Scholars LITERATURE

La Prensa Medica Argentina

Review Article

DOI: https://doi.org/10.47275/0032-745X-412
Volume 110 Issue 2

Personalized Medicine and Oral Cancer

Pinelopi Petropoulou

Department of Nursing, University of West Attica, Aigaleo, Greece

Abstract

Oral cancer (OC) is one of the most frequent malignancies worldwide, is constantly increasing especially in developing countries and is associated with high morbidity and mortality. Early diagnosis and treatment play a decisive role in survival outcomes and are directly influenced by socio-economic factors. According to studies, the worst pattern of invasion could be an important prognostic factor in oral squamous cell cancer, may be useful for risk stratification and treatment decision making and can help more personalized and effective treatment strategies. Moreover, studies have shown that the status of Bcl-2 protein is related to successful head and neck cancer (HNC) treatments and prognosis for survival, when saliva as a liquid biopsy is an emerging approach for screening and early diagnosis of cancer. In addition, immunologically active saliva substitutes appear more effective in treating dry mouth, while acyclovir and valacyclovir are effective in preventing and treating oral herpes in patients receiving cancer treatment. Furthermore, oral mucositis (OM) is an important side effect in patients receiving any type of systemic antineoplastics and radiation therapy, degrades their quality of life, causes delays or changes in anticancer treatment, and must be treated immediately due to its high frequency regardless of its staging. In the future, tissue electrical parameters could be used to predict side effects of radiotherapy (RT). Also there appear to be 2 subgroups of patients with HNC that are molecularly and clinically distinct from each other and this helps to develop individualized effective therapies. Finally, Tele-Dentistry can offer possibilities for detection, early diagnosis, treatment, and remote monitoring of potentially malignant disorders by a specialist.

Keywords: Personalized dentistry, Oral cancer, Salivary biomarkers, Head and neck cancer, Prevention, Oral microbiome, Mucositis

[*] ***Correspondence to*:** Pinelopi Petropoulou, Department of Nursing, University of West Attica, Aigaleo, Greece, E-mail: ppetropoulou@uniwa.gr

Citation: Petropoulou P (2024) Personalized Medicine and Oral Cancer. Prensa Med Argent, Volume 110:2. 412. DOI: https://doi.org/10.47275/0032-745X-412

Received: February 17, 2024 **; Accepted:** March 04, 2024 **; Published:** March 06, 2024

Introduction

OC is a serious public health problem, due to increased morbidity and mortality rates. It has a multifactorial etiology and is shaped by biological, social, economic, cultural, and environmental factors. In addition, unhealthy eating practices and the presence of comorbidities further aggravate the problem. In developing countries as well as in lower socio-economic strata, it shows a significant increase. Exogenous factors such as smoking, alcohol consumption, solar radiation, and endogenous factors such as immunodeficiency, iron deficiency anemia, malnutrition are risk factors that promote the occurrence of OC. Additional temperamental and genetic factors appear to play a significant role [1].

Its frequency increases with age, it occurs more in men than in women and 90% is squamous cell carcinoma. Intraoral cancer in total is 4 times more common than lip cancer and approximately 1 in 5 patients shows cervical metastases at the time of diagnosis due to late appearance to a doctor. Patients with previous oral or respiratory tract cancer have a 5 - 40% increased risk of developing a new second cancer in the mouth or other locations. The highest percentages concern smokers who continue smoking after the treatment of the first tumor [2].

Smoking and alcohol have long been directly linked to cancers of the mouth and pharynx but according to new studies the same link exists with poor oral hygiene. People with poor oral hygiene and dental care are at greater risk for oral and pharyngeal cancer according to newer research. People with poor oral health are defined as those who have lost their teeth and have full or partial dentures or persistent bleeding gums.

OC has also been found to develop in the mouth, in places of chronic injury from broken teeth, bridges, and dentures. Prevention and timely diagnosis and treatment are decisive factors for the outcome of the disease, survival rate and the quality of patient's life. Chemo-RT that cancer patients receive has severe effects on the oral cavity and if they are not treated immediately, antineoplastic treatment will be delayed or may even be stopped temporarily while the patient's quality of life is certainly degraded [3].

Methodology

The purpose of this systematic study is to investigate the role of personalized medicine in the prevention and treatment of OC. According to the PRISMA method, the PubMed database was searched for the terms "Personalized Dentistry" and "Oral Cancer" with free full text from 2018 to 2023. 68 results were found and 15 were included in the study according to the selection criteria.

Study limitations

The present study was limited to the English language literature, with a time limit of 5 years, to a single database and to adult patients.

Results

Early diagnosis and treatment of OC is considered to play a key role in patient outcomes. This is usually assessed by estimating the time elapsed between key events in the cancer care pathway. Specifically, three intervals describe the time elapsed between the onset of symptoms and until the start of treatment. The patient interval includes the time

from symptom onset to first presentation to a healthcare professional, the diagnostic interval, time from first presentation to a clinician until diagnosis and the treatment interval, time from diagnosis to initiation of treatment. The length of time in the OC care pathway is influenced by socio-economic factors and may impact patient outcomes. In particular, in lower-income countries, patient-treatment intervals were longer and longer patient intervals were associated with a later stage of diagnosis. Studies in high-income countries found that longer treatment intervals were associated with lower survival. Further research is needed particularly in resource-poor settings in relation to survival rates [4].

Many studies have concluded that the worst pattern of invasion (WPOI) is associated with an unfavorable outcome in patients with oral squamous cell carcinoma. Depth of invasion is associated with oral squamous cell carcinoma prognosis, lymph node metastasis, local recurrence and gives postoperative prognostic results. The worst pattern of invasion also serves as a prognostic factor for oral squamous cell carcinoma, can give results preoperatively and may be useful for risk stratification and treatment decision making.

Depth of invasion and WPOI have been shown to be the most important pathologic predictors for local recurrence. Studies have shown that patients with a high WPOI [4, 5] had high rates of mortality and local invasion and worse outcomes in overall survival, disease-specific survival, and local recurrence rate. Based on WPOI local recurrence is evaluated, which implies increased morbidity, mortality, and quality of life degradation, as well as the survival without local recurrence, which entails better prognosis, reduced morbidity, and better quality of life. These results have important implications for clinical practice as individualized treatments can be planned for each patient's cancer management needs [5].

Leukoplakia is the most common pre-cancerous condition in the oral mucosa in the form of white plaque and transforms to squamous cell OC. It has been linked to smoking and when it occurs, a biopsy is needed immediately since the greater the degree of dysplasia, the higher the risk of occurrence of squamous cell OC. According to modern studies, the occurrence of squamous cell OC is increasing rapidly as is the mortality due to it and early diagnosis and intervention when white plaque is diagnosed is critical. The highest rates appear in Asia and Europe, more common in men than women, as is OC, and in people over 60 who smoke and drink alcohol. Screening of these high-risk patients and development of strategies and policies in primary care to inform and change patients' habits is needed [6].

Bcl-2 protein is a non-decreasing protein that has been detected in HNC as well as other cancers and has been associated with primary tumors. It is considered an independent predictor of risk and survival and is not related to TNM staging and the histological grade. A better survival rate is observed in tumors with positive Bcl-2 expression and no association with overexpression of the protein appears in cancer recurrences.

High tumor response rates were also observed in patients positive for Bcl-2 protein while response to chemotherapy with cisplatin appeared to worsen in patients with overexpression of the protein. Bcl-2 expression was the most important index for survival rate and disease-free survival within 5 years in early-stage HNC patients treated primarily with RT. Further research is needed to correlate Bcl-2 protein expression with the prognosis and survival from HNC [7].

Oral mucosal toxicity appears to be an important side effect in non-irradiated cancer patients and has high prevalence in patients receiving systemic antineoplastic therapy. No significant differences were found in the effects on the oral mucosa between traditional chemotherapy alone, targeted therapies or their combination. These findings support the need to evaluate the oral mucosa in patients receiving any type of systemic antineoplastic agents in the same way to avoid underdiagnosis because mucosal toxicity is an extremely common side effect of cancer therapy [8].

OM is one of the most common complications of chemotherapy and radiation and displays as an erythema and ulceration of oral mucosa. If not treated immediately, it not only impairs the quality of life of patients but also triggers other complications in the oral cavity and causes delays or changes in antineoplastic therapy. The severity of OM was positively related to disease severity, age, and chemotherapy dosage. Studies have proven that curcumin, one of the components of turmeric, appears to have anti-inflammatory and antioxidant properties. Curcumin can improve oral hygiene and the ability to open the mouth. It seems to be more effective in the treatment and prevention of oral mucosa seen in patients receiving chemotherapy alone, compared to those receiving combination therapy, while it seems to be ineffective in the destruction of salivary glands and in the treatment of dry mouth [9].

Xerostomia is directly related to radiation therapy for HNC and negatively affects all mouth functions, chewing, swallowing, taste, speech. It affects nutritional habits and degrades the quality of life. Patients with dry mouth may also have more frequent fungal infections and dental caries. In the past, mucosal lubricants, saliva substitutes and surgical treatment of the salivary glands have been proposed to treat the symptoms.

New studies show that immunologically active saliva substitute with immunologically active natural enzymes improves objectively measured salivary flow in irradiated patients compared to non-immunologically active mouthwash. Calculating the unstimulated whole saliva seems that immunologically active saliva substitute is significantly more effective in improving subjective and objective measurements of dry mouth. This treatment is very safe, with high-quality side effect profiles and it is indicated to be taken for the rest of life [10].

To enable optimal dental care for patients with HNC before, during, and after radiation therapy, close multidisciplinary communication and collaboration between radiation oncologists, dentists, medical oncologists, and oral surgeons is absolutely necessary. Clinicians should have knowledge of oral signs and symptoms so that appropriate clinical assessment and timely medical referral for treatment can be made [11].

Clinicians should inform and educate patients with OC about the potential risk of oral side effects after chemotherapy and radiation, preventive programs for dry mouth, scrupulous oral hygiene, changes in dietary habits, control of the microbial flora and the use of prescribed oral medical preparations. Additionally, Tele-Dentistry can offer possibilities for detection, early diagnosis, treatment, and remote monitoring of potentially malignant lesions so that they do not develop into cancer but also of other oral disorders by a specialist with free chat applications and taking photos [12].

HNC treatment has some side effects that are painful and difficult to manage. OM, dry mouth, sticky saliva, difficulty swallowing solid foods and dysgeusia are common complications of radiation therapy in the treatment of HNC.

OM is classified into 4 grades depending on its severity. Grade 2 lesions are associated with pain, but the patient can swallow solid foods, while grades 3 and 4 involve difficulty in swallowing food, according to the objective assessment with a special scale by a doctor with special

training and monitoring with frequent re-examination. Thus, ulcerative OM may require modifications to the radiation therapy regimen and indeed high degrees of OM require treatment interruption and topical analgesics for paroxysmal pain several times a day. Discontinuation of RT is associated with decreased local tumor control rates and decreased survival [13, 14].

Despite the unpleasant effects of OM on the patient's quality of life, there are no diagnostic tools for predicting it after RT in HNC. Research has shown that local electrical parameters of tissues measured after the 1st week of RT such as resistance, phase angle, impedance module and reactance have higher values in the irradiated regions. They could therefore be used in the future to predict OM, assess the risk of its occurrence in irradiated patients and plan preventive strategies to avoid a poor prognosis resulting in the discontinuation of RT. In the future, tissue electrical parameters could be used to predict side effects of radiation therapy [15, 16].

Immunodeficiency and immunosuppression from various forms of anticancer therapy are the main predisposing factors for oral herpes or HSV reactivation. Acyclovir (topical, per os or intravenous) and valacyclovir (requires less frequent dosing and is less expensive) have been found to be particularly effective in preventing HSV-1 in patients undergoing cancer treatment. Acyclovir (800 mg/day) is superior compared to valacyclovir in the results of virus prevention, and therapeutically, the administration of antiherpetic treatment as early as possible reduces the patient's morbidity as well as the complications in his antineoplastic treatment, ulceration, and malnutrition [17].

Studies have already been carried out on the molecular diagnosis of cancer by liquid biopsy and the analysis of circulating cancer cells for the detection of residual disease, the prediction of recurrent disease and the monitoring of the patient after treatment. Saliva represents a promising non-invasive source of new biomarkers for the diagnosis and prognosis of cancer. It seems to have biochemical advantages in relation to blood, easy collection and storage and with less disturbance in monitoring the patient. Changes in the concentrations of certain biomarkers in saliva contribute to the diagnosis, prognosis, individual risk assessment and monitoring of HNC and distant cancers. The application of saliva as a novel liquid biopsy for screening and early diagnosis is an emerging approach, with sufficient sensitivity and specificity relative to plasma, to develop personalized medical strategies. Diagnosis based on saliva in cancer is still in its infancy for many types of tumors. Future larger and randomized studies are needed to validate salivary biomarkers for tumor diagnosis, characterization, and monitoring of the tumor [18].

Bad oral hygiene has long been associated with OC. More recent research has found a direct link between the incidence of OC and moderate and advanced periodontal disease. Alcohol, smoking, aging, and poor oral hygiene are common risk factors for periodontitis and OC, but periodontitis should be considered as a separate risk factor in OC but also in distant cancers. The severity of periodontitis promotes changes in the oral microbiome and thus creates a suitable environment for the appearance and development of oral squamous cell carcinoma. Men seem to neglect their oral health more than women and have higher rates of periodontal disease and OC. Dentists play an important role in the prevention of cancer, since they can also assess the socio-economic status of patients as well as their habits, lifestyle, and education. Structured preventive programs would reduce the rate of morbidity and mortality related to OC, focusing on the high level of oral hygiene education, changing harmful habits, and informing and educating about the disease [19].

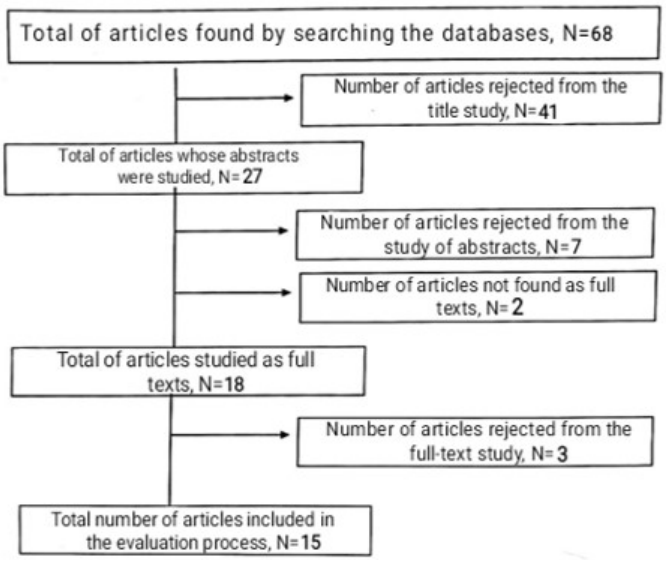

Figure 1: The process of searching and locating research articles.

Conclusion

By studying the oral microbiome from biofilms, it seems that oral dysbiotic conditions can contribute to tumorigenesis in the mouth but also in distant parts of the body. Periodontitis, according to recent research, is a separate risk factor for the development of OC and in high-risk patients, the maintenance of good periodontal health with appropriate oral hygiene and follow-up minimizes the risks of cancer. Dentists play an important role in the precaution and treatment of OC as well as to avoid the disturbing effects in the oral cavity of antineoplastic treatment such as mucositis, dry mouth, herpes infection or other microbial infections. The cooperation of dental and medical teams in the treatment of cancer, promotes the general and oral health of patients receiving cancer treatment and regardless of the site, type, stage of cancer, effective prevention and management of caries and periodontal disease must be implemented.

According to recent research, saliva as a liquid biopsy is an emerging approach for screening and early diagnosis of cancer and future research should aim to test and validate saliva biomarkers as a diagnostic and preventive tool. Finally, it appears that in HNC patients there are two subgroups, which differ molecularly and clinically from each other. This knowledge can help develop personalized treatments to improve outcomes for these patients.

Acknowledgements

None.

Conflict of Interest

None.

References

1. Kwaśniewska A, Wawrzeńczyk A, Brus-Sawczuk K, Ganowicz E, Strużycka I (2019) Preliminary results of screening for pathological lesions in oral mucosa and incidence of oral cancer risk factors in adult population. Przegl Epidemiol 73: 81-92.
2. Su WWY, Lee YH, Yen AMF, Chen SLS, Hsu CY, et al. (2021) Impact of treatment delay on survival of oral/oropharyngeal cancers: results of a nationwide screening program. Head Neck 43: 473-484. https://doi.org/10.1002/hed.26504
3. Fleming E, Singhal A (2020) Peer reviewed: chronic disease counseling and screening by dental professionals: results from NHANES, 2011-2016. Prev Chronic Dis 17: E87. https://doi.org/10.5888/pcd17.200152

4. Fernández-Martínez NF, Petrova D, Špacírová Z, Barrios-Rodríguez R, Pérez-Sayáns M, et al. (2023) The duration of intervals on the oral cancer care pathway and implications for survival: a systematic review and meta-analysis. Front Public Health 11: 1183244. https://doi.org/10.3389/fpubh.2023.1183244

5. Binmadi NO, Mohamed YA (2023) Impact of worst pattern of invasion on prognosis of oral squamous cell carcinoma: a systematic review and meta-analysis. J Int Med Res 51: 1-6. https://doi.org/10.1177/03000605231206260

6. Zhang C, Li B, Zeng X, Hu X, Hua H (2023) The global prevalence of oral leukoplakia: a systematic review and meta-analysis from 1996 to 2022. BMC Oral Health 23: 645. https://doi.org/10.1186/s12903-023-03342-y

7. Silva FFVE, Caponio VCA, Camolesi GCV, Padín-Iruegas ME, Lorenzo-Pouso AI, et al. (2023) Correlation of Bcl-2 expression with prognosis and survival in patients with head and neck cancer: a systematic review and meta-analysis. Crit Rev Oncol Hematol 187: 104021. https://doi.org/10.1016/j.critrevonc.2023.104021

8. Rodríguez-Fuentes ME, Pérez-Sayáns M, Carreras-Presas CM, Marichalar-Mendia X, Bagán-Debón L, et al. (2023) Prevalence of acute oral mucosal damage secondary to the use of systemic antineoplastics: a systematic review and meta-analysis. Oral Surg Oral Med Oral Pathol Oral Radiol 135: 385-395. https://doi.org/10.1016/j.oooo.2022.11.016

9. Kia SJ, Basirat M, Saedi HS, Arab SA (2021) Effects of nanomicelle curcumin capsules on prevention and treatment of oral mucosits in patients under chemotherapy with or without head and neck radiotherapy: a randomized clinical trial. BMC Complement Med Ther 21: 232. https://doi.org/10.1186/s12906-021-03400-4

10. Marimuthu D, Han KM, Mohamad MSF, Azman M (2021) Saliva substitute mouthwash in nasopharyngeal cancer survivors with xerostomia: a randomized controlled trial. Clin Oral Investig 25: 3105-3115. https://doi.org/10.1007/s00784-020-03634-5

11. Lee HJ, Han DH, Kim JH, Wu HG (2021) The effect of comprehensive oral care program on oral health and quality of life in patients undergoing radiotherapy for head and neck cancer: a quasi-experimental case-control study. Medicine 100: e25540. https://doi.org/10.1097/MD.0000000000025540

12. Uhrin E, Domokos Z, Czumbel LM, Kói T, Hegyi P, et al. (2023) Teledentistry: a future solution in the diagnosis of oral lesions: diagnostic meta-analysis and systematic review. Telemed E Health 29: 1591-1600. https://doi.org/10.1089/tmj.2022.0426

13. Ueno T, Yatsuoka W, Ishiki H, Miyano K, Uezono Y (2022) Effects of an oral mucosa protective formulation on chemotherapy-and/or radiotherapy-induced oral mucositis: a prospective study. BMC Cancer 22: 90. https://doi.org/10.1186/s12885-021-09107-6

14. Ueno T, Zenda S, Konishi T, Yurikusa T, Shibasaki Y, et al. (2019) The post hoc analysis comparing the severity grades of chemoradiotherapy-induced oral mucositis scored between the central and local assessors in a multicenter, randomized controlled trial of rebamipide for head and neck cancer. Int J Clin Oncol 24: 241-247. https://doi.org/10.1007/s10147-018-1355-7

15. Qadir F, Lalli A, Dar HH, Hwang S, Aldehlawi H, et al. (2019) Clinical correlation of opposing molecular signatures in head and neck squamous cell carcinoma. BMC Cancer 19: 830. https://doi.org/10.1186/s12885-019-6059-5

16. Sanches GLG, da Silva Menezes AS, Santos LI, Durães CP, Fonseca LL, et al. (2020) Local tissue electrical parameters predict oral mucositis in HNSCC patients: a diagnostic accuracy double-blind, randomized controlled trial. Sci Rep 10: 9530. https://doi.org/10.1038/s41598-020-66351-9

17. Aribi Al-Zoobaee FW, Yee Shen L, Veettil SK, Gopinath D, Maharajan MK, et al. (2020) Antiviral agents for the prevention and treatment of herpes simplex virus type-1 infection in clinical oncology: a network meta-analysis. Int J Environ Res Public Health 17: 8891. https://doi.org/10.3390/ijerph17238891

18. Rapado-González Ó, Martínez-Reglero C, Salgado-Barreira Á, Takkouche B, López-López R, et al. (2020) Salivary biomarkers for cancer diagnosis: a meta-analysis. Ann Med 52: 131-144. https://doi.org/10.1080/07853890.2020.1730431

19. Komlós G, Csurgay K, Horváth F, Pelyhe L, Németh Z (2021) Periodontitis as a risk for oral cancer: a case–control study. BMC Oral Health 21: 640. https://doi.org/10.1186/s12903-021-01998-y