords: oral health, geriatrics, integrative oncology.

Resumo

O câncer é uma doença da idade avançada; 60% dos diagnósticos de câncer e 70% das mortes por câncer ocorrem em indivíduos ≥ 65 anos. O envelhecimento oral normal pode tornar-se patológico na presença de um ou mais fatores modificadores em potencial, como um novo diagnóstico ou tratamento oncológico. As afecções orais causam morbidade significativa em pacientes com câncer. Pesquisas anteriores sugerem que as afecções orais não são bem questionadas, (re)avaliadas, manejadas ou investigadas em pacientes idosos. As afecções orais mais frequentemente relatadas em pacientes submetidos à terapia oncológica incluem xerostomia, disgeusia, candidíase, mucosite e cárie dentária. Alguns tratamentos oncológicos, como o transplante de células-tronco hematopoiéticas ou a quimiorradioterapia para cânceres de cabeça e pescoço, acarretam maior risco de complicações orais. Não há recomendações específicas para pessoas idosas com afecções orais associadas ao câncer. As recomendações de tratamento são baseadas em evidências de baixo nível e/ou extrapoladas de pacientes oncológicos mais jovens.

Palavras-chave: saúde oral, geriatria, oncologia integrativa.



INTRODUCTION

Oral health is complex. According to the FDI/World Dental Federation, it comprises the abilities to speak, smell, taste, touch, chew, swallow, and convey a range of emotions through facial expressions with confidence and without pain, discomfort, and disease of the craniofacial complex (head, face, and oral cavity).¹ It is fundamental to overall health, as it contributes to quality of life, longevity, and functionality. It allows taste and smell, supports swallowing and nutrition, and maintains facial anatomy and self-esteem. Oral aging is especially relevant in the context of cancer, since it contributes to a lower threshold for developing oral disease, nutritional and swallowing disorders, taste and smell impairments, and chronic pain, as well as other adverse outcomes.²

Although aging is a normal process, individuals, systems, and tissues age at different rates. In addition, changes associated with age are multifactorial in nature in such a way that their expression depends on lifestyle, environment, and genetics, among other determinants.²

In the oral cavity, changes to dentition include enamel wear, chipping, appearance of fracture lines, staining, dentin exposure, and deposition of secondary dentin that reduces the size of the pulp chamber and canals. In older populations, teeth are generally darker, which results from a combination of secondary dentin deposition, enamel thinning, and staining. A modest reduction in periodontal support is also part of normal aging, often manifesting as attachment loss (observed as gingival recession ≥ 3 mm on the buccal surfaces). Although frequent, neither dental caries nor periodontal disease are normal changes associated with aging. The increase of dental caries in older adults is associated with the presence of root caries, representing the effect of increased tooth retention and root surfaces exposed due to the loss of periodontal support. In older adults, risk factors for periodontitis are often substantial, especially in those unable to fully remove plaque deposits due to reduced dexterity and/or reduced visual acuity and in those with other health conditions, such as diabetes mellitus or cancer.²

With aging, the oral mucosa undergoes a loss of elastic fibers and thickening and disorganization of collagen bundles. In consequence, it becomes less resistant, which, accompanied by a reduction in the microvasculature, leads to impaired healing.^{2,3}

Up to half of older adults experience xerostomia, the subjective complaint of a dry mouth sensation; most such cases are caused by medication, particularly cardiovascular and anticholinergic drugs.^{2,4,5}

There is still controversy regarding aging-related changes in salivary gland function. Previous work has identified changes in the composition of saliva, with increased concentrations of IgA and diminished protein concentration. Although atrophy of the acinar cells and replacement of the gland parenchyma with fibrous or/and adipose tissue do occur, studies regarding salivary flow rates in older adults have reported mixed results.

Nutritional intake and adequate mastication are essential to healthy aging, and depend on the appropriate function of dentition, the temporomandibular joint, mastication muscles, and swallowing processes. As masticatory function is diminished with aging because of reduced muscle mass, the number of chewing strokes needed to reduce each food bolus for swallowing increases, making grinding less efficient. Under certain circumstances, this normal change may lead to dietary modifications resulting in lower fiber, lower protein, and higher carbohydrate intake, which can be handled by a less efficient chewing mechanism.²

As proposed by Lamster et al,² in the presence of one or more potential modifiers, such as poor general health status, a new cancer diagnosis, or a new treatment, normal oral aging may transition to disease (Figure 1).

Along the same lines, cancer is a disease of older adults, with 60% of cancer diagnoses and 70% of cancer deaths occurring in older individuals.⁶ Oral conditions are common in patients with advanced cancer and cause significant morbidity;⁷ they are particularly troublesome in patients receiving oncological treatment for head and neck tumors (more than 95% of patients receiving chemotherapy/radiotherapy for this reason develop mucositis and 100% report xerostomia)⁸ and in patients undergoing hematopoietic stem cell transplantation (adverse effects of the transplantation regimen affecting the oral cavity occur in approximately 80% of patients).⁹

Some types of chemotherapy entail higher risks for the development of oral conditions. For example, agents affecting DNA synthesis (S phase-specific agents such as fluorouracil, methotrexate, and cytarabine) carry a higher risk of mucositis.¹⁰ Extensive oral adverse effects have also been reported in association with the use of new anticancer therapies (affecting more than 20% of treated patients). Some have been better characterized, such as mammalian target of rapamycin (mTOR) inhibitor-associated stomatitis (mIAS), while others remain to be further studied, including various types of stomatitis, benign migratory glossitis, and osteonecrosis of the jaw associated with multi-target kinase inhibitors of the vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) receptors; mucositis induced by epidermal growth factor receptor (EGFR) inhibitors (alone or in the context of radiotherapy and/or

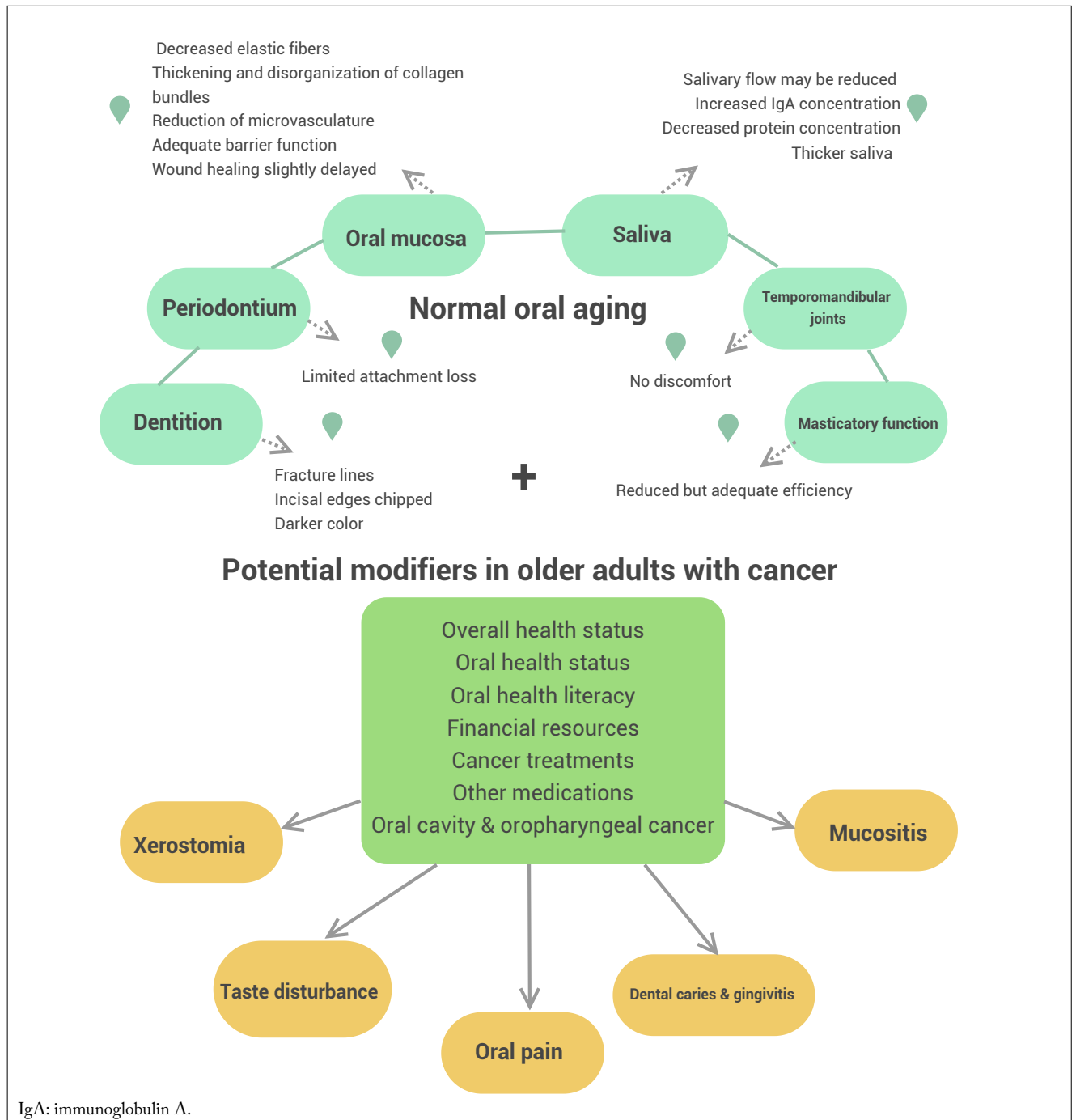


FIGURE 1. Normal aging of the mouth and its potential modifiers in older adults with cancer.

chemotherapy); hyperkeratotic lesions associated with BRAF inhibitors; and discoloration and lichenoid reactions secondary to imatinib.¹¹

Oral conditions occurring more frequently in patients diagnosed with cancer include dysgeusia, mucositis, and infections.^{11,12} However, previous work suggests that oral conditions are neither elicited/assessed/reassessed nor well-managed in patients with advanced cancer.^{6,7} Therefore, it is essential that

healthcare professionals involved in the care of older adults with cancer become knowledgeable about the principles of oral care. The aim of this paper is to review common oral conditions in older patients with cancer and the available evidence supporting assessment and treatment recommendations. Since this is a literature review, neither the approval of an ethics committee nor the obtainment of written consent was required. Cited articles were retrieved from various

libraries and search engines, including EMBASE, Google Scholar, PubMed, Science Direct, and Scopus. Using free-text term searches, the search syntax was adapted for different databases. There were no restrictions on date of publication or study type. However, retrieved articles were written either in English or in Spanish. Finally, the articles included in each section were selected at the authors' discretion.

Etiology

Oral disorders in patients with cancer may be associated with direct damage from cancer (anatomical), indirect effects of cancer (e.g., difficulty performing oral hygiene due to fatigue), adverse effects of cancer treatment (e.g., gland hypofunction due to irradiation of head and neck fields), comorbidities or their treatment, or any combination of the aforementioned factors.^{7,13}

Epidemiology

There is a lack of information regarding the epidemiology of oral conditions in older adults with cancer. A recent cross-sectional study in India assessed the prevalence of oral complications in patients undergoing chemotherapy and reported that 60% of patients had at least one or more oral conditions, with a higher prevalence among those aged ≥ 61 years. The most frequent oral conditions were xerostomia (29.71%), dysgeusia (21.74%), candidiasis (18.84%), mucositis (10.14%), and dental caries. In addition, an association between older age and a higher frequency of oral mucositis was described.¹⁴

A prospective study following patients with head and neck cancer for a 6-month period after radiation therapy found a decline in salivary flow from 1.09 to 0.47 mL/min (56.89%), reduction in maximal mouth opening from 45.58 to 42.53 mm (6.69%), mucositis in 8.1%, and oral ulcers in 3.8%. In this cohort, oral health-related quality of life was lessened due to complaints related to dry mouth, sticky saliva, difficulty swallowing solid food, and impaired sense of taste.¹⁵

Some of these oral conditions become more prevalent and severe with time and disease progression. A study of 314 patients with nonmetastatic nasopharyngeal carcinoma treated with radiotherapy reported an incidence of dental toxicity (pain, fractures, mobility, loss, caries, and dental and alveolar radionecrosis) that increased with time, from 16% in the first year to 74% at 7 years.¹⁶

Moreover, a study of women examined after chemotherapy for breast cancer showed a higher risk of missing teeth and apical lesions compared with healthy controls,¹⁷ which highlights the crucial implications of a dental examination prior to starting treatment. In patients with head and neck cancer, although the prevalence of at least one tooth with caries was 37.2% at baseline (before radiotherapy), only about

half of the patients (49.5%) were advised to undergo dental treatment before starting cancer treatment.¹⁸ Among older adults, receiving chemotherapy is associated with a higher likelihood of oral disease and malnutrition.¹⁹

Specific issues

Hyposalivation and xerostomia

Saliva is essential for the preservation of oropharyngeal health and participates in biological and protective functions. It is rich in food-processing enzymes, such as lipase, amylase, DNase and RNAase; antimicrobial molecules, such as IgA, histatins, lactoperoxidase, lactoferrin, and secretory leukocyte protease inhibitor; and substances with lubricating and remineralizing functions, such as mucin, water, statherin, and proline-rich proteins.^{20,21}

The average rate of salivary production ranges from 0.3 – 0.5 mL/min in healthy individuals,¹⁷ increasing to 0.7 – 1 mL/min with sympathetic stimulation, mainly through β -adrenergic receptors, for a total daily output of 500 – 600 mL.^{22,23} However, older adults may experience a decrease in salivary flow rate of 40 to 50%,²⁴ which may or may not be associated with xerostomia.²⁵ The prevalence of xerostomia/hyposalivation in community-dwelling and institutionalized older adults varies by etiology and setting, ranging from 18 to 72%.^{26,27}

Hyposalivation (the objective finding of decreased salivary production) can lead to oral and systemic health issues, and can be classified according to its cause as primary (caused by conditions that directly affect the salivary glands) or secondary (e.g., caused by side effects of cancer treatment, including chemoradiation and some medications).²⁸ In older adults, its etiology is generally multifactorial, with multiple simultaneous conditions implicated, such as commonly prescribed medications (anticholinergics, tricyclic antidepressants, sedatives, antihypertensives, antiparkinsonians, and anticonvulsants) and systemic diseases (including Sjögren's syndrome, diabetes mellitus, HIV/AIDS, scleroderma, sarcoidosis, lupus, Alzheimer's disease, and dehydration).²⁹ Hyposalivation can lead to oral and general health problems, including dental caries, dry lips, dysphagia, dysgeusia, halitosis, gingivitis, mucositis, chewing problems, slurred speech, oropharyngeal candidiasis, difficulty sleeping, traumatic oral injuries, and nutritional deficits.^{25,30}

The management of both hyposalivation and xerostomia includes the treatment of the underlying cause (if possible), non-pharmacological (chewing gum, topical fluoride, mouthwashes, artificial saliva, lubricants, a low-sugar diet, and nightly use of humidifiers) and pharmacological

measures.³¹ In patients with advanced cancer, oral clinical care of hyposalivation and xerostomia has been often based on anecdotal remedies.³² However, recent guidelines recommend non-pharmacological treatments, including artificial saliva and chewing gum (level II evidence),³³⁻³⁵ and the use of pilocarpine, a salivary stimulant, as a pharmacological intervention.³⁵

It should be noted that the evidence on managing xerostomia and hyposalivation is of limited quality and not specific for older adults.^{13,36,37}

Taste disturbances

Older adults are prone to developing taste disturbances.³⁸ These can be classified into: ageusia, a total lack of taste; hypogeusia, decreased sensitivity to taste; hypergeusia, increased sensitivity to taste; and dysgeusia, distortion of normal taste sensation. Altogether, they occur in 56 – 76% of patients being treated for cancer, depending on the type of therapy.³⁹⁻⁴¹ Taste disturbances can significantly affect quality of life and oral intake, which has wide-ranging implications due to possible dietary changes, leading to decreased nutrient intake and a higher prevalence of malnutrition.^{42,43}

Taste disturbances in older people with cancer are frequently multifactorial in nature.³⁵ Causes include cytotoxic damage to rapidly dividing taste receptor cells, poor oral hygiene, medications, and nutritional deficiencies (zinc).⁴⁴ Cancer treatment is the leading cause of taste disturbances; chemotherapy (mainly taxanes, platinum salts, and anthracyclines), immunotherapy, and radiotherapy have all been implicated.^{39,45}

Changes in taste can be assessed objectively and subjectively. Objective measurements (chemical and electrogoniometry) provide more information; however, they are not frequently performed in the clinic. Subjective measurements in the form of validated questionnaires (EORTC, OHIP-14) can also be valuable.^{46,47} Nevertheless, self-reporting is a good way to assess these disorders in the clinical setting.⁴⁸

The management of dysgeusia must be personalized. Non-pharmacological measures are the mainstay of management, alongside correction of the underlying cause whenever possible.³⁹ People with taste disturbances should be referred to a nutritionist. Recommendations such as consuming cold foods and frozen fruits, adding more condiments and/or sugar to foods, avoiding bitter or metallic-tasting foods, and avoiding foods with strong odors have been shown to be helpful.^{39,49} Some pharmacological interventions that have proven useful include zinc supplements, tetrahydrocannabinol, and megestrol acetate; however, there is no specific evidence in older adults, and efficacy and safety are still unclear.^{50,51}

Oral candidiasis

Oral candidiasis, or thrush, is an opportunistic infection. It is common in patients with cancer, particularly those with hematological malignancies and those receiving systemic chemotherapy or head and neck radiotherapy.⁵² Its prevalence ranges from 13 to 34%.⁵³ Incidence increases with aggressive systemic treatments, high radiation doses, irradiation of the entire oral cavity, and concomitant oral mucositis.⁵⁴ An association between denture wearing and oral candidiasis has also been described, which is consistent with an environment suitable for yeast proliferation.⁵⁵ The relationship between systemic steroid therapy and oral candida carriage or infection is unclear. Some studies reported that the frequency of candidiasis was directly related to the use of stronger topical corticosteroids over prolonged periods of time and at high concentrations, but the evidence is weak.⁵⁶ Salivary gland dysfunction is also a recognized predisposing factor, due to decreased antifungal activity of saliva.⁵⁷

Oral candidiasis is a spectrum of several clinical entities: pseudomembranous candidiasis (most prevalent), erythematous candidiasis, denture stomatitis, and angular cheilitis.⁵⁸ Up to 67% of patients receiving hospice care show microbiological evidence of oral yeast carriage; in those with clinical evidence of a fungal infection (38%), *Candida albicans* was the predominant organism.⁵⁹

The clinical features of oral candidiasis are relatively non-specific; oral discomfort and pain with white plaques and red patches may occur. These symptoms lead to poor nutrition, delays in drug administration, prolonged hospital stays and increased hospital costs and, in some patients, life-threatening infection.⁶⁰ Definitive diagnosis depends on a combination of clinical features and microbiological investigations (swabs and imprints of lesions).⁶¹

The management of confirmed oral candidiasis primarily involves the use of antifungal medication (polyenes, azoles), combined with treatment of predisposing factors (e.g., disinfection of dentures).⁶² Other options for patients with recurrent/resistant oral candidiasis include chlorhexidine and tea tree oil, but these remain controversial.⁶³

Oral pain

The evaluation and management of older adults with cancer-related oral pain is a significant challenge, since it can be caused by a wide array of conditions, making optimal control difficult to achieve. In addition, changes that occur with aging contribute to the high prevalence of oral pain in older adults.⁶⁴⁻⁶⁶

Pain is often the initial symptom of cancer and has different dynamics throughout the disease continuum. Orofacial pain and discomfort are significant factors that add to the

burden of patients with cancer and are detrimental to overall health, nutrition, behavior, and quality of life. It has been deemed the most debilitating side effect of cancer therapy.^{64,67-70}

Primary neoplasia, tumor infiltration, paraneoplastic syndromes (e.g., paraneoplastic autoimmune multiorgan syndrome), oral mucositis, chemotherapy-induced neurotoxicity, osteonecrosis of the jaw, and post-surgical pain are the leading causes of oral pain in older adults with cancer. Conditions such as temporomandibular joint disease, vitamin deficiencies, burning-mouth syndrome, and salivary gland and tooth disorders cause chronic discomfort and may be present concomitantly.^{64,67,69}

Many tools help assess pain in older adults. Instruments such as the Oral Symptom Assessment Scale (OSAS) and Oral Problems Scale (OPS) can be of utility.⁷¹⁻⁷³

Effective pain management requires an interprofessional approach, and realistic treatment goals should be set. Treatment of oral pain varies depending on the underlying cause of the symptom. Behavioral, pharmacological, and invasive interventions can be attempted to palliate symptoms. Clinicians should routinely carry out a pain control evaluation to ascertain whether goals are being achieved.^{64,67,73}

Opioid and non-opioid analgesics are useful for nociceptive pain; antidepressants and anticonvulsants, for neuropathic pain; topical treatments such as anesthetics and analgesics (e.g., morphine, lidocaine, and benzydamine), coating agents, bland rinses, and ice chips are commonly used for patients with ulcers and oral mucositis; cannabinoids could be considered in certain cases. Adenosine A3 receptor agonists are a promising drug class that reduces central sensitization leading to nociceptive pain, but efficacy has not yet been proven. Finally, carers could attempt complementary therapies in patients for whom conventional treatment has not provided adequate pain relief. However, evidence is lacking, and further studies are needed to comprehend the benefits of each therapy in this specific population.^{13,69,73,74}

Dental caries and gingivitis

Periodontal disease and caries are highly prevalent in older adults with cancer. Oral changes associated with the aging process (gum atrophy, loss of masticatory force, changes in saliva production) and treatment options (chemotherapy, radiotherapy, drugs for primary comorbidities) could explain this phenomenon.⁷⁵

The overall prevalence of dental caries is 28%. The weighted prevalence in patients who receive chemotherapy is 37%, and after radiotherapy, 24%. For gingivitis, the weighted prevalence is 20%, with an increase in both the plaque index (1.46, SD 0.23) and gingival index (1.02, SD 0.15), which are considered risk factors for periodontal disease. Exact data for older adults are not available.⁷⁶

In patients with periodontal conditions, scaling and prophylaxis combined with good oral hygiene and dietary advice should be promoted, with particular emphasis on adequate hydration. Deep scaling and root planing should preferably be performed at least 14 days before any cancer treatment. Mouth rinses with aqueous (alcohol-free) chlorhexidine gluconate are appropriate for short-term use.⁷⁵

Restorative treatment in older adults with cancer includes caries removal and dental restorations as appropriate. If necessary, defective restorations should be removed and replaced. As in other patients with periodontal disease, necessary extractions should be undertaken at least 2 weeks before the start of cancer treatment.

Quality of life, aesthetics, and function are linked to retained vital and viable teeth,⁷⁵ and a comprehensive oral evaluation and identification of dental caries and gingivitis prior to any cancer treatment is mandatory. This should occur several days before starting chemotherapy (if the case allows it) to promote adequate healing. Oral examinations should be part of a comprehensive geriatric assessment, which is a fundamental tool for the management of older patients with cancer.⁷⁷

Denture retention and denture problems

The prevalence of denture problems in patients with advanced cancer ranges from 57 – 83%.¹³ Their presence leads to cumbersome symptoms such as dry mouth, difficulty chewing, dysphagia, decreased nutritional intake, impaired speech, anorexia, poor oral hygiene, halitosis, oral candida infection, and bone density loss.⁷⁸

Oral health is closely associated with orofacial appearance. Even if oral care is an essential aspect, dentures are often not considered a priority, especially in patients with advanced cancer when various complex needs must be managed. The aforementioned symptoms may compromise different aspects of daily living, such as eating and sleeping, and may cause embarrassment, anxiety, depression, and social isolation, with a negative impact on quality of life.⁷⁹

Even effective oral care may be undermined if care of dentures is inadequate. Since dentures may act as a reservoir for oral pathogens and lead to repeated infection of the oral environment, removing denture plaque is essential for maintaining oral health.⁷⁸ Denture care in patients with advanced cancer includes removing dentures overnight and mechanical cleaning once a day (brushing with soap to remove debris and then rinsing with water). Toothpaste or denture cream can be used if preferred by the patient.⁷⁸ Biochemical cleaning should also be performed once daily; however, many proprietary denture cleaning solutions are ineffective against candida. Therefore, the most appropriate solution is a broad-spectrum,

antimicrobial agent such as dilute sodium hypochlorite (for non-metallic dentures only) or chlorhexidine, which has antibacterial, antifungal, and antiplaque properties and is suitable for all dentures. Chlorhexidine is sometimes used for routine mouth washing; in this setting, it can be unpalatable and lead to taste disturbances, although this can be reduced by diluting with an equal volume of water with no loss of efficacy. Oral rinsing with chlorhexidine should not be done more than once every 12 hours. At night, dentures should be cleaned and stored in a denture box.^{13,80}

Mucositis

Mucositis is defined as erythema and ulceration of the mucosal lining at any part of the gastrointestinal tract.⁷⁷ It is a common complication of cancer treatment, with an incidence ranging from 20 to 95%.^{81,82} Oral mucositis (OM) has a heavy toll on patients' quality of life since it may lead to pain, dysphagia, need for enteral or parenteral nutrition, increased opioid consumption, interruptions in treatment

and, among immunosuppressed patients, increased mortality rates.⁸³⁻⁸⁵ The prevalence of oral mucositis in older adults ranges from 22.3% in patients with solid advanced tumors receiving chemotherapy to 95% in patients with head and neck cancer receiving chemoradiotherapy.^{86,87}

Several studies have identified extremes of age as a risk factor for severe oral mucositis, as well as female gender, high body mass index, preexisting periodontal disease, poor baseline nutritional status, and genetic susceptibility.⁸⁸ The association between young age and oral mucositis is attributed to a higher epithelial mitotic rate, and in older adults, while the reason is still unclear, to a higher prevalence of hyposalivation.

Even though research on the prevention and treatment of oral mucositis has gained relevance in the last decades, data for older patients is limited,⁸⁹ and most decisions are extrapolated from evidence in younger adults. Recent guidelines recommend a holistic approach to patients at risk of oral mucositis, including participation of dentists, oncologists, and nurses.⁹⁰ Interventions included in Table 1^{77,81,90-104} have

TABLE 1. Recommendations for the prevention and treatment of oral mucositis.

Intervention	Recommendation	Level of evidence	Recommendations for older adults
Basic oral care	High-quality evidence is limited. ^{81,91} Multiagent combination oral care protocols: prevention of OM during CT, head and neck RT, and hematopoietic stem cell transplantation	III	Remove dentures before performing oral care; defer wearing dental prosthetics as long as possible until the lining tissues are healed. ⁹²
Benzydamine mouthwash	Prevention of OM in patients with head and neck cancer receiving RT-CT. ⁷⁷	I	The mean age across studies was 53 ± 11.2 and 56 ± 16 years. ⁹³⁻⁹⁵
Low-level laser therapy	Prevention of OM in adults receiving RT-CT for head and neck cancer.	I	In older adults with head and neck tumors receiving RT-CT, a significant reduction in the incidence and severity of OM, pain, and weight loss was reported. ⁹⁶
Cryotherapy (30 minutes)	Prevention of OM in patients receiving bolus 5-fluorouracil.	II	The mean and median age at the clinical trials ranged from 36 to 63 (8 – 85) years. ^{97,98}
Honey	Prevention of OM in patients with head and neck cancer who receive either RT or RT-CT. ^{81,99}	II	Small studies, with median age ranging from 63 (19 – 89) to 59 (39 – 85) years. ⁹⁹
Dexamethasone-containing mouthwash	Reduction of the incidence and severity of OM in women with breast cancer receiving everolimus and exemestane. ¹⁰⁰	II	Median age 61 (56 – 67) years. ¹⁰⁰
Topic morphine 0.2% mouthwash	Treatment of OM-associated pain in patients with head and neck cancer who receive RT-CT.	III	The mean age across studies was 49.5 ± 13.2 and 58.8 (44 – 80) years; ECOG performance status was 1 in 57% and 2 in 43%. ^{101,102} Adverse effects (itching, burning, foul taste) did not lead to discontinuation. No systemic adverse effects reported. ¹⁰¹
Methylene blue rinse	A randomized phase 2 clinical trial ¹⁰³ and an uncontrolled cohort study ¹⁰⁴ demonstrated a significant reduction in pain and improved oral functioning in patients aged 18-83 years.	II	-

OM: oral mucositis; CT: chemotherapy; RT: radiotherapy; ECOG: Eastern Cooperative Oncology Group Performance Status.

proven beneficial in the prevention and treatment of mucositis and are recommended by the Multinational Association for Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO).

Osteonecrosis of the jaw

Medication-related osteonecrosis of the jaws (MRONJ) is the necrosis of bone resulting from impaired blood supply. It is an adverse effect of bone-targeted therapies (BTT) such as denosumab and bisphosphonates, which are used to prevent symptomatic skeletal events following bone malignancy, including multiple myeloma and bone metastases from solid tumors such as prostate, breast, or lung cancers.¹⁰⁵ Up to 5% of patients with cancer develop MRONJ as late as 3 years after bone-targeted therapy.¹⁰⁶

Previous work suggests the risk of MRONJ is higher in patients diagnosed with cancer (< 5%) than in those diagnosed with osteoporosis (< 0.05%). Regardless of indication, time of exposure to BTT is associated with increased risk for developing MRONJ, with cumulative hazards increasing from 1% after 12 months of treatment up to 11% after 4 years.

Systemic risk factors which increase the risk of MRONJ include the type of disease (multiple myeloma patients have the highest incidence, at around 10%) and the administration of concomitant therapies (for example, chemotherapy, glucocorticoids, antiangiogenic agents).¹⁰⁷

Locally, dentoalveolar surgery and dental extraction during BTT are the most common identifiable risk factors; up to 27.5% of individuals thus exposed can develop MRONJ.^{108,109}

The clinical diagnostic criteria for MRONJ include all of the following: current or previous treatment with antiresorptive agents; persistently (> 8 weeks) exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region; and no history of radiation therapy to the region or metastatic disease to the jaws.¹⁰⁷

Clinically, MRONJ is characterized by pain, soft tissue swelling, erythema, discharge, tooth loss, deformity, pain, and dysesthesia. Other manifestations are unexplained jaw pain, fistula/sinus tract, loose teeth, and pathological fractures.¹¹⁰

The best preventive strategy is for patients to undergo an exhaustive dental and oral examination before starting BTT, to address any preexisting issues (dental and periodontal infection foci) and maintain oral health. BTT should be delayed until oral mucosal healing is complete. Once started on BTT, patients should continue dental and periodontal infection prevention strategies and supportive periodontal therapy.

Earlier stages of MRONJ are usually treated conservatively with pain and infection control (antimicrobial mouthwash and oral antibiotics). The decrease of the intraoral bacterial

load minimizes the risk of exposed bone infection and disease progression. In the presence of exposed bone (latter stages), surgical treatment, which ranges from superficial debridement to complete resection, should be considered. In addition, a 10-day to 3-week course of broad-spectrum oral antibiotic therapy is also recommended for latter stages of MRONJ. Even though there is no conclusive evidence, BTT should be carefully reconsidered in these patients.^{107,111}

The surgical resection of necrotic jawbone is indicated in patients with advanced who are unresponsive to supportive treatment, and it is palliative rather than curative. Conservative surgical treatments (debridement or bone curettage and sequestrectomy) differ from surgical resection in that the removal and curettage of necrotic bone is performed without the intention of including a margin of normal surrounding bone.¹¹²

Some proposed adjunctive treatments are biostimulation (ozone or laser therapy), hyperbaric oxygen therapy, and teriparatide (only in patients with osteoporosis), but evidence is poor.^{107,113}

Strengths, limitations, and implications

Several limitations of this study must be acknowledged. This is a narrative literature review, which enabled us to identify gaps and shape new research questions, but lacks the methodology needed to answer highly structured or specific research questions or to draw conclusions or detect patterns between findings. In addition, this review relied on the judgment of the authors for its contents, as no restrictions were applied with regards to timing of publication and study type and the quality of the cited manuscripts was not assessed. However, it clearly demonstrates the lack of evidence regarding oral conditions associated with cancer and cancer treatment in older adults and underlines the need for high-quality research in this population. Knowledge gaps are numerous and include lack of epidemiological data, description of specific risk factors, possible interventions, and their matching economic-evaluation studies; prevention and treatment guidelines for older adults with cancer are also lacking. Previous work on younger populations diagnosed with head and neck cancer has shown significant improvements in clinical and radiographic periodontal parameters and better oral hygiene habits when a multidisciplinary approach is taken.¹¹⁴ Similar studies in older adults with cancer are urgently needed.

CONCLUSIONS

Oral conditions are common in patients with advanced cancer and cause significant morbidity. However, although cancer is

a disease of older adults, there is a lack of information regarding oral conditions among older individuals with cancer. Frequently reported oral conditions in patients undergoing cancer therapy include xerostomia, dysgeusia, candidiasis, mucositis, and dental caries. Older age has been shown to be a risk factor for severe mucositis in the oncological context.

Even though formal guidance provides an evidence-based framework for the management of these common problems in patients with cancer, individualized management is always required, with preventive measures, assessment, and reassessment as the cornerstones. Unfortunately, many recommendations are based on evidence of low quality and/or extrapolated from younger patients with cancer. Further research into the oral health of older adults with cancer is warranted, with improvement of patients' quality of life as the ultimate goal.

Conflict of interests

Dr. García-Lara has received honoraria for lectures from Ferrer Laboratories during the last 36 months. Dr. Chavarri-Guerra

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Authors' contribution

APNR: conceptualization, supervision, visualization, writing – original draft, writing – review & editing. JPNN: writing – original draft. GCK: writing – original draft. JGC: writing – original draft. YJC: writing – original draft. LGLM: writing – original draft. RRT: writing – original draft. JARN: writing – original draft. CARM: writing – original draft. DASV: writing – original draft. ACTP: writing – original draft. JMAGL: writing – original draft. ESPC: visualization, writing – review & editing. YCG: visualization, writing – review & editing.

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