



Review Article

Stress, inflammation, and resilience among patients with oral squamous cell carcinoma undergoing multimodal therapy: Current knowledge and future directions

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ABSTRACT

Oral squamous cell carcinoma represents a significant public health challenge in Asia, where multimodal therapies, while extending survival, impose substantial biologic and psychosocial stress. Sustained activation of the sympathetic–adrenal–medullary axis and dysregulation of the hypothalamic–pituitary–adrenal axis increase catecholamines, cortisol, interleukin-6, and C-reactive protein, accelerating tumor progression, impairing treatment tolerance, and increasing cardiovascular risk. Betel quid chewing, prevalent in the region, exacerbates inflammation and contributes to cardiovascular comorbidities. Resilience, defined as the ability to restore physiologic and emotional homeostasis, modulates these pathways, with higher resilience linked to improved recovery, quality of life, and survival. Current evidence supports interventions including structured psychoeducation, cognitive-behavioral therapy, and peer mentoring to reduce anxiety and enhance treatment adherence. Smoking and betel quid cessation, alongside cardiometabolic optimization, mitigate inflammatory burden. Nonopioid strategies, including acupuncture, transcutaneous vagus nerve stimulation, and mindfulness, recalibrate neuro-immune signaling while minimizing opioid reliance. Enhanced recovery surgical protocols and omega-3 supplementation attenuate inflammatory responses and preserve lean mass. Emerging biomarkers such as heart rate variability and neutrophil–lymphocyte ratio show promise for real-time stress and inflammation monitoring. Digital health technologies and telerehabilitation extend intervention benefits postdischarge. Future research should focus on validating predictive biomarkers, developing resilience-stratified trials, integrating cardio-oncology surveillance, and implementing precision supportive care models that incorporate stress, inflammation, and resilience metrics to optimize oncologic and cardiovascular outcomes in this high-risk population.

KEYWORDS: *Inflammation, Integrative interventions, Oral squamous cell carcinoma, Resilience, Stress*

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INTRODUCTION

Oral squamous cell carcinoma (OSCC) remains a major global health burden, with disproportionately high incidence and mortality in Asian populations [1]. Taiwan reports the highest age-standardized incidence of lip and oral cavity cancer among South and Southeast Asian nations [2]. Notably, OSCC ranks as the second leading cause of cancer-related death in Taiwanese adults aged 45–54 years [3], reflecting a concerning rise in younger cohorts. Surgery remains the primary treatment for OSCC, with adjuvant radiotherapy (RT) or concurrent chemoradiotherapy (CRT) selected on the basis of tumor stage and pathological invasion [4].


Multimodal therapy often induces lasting toxicities that cause substantial physical and psychological distress and may accelerate disease progression [5,6]. Patients with OSCC face heavy health burdens, with the highest suicide rates and most severe pain among all cancers [7,8]. Stress and inflammation interact synergistically, impairing quality of life (QoL); worsening prognosis; and driving cancer onset, growth, and

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metastasis [6]. Resilience, which is the ability to adapt and maintain psychological, cognitive, and physical stability after a cancer diagnosis, is linked to enhanced survival [5,9]. Higher resilience is linked to better survival rates, highlighting the roles of immune and neuropsychological mechanisms in reducing stress and supporting recovery [10-12]. However, evidence on the interplay among stress, inflammation, and resilience and on strategies to assess and enhance resilience in patients with OSCC undergoing multimodal therapy is limited.

In this article, recent evidence on the interplay of stress, inflammation, and resilience in patients with OSCC undergoing multimodal therapy was reviewed. Neuroendocrine-immune dysregulation mechanisms that affect disease course and cardiovascular risk were examined. Emerging interventions, including psycho-behavioral support, inflammatory modulation, and nonopioid pain management, were evaluated. Challenges in developing precision supportive care models that incorporate point-of-care biomarkers and resilience metrics to optimize oncologic and QoL outcomes were addressed.

STRESS AND INFLAMMATION: A COMPLEX SIGNALING NETWORK IN ORAL CANCER PROGRESSION

Stress and inflammation form a mutually reinforcing network that drives OSCC progression. Patients experience psychological stress from diagnosis, physical burden from invasive treatments, and persistent anxiety about recurrence and social disruption [5]. Acute stress activates the sympathetic nervous system (SNS), releasing epinephrine and norepinephrine, which bind to β_2 -adrenergic receptors (β_2 -ARs) to mobilize energy for immediate responses. On the other hand, chronic stress induces sustained activation of the hypothalamic–pituitary–adrenal (HPA) axis, increasing glucocorticoids that suppress immune function and promote systemic inflammation [12].

Stress hormones, particularly through β_2 -AR, accelerate the growth of oral squamous carcinoma cells and stimulate secretion of interleukin (IL)-6, enhancing tumor-associated inflammation. Tumor-derived cytokines, such as IL-6 and IL-1 β , can disrupt central nervous system function, leading to HPA axis dysregulation and symptoms such as depression, insomnia, and pain [13]. Stress hormones and tumor cytokines amplify each other, worsening cancer outcomes and patient well-being [12,14].

Cigarette smoking, betel quid chewing, and alcohol consumption increase carcinogenic risk through bioactive compounds that trigger chronic inflammation, promoting tumor growth [14]. In Taiwan, approximately 90% of OSCC cases are associated with long-term betel quid use. Key alkaloids, such as arecoline and arecaidine; damage oral epithelial cells; induce systemic inflammation; and contribute to cardiovascular comorbidities, including hyperlipidemia, metabolic syndrome, and atherosclerosis [14].

PSYCHOLOGICAL DISTRESS AND FUNCTIONAL IMPAIRMENT

Many patients with OSCC face considerable anxiety and uncertainty due to insufficient knowledge regarding their illness

and treatment options [15]. This psychological burden impairs informed decision-making and reduces therapy adherence [15]. Postoperative changes, such as altered facial appearance and impaired speech or eating, harm body image, self-esteem, and worsen depressive symptoms [16]. Depression, anxiety, and posttraumatic stress are markedly higher than in the general population, increasing with disease advancement and adversely affecting treatment outcomes and survival [17].

Psychological distress closely correlates with clinical symptoms. Before treatment, 33% of patients report stress from oral ulcers and eating difficulties, rising to 77% during RT [18]. Notably, 15.7% experience suicidal ideation within 1 year of diagnosis [7]. Despite these challenges, few patients access psychological support [19], highlighting a critical gap in psycho-oncological care.

SURGICAL STRESS AND INFLAMMATORY RESPONSES

Surgical procedures elicit a systemic inflammatory response involving pro-inflammatory cytokines, endothelial dysfunction, and neutrophil activation, potentially leading to organ dysfunction and adverse outcomes [20]. Surgical procedures activate the HPA axis and SNS, increasing cortisol and catecholamine levels [6,11]. Even short procedures can induce substantial inflammation due to tissue trauma, hypothermia, transfusions, and anesthetic effects. These responses upregulate cytokines that affect wound healing, infection risk, and tumor immunology [21].

OSCC surgeries, often involving complex resections and neck dissections, have postoperative complication rates of 20%–50% [22]. Increased inflammatory markers after surgery correlate with reduced QoL and increased complication rates, underscoring the need for targeted anti-inflammatory strategies [23]. Complication risk increases with comorbidities, poor nutrition, and surgical complexity. Advanced tumors or those affecting critical structures require extensive resections, causing increased functional deficits and prolonged rehabilitation [5].

STRESS INDUCED BY RADIOTHERAPY AND CHEMOTHERAPY

Postoperative CRT remains the standard treatment approach for patients with locally advanced OSCC [4]. RT utilizes high-energy ionizing radiation to damage the DNA of cancer cells and inhibit their proliferation. However, this process also affects normal tissues, inducing various forms of cellular stress, including oxidative stress, DNA damage responses, and endoplasmic reticulum stress, which contribute to further tissue damage and inflammation [24]. These stress pathways exert a double-edged effect, promoting tumor cell death while simultaneously heightening normal-tissue susceptibility to inflammation and damage, which ultimately limits treatment tolerability. Chemotherapeutic agents, such as cisplatin and 5-fluorouracil (5-FU), enhance radiosensitivity and induce cancer cell apoptosis but cause oxidative damage to healthy cells.

CRT is associated with severe side effects, including bone marrow suppression, mucocutaneous inflammation, and

vascular toxicity. It frequently causes grade ≥ 3 acute adverse events, which reduce treatment adherence, leading to dose reductions, interruptions, or early termination, and ultimately worsen prognosis and survival [24].

PAIN MECHANISMS AND CHALLENGES IN ORAL CANCER

Despite the WHO guidelines, cancer pain remains undertreated, with patients with OSCC particularly experiencing a high burden. Pain affects up to 83.4% of patients during treatment and persists in 38%–45% 1 year after diagnosis [25]. These pain statistics reflect the dense innervation of the oral cavity, aggressive tumor invasion, and considerable psychological stress [26].

OSCC pain, often accompanied by sensory disturbances or motor dysfunction, evolves with disease and treatment, defying conventional classification systems for facial pain or headaches [26]. Within the tumor microenvironment, cancer cells release cytokines and prostaglandins, sensitizing nociceptors, lowering pain thresholds, and amplifying nociceptive signaling [27]. Tumor invasion into tissues and bone causes nerve damage, leading to hyperalgesia and widespread pain. Emotional stress activates the thalamo-limbic system, worsening anxiety and depression, which intensify pain perception and perpetuate physical and psychological distress.

Treatment-related pain in OSCC arises from tissue injury, inflammation, and neuropathic damage. Surgery induces acute postoperative pain via localized trauma, typically resolving with healing. CRT causes mucositis, xerostomia, and ulceration, exacerbating discomfort. Neuropathic pain, marked by burning or tingling, affects 25%–60% of patients, with RT contributing in 20% [25,28]. Both treatments trigger prostaglandin and cytokine release, activating nociceptors [28,29].

Additional complications include shoulder dysfunction after lymph node dissection or RT, causing pain and restricted mobility [30]. Chronic pain increases cardiovascular disease risk, with a dose–response link between pain severity and cardiovascular events, particularly in patients with preexisting conditions [31].

HIDDEN CARDIOVASCULAR RISKS IN PATIENTS WITH ORAL CANCER

Cardiovascular disease accounts for approximately 22% of deaths among cancer survivors, making it a major cause of mortality [32]. In Eastern Taiwan, 35.3% of newly diagnosed patients with OSCC have coexisting hypertension [33]. Arecoline in betel quid induces sympathetic activation, causing tachycardia and hypertension while triggering inflammation and coagulation cascades that disrupt lipid metabolism and vascular homeostasis, increasing vascular stress [14].

Extensive OSCC surgeries, often lasting 8–16 h, impose considerable anesthetic and hemodynamic burdens, increasing venous thromboembolism risk from 0.5% to 13% [34,35]. Cervical lymphadenectomy may cause lymphedema and increased venous pressure, impairing local

circulation. Cisplatin-based chemotherapy is associated with arrhythmias and ischemic events, particularly in vulnerable patients [36], and 5-FU causes cardiotoxicity in up to 68% of cases [37]. Targeted therapies (e.g., cetuximab and PD-1 inhibitors) and RT further heighten cardiovascular risk by accelerating carotid atherosclerosis and increasing stroke risk [36]. These treatment-related effects, combined with lifestyle factors and chronic stress, contribute to substantial long-term cardiovascular morbidity. Prospective cohorts using multimodal vascular imaging and autonomic profiling could elucidate treatment-related cardiotoxicity and inform preventive strategies for high-risk OSCC survivors.

PSYCHOLOGICAL DISTRESS AND QUALITY OF LIFE ASSESSMENT

The National Comprehensive Cancer Network recommends routine screening for psychological distress in patients with cancer to enhance supportive care [38]. The Distress Thermometer, a 0–10 Visual Analog Scale paired with a 39-item problem checklist, is widely used to screen for distress. A score of ≥ 4 prompts referral for psychosocial or psychiatric evaluation [38]. The Depression, Anxiety, and Stress Scale-21 measures symptom severity across three domains, enabling longitudinal monitoring of psychological well-being [39]. Health-related QoL is evaluated using disease-specific and generic tools. Cancer-specific QoL instruments [40], and the 12-item Short-form Health Survey (SF-12) are commonly employed. With its brevity and robust psychometric properties, SF-12 is particularly suitable for patients with oral cancer [41].

PHYSIOLOGICAL STRESS AND INFLAMMATION ASSESSMENT

Physical function and nutritional status remarkably affect patients' ability to tolerate oncological treatment and manage associated stress. The Malnutrition Universal Screening Tool reliably predicts postoperative complications and long-term survival [42]. Pain, inflammation, and nutritional decline are bidirectionally linked. Persistent nociceptive and inflammatory processes accelerate catabolism and reduce oral intake, creating a cycle that hinders clinical recovery [43]. Increased inflammatory burden can reduce the efficacy of nutritional interventions, limiting their benefits despite appropriate use. Comprehensive pain assessment, incorporating multiple tools and evaluating neuropathic features when relevant, is thus essential for effective patient care [44].

The neutrophil–lymphocyte ratio (NLR) is a cost-effective prognostic biomarker in oral cancer. Increased preoperative NLR is associated with advanced tumor staging, poor differentiation, lymphovascular invasion, and reduced overall survival in patients with OSCC [45], and structural brain changes linked to depression [46,47].

CARDIOVASCULAR AND AUTONOMIC STATUS

Noninvasive tools such as the ankle–brachial index and pulse wave velocity (PWV) assess arterial stiffness and thromboembolic risk in patients with cancer. A meta-analysis found higher PWV in patients with cancer than in healthy

controls, supporting its role in predicting cardiovascular events [48]. Routine head-and-neck computed tomography scans for cancer surveillance can detect vascular abnormalities, such as carotid wall thickness >2 mm, luminal narrowing $>50\%$, or noncalcified soft plaques, which pose greater stroke risk than calcified lesions [49]. Doppler ultrasound, which measures intima-media thickness, is the primary screening method [50].

Heart rate variability (HRV) reflects autonomic nervous system function and physiological adaptability. Higher HRV is linked to better survival in patients with cancer [51], whereas reduced variability, indicating sympathetic dominance, is common across cancer types. Although HRV research in OSCC is limited, studies in nasopharyngeal carcinoma show its utility in detecting subclinical cardiotoxicity during CRT [52]. Future research should develop real-time monitoring platforms integrating wearable HRV data with inflammatory markers, such as IL-6 and NLR, to enable early detection of stress – inflammation surges and timely interventions.

MULTIDIMENSIONAL RESILIENCE ASSESSMENT

Resilience reflects psychological adaptability and physiological robustness in facing adversity [5]. The 25-item Resilience Scale assesses domains, such as inner strength, social support, life purpose, and problem-solving, with higher scores linked to better disease adaptation and fewer depressive symptoms [53]. The 14-item Resilience Scale (RS-14) is more concise than the original 25-item version [54], requiring only 3 min to complete, with validated reliability in Chinese populations [55]. Higher resilience correlates with better QoL, reduced psychological distress, and greater hope and optimism in patients with oral cancer [56].

Current psychosocial interventions for cancer patients integrate cognitive-behavioral therapy (CBT), maladaptive-response modification, and positive coping strategies to cultivate positive thinking and optimism, which in turn foster hope and adaptive coping [57]. However, existing tools struggle to capture resilience's multidimensional nature, posing methodological challenges [58]. Advancing understanding of stress, inflammation, and resilience interactions requires integrating subjective and objective assessments with targeted interventions [59]. Randomized controlled trials (RCTs), stratified by baseline resilience phenotypes, are needed to evaluate whether tailored CBT, HRV biofeedback (HRV-BFB), or mindfulness programs yield resilience-dependent benefits.

Future studies should integrate subjective assessments, such as RS-14, with objective physiological markers, such as HRV, to establish clinical practice value. An online platform incorporating electronic health records and 5 min HRV measurements during routine vital sign monitoring could minimize clinical burden while enabling individualized precision interventions. Table 1 lists key stress–resilience–inflammation metrics and their assessment timings, and Table 2 shows an overview of vascular and inflammatory biomarkers monitored in oral cancer.

STRESS MANAGEMENT AND RESILIENCE-ENHANCING STRATEGIES

Psychosocial interventions

Stress management interventions improve cancer prognosis, QoL, and resilience by regulating psychological, physiological, and immune responses [13]. Interdisciplinary strategies enable tailored care models for patients with OSCC, enhancing clinical and rehabilitation outcomes. Psychosocial interventions, including support networks, psychoeducation, and psychotherapy, reduce anxiety, promote adaptation, and improve treatment engagement. Multimodal approaches are increasingly effective for managing psychological stress in patients with OSCC. Support from healthcare providers, family, and peers reduces preoperative anxiety and aids treatment adaptation [61]. A survey found that 40% of patients with cancer reported unmet needs for personalized information and coping strategies at diagnosis [15]. Peer support programs reduce isolation and boost self-efficacy through shared experiential knowledge [62].

Psychoeducational interventions, often delivered by advanced practice nurses, address gaps in understanding disease progression, treatment side effects, and functional outcomes. RCTs show that preoperative counseling reduces anxiety, enhances surgical preparedness, improves pain control, and shortens hospital stays [63]. Psychoeducation promotes treatment adherence and informed decision-making, reducing fear and improving body image adaptation. Meta-analyses suggest improved 1-year survival, likely due to enhanced compliance [62].

Psychotherapeutic approaches yield varied results. CBT, which targets maladaptive stress responses, shows inconsistent long-term benefits, possibly due to communication barriers limiting engagement [64]. Physiologically based interventions, such as HRV-BFB, are more promising. A systematic review of 19 controlled trials found that resonant frequency breathing improved autonomic regulation, reducing pain, fatigue, emotional distress, and sleep disruption, highlighting neurophysiological modulation's role in psychological outcomes [65].

LIFESTYLE MODIFICATIONS AND COMORBIDITY MANAGEMENT

Ceasing betel quid use reduces OSCC risk, with over 10 years of abstinence aligning risk levels with never-users [66]. Nurse-led smoking cessation programs, combining brief counseling and structured education, remarkably boost quit rates, even with short interventions [66,67]. Strict management of hypertension, hyperlipidemia, and diabetes reduces chronic inflammation and postoperative complications [68]. Proactive prevention of thrombosis and stroke is critical because chemoradiation increases cardiovascular strain. The American Heart Association's ABCDE framework provides a practical approach: A: risk awareness and aspirin for high-risk patients, B: blood pressure control, C: cholesterol management and sustained smoking cessation, D: diet optimization and diabetes control, and E: regular exercise [69]. Comprehensive oral

Table 1: Summary of clinical tools and biomarkers for assessing stress, inflammation, and resilience in oral cancer

Biomarker/Tool	Type	Clinical purpose	Timing of use	References
NLR	Blood biomarker	Systemic inflammation index	Pre/postsurgery, during CRT	[45]
HRV	Physiological monitoring	Autonomic function and adaptation; prognostic value	Pre/posttreatment, remote monitoring	[51,52]
PWV	Vascular health measure	Assessment of arterial stiffness and cardiovascular risk	Prognosis, comorbidity assessment	[48]
DT	Psychological scale	Rapid screening for psychological distress	Diagnosis, during and posttreatment	[38]
DASS-21	Psychological scale	Assessment of depression, anxiety, and stress	Throughout treatment and follow-up	[39]
RS-14	Psychological scale	Evaluation of resilience/adaptive capacity	Pre- and postintervention	[54]
SF-12	QoL scale	Brief, validated measure of health-related QoL	Throughout treatment	[41]

CRT: Chemoradiotherapy, DASS-21: Depression, Anxiety, and Stress Scale-21, DT: Distress Thermometer, HRV: Heart rate variability, NLR: Neutrophil-to-lymphocyte ratio, PWV: Pulse wave velocity, RS-14: 14-item Resilience Scale, SF-12: 12-Item Short-Form Health Survey, QoL: Quality of life

Table 2: Inflammation and cardiovascular risk biomarkers in oral cancer: Assessment and clinical significance

Biomarker	Clinical significance	Changes in oral cancer	References
IL-6	Tumor-related inflammation; associated with depression and pain	Increased under stress; drives progression	[60]
NLR	Systemic inflammation; predicts survival	Increased in patients with advanced disease	[45]
HRV	Autonomic function; predicts survival and cardiotoxicity	Reduced, indicating sympathetic dominance	[51,52]
PWV	Arterial stiffness; predicts cardiovascular events	Increased in patients with vascular injury	[48]

HRV: Heart rate variability, IL-6: Interleukin-6, NLR: Neutrophil-lymphocyte ratio, PWV: Pulse wave velocity

health care supports optimal postoperative function and rehabilitation [70].

Cardio-oncology guidelines [71] recommend utilizing the Heart Failure Association-International Cardio-Oncology Society risk scoring system [72] for all patients receiving potentially cardiotoxic cancer therapies, with proactive cardioprotective strategies established for those classified as high or very high risk. For patients undergoing anthracycline chemotherapy, early initiation of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before treatment commencement is advised, potentially supplemented with beta-blockers and/or statins on the basis of individual risk profiles [71]. Regarding anticoagulation management, patients with atrial fibrillation or flutter should receive direct oral anticoagulants or low-molecular-weight heparin (LMWH) as first-line therapy, and aspirin or LMWH monotherapy is not recommended for primary thromboprophylaxis [71]. For patients with OSCC, LMWH combined with statins is recommended as the preferred peri-operative antithrombotic prophylaxis [73].

INTEGRATIVE APPROACHES FOR CANCER PAIN MANAGEMENT

Pharmacologic management, primarily with opioids, is essential for cancer pain relief, but a multimodal approach combining opioids, nonopioids (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]), and co-analgesics (e.g., antidepressants and anticonvulsants) optimizes outcomes [74]. Despite available treatments, cancer pain is often undertreated due to limited education and fear of side effects, necessitating regular reassessment to balance relief and adverse effects [74].

Nonpharmacologic strategies complement pharmacologic treatments. Transcutaneous electrical nerve stimulation (TENS) and transcutaneous auricular vagus nerve stimulation (ta-VNS) with pregabalin reduce pain intensity, with TENS promoting endogenous opioid release and ta-VNS alleviating neuropathic

pain [75]. Functional relaxation eases pain, anxiety, insomnia, fatigue, and nausea during CRT [76]. Acupuncture and acupressure reduce pain and opioid use while improving QoL, with combined acupuncture and drug therapy outperforming drug therapy alone [77]. Exercise programs, especially those exceeding 8 weeks, decrease pain and improve physical function, fatigue, and psychological symptoms [78]. Mindfulness-based interventions reduce pain intensity and psychological distress in short- and long-term follow-up [79]. These modalities, used alone or alongside pharmacologic treatments, reduce opioid dependence and support holistic pain management [80].

NUTRITIONAL COUNSELING AND SUPPORT

Nutritional support is vital in OSCC treatment. High-calorie, protein-rich oral supplements are recommended, with enteral nutrition or prophylactic gastrostomy considered case by case [81]. During adjuvant therapy, particularly 1–1.5 months post-RT, weekly nutritional assessments manage mucositis and dysphagia to maintain weight and support treatment precision [82]. Early postoperative nutrition, started within 24 h, enhances wound healing and reduces stress responses [83].

Supplementation with N-3 polyunsaturated fatty acids during treatment helps prevent malnutrition and improves outcomes [82]. Nutritional interventions during CRT support body weight maintenance [84]. Systematic reviews show that nutritional counseling increases energy and protein intake in patients with cancer undergoing treatment [85]. In home-based care, personalized plans and anti-inflammatory diets, such as the omega-3-rich Mediterranean diet, are beneficial. This diet improves metabolic indices, including reduced body weight, fat mass, and body mass index (BMI), while enhancing QoL in patients with cancer [86]. These nutritional strategies bolster physiological function and resilience throughout treatment.

PERIOPERATIVE CARE: MITIGATING INFLAMMATION AND STRESS

Surgery, a key treatment for OSCC, triggers considerable inflammation and stress, increasing thrombosis and infection risks. Postoperative infections occur in 10%–50% of cases, and they are linked to low BMI, diabetes, and hypoalbuminemia [87]. Prophylactic antibiotics, such as penicillin (e.g., ampicillin/sulbactam) or cephalosporins, given 30–60 min preoperatively and continued for 24–48 h, reduce infection risk without overuse [23]. Enhanced recovery after surgery (ERAS) protocols target inflammation through early mobilization to lower pro-inflammatory cytokines, optimized analgesia to reduce stress, and nutritional supplementation to support anti-inflammatory processes [88]. ERAS protocols, supported by 18 studies on oral and maxillofacial reconstruction, decrease readmissions, complications, and hospital stays [89]. Effective management of stress and inflammation enables chemoradiation initiation within 6 weeks, improving outcomes [90].

ADJUVANT THERAPY SHIFT TO HOME-BASED REHABILITATION

Chemoradiation-induced mucositis, affecting 20%–80% of patients with OSCC, is managed at home with oral hygiene, saline rinses, and topical analgesics like palifermin [91]. Prophylactic swallowing exercises and resistance training improve functional and psychological outcomes [92]. Cervico-scapular syndrome, caused by RT-related soft-tissue inflammation, responds to physiotherapy with anti-inflammatory myofascial techniques [30]. Cardiovascular toxicity monitoring by multidisciplinary teams includes baseline assessments and targeted interventions [69].

Digital health technologies enhance communication, education, and self-management between patients with cancer and healthcare providers [93]. Deinstitutionalized remote care models help address specialist service accessibility inequities, particularly for patients in remote areas, to optimize health outcomes and effectively utilize limited healthcare resources [94]. Telerehabilitation platforms with biomarker tracking can achieve functional outcomes comparable to in-person programs while maintaining high adherence [93]. Telehealth exercise-based rehabilitation improves cardiorespiratory fitness and physical activity in cancer survivors [93,94]. A meta-analysis of 18 online mindfulness-based intervention trials reported small-to-moderate reductions in IL-6 and C-reactive protein (CRP), alongside improvements in mood and pain [60]. Traditional Chinese medicine, such as acupoint stimulation, shows preliminary benefits in reducing pro-inflammatory cytokines, fatigue, and depressive symptoms, though larger trials are needed. Psychoneuroimmunology-based interventions, including CBT and mindfulness-based stress reduction, consistently downregulate key inflammatory mediators such as IL-6, CRP, tumor necrosis factor-alpha, and Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) [95].

INFLAMMATORY MODULATION THERAPIES

Inflammation promotes tumor growth and metastasis in OSCC,

with β_2 -AR activation driving pro-inflammatory cytokine release and worsening the tumor microenvironment [96]. Beta-blockers, which block β_2 -AR, showed preclinical potential but yielded mixed clinical results, including no reduction in cancer risk and worsened survival in some oncological studies [97,98]. NSAIDs, which inhibit COX pathways, have unclear benefits because postdiagnosis use is associated with increased mortality [99]. These inconsistent findings underscore the need for RCTs to define the role of beta-blockers, NSAIDs, and cytokine-modulating agents, optimizing timing, dosage, patient selection, oncologic efficacy, and cardiovascular safety [96-99]. Given these uncertainties, clinical decision-making should prioritize established cardiovascular indications rather than cancer-specific outcomes when prescribing β -blockers and NSAIDs. For patients with OSCC with cardiovascular comorbidities, β -blockers remain indicated for hypertension, heart failure, or postmyocardial infarction management according to established cardiology guidelines [71]. Evidence-based integrative interventions and their effects on inflammation, stress, and QoL are presented in Table 3.

FUTURE DIRECTIONS

Critical gaps persist despite advances in oral cancer supportive care. Can HRV and NLR be validated to predict stress-induced inflammatory surges? Which interventions, such as psychoeducation, biofeedback, or mindfulness, provide the greatest benefit for low-versus-high-resilience patients stratified by self-report and HRV NLR metrics? How can echocardiography, computed tomography, and PWV be integrated into cardio-oncology surveillance? Do beta-blockers, statins, or anti-inflammatory agents prevent betel quid-related cardiotoxicity? Which telerehabilitation features with integrated biomarker tracking best manage stress-induced inflammatory surges? How can tiered biomarker strategies prioritize self-reported symptoms while using laboratory testing as supplementary support? How can phase-adaptive monitoring systems dynamically adjust support intensity throughout treatment timelines? What combination of automated reminders, caregiver platforms, and hybrid education can bridge digital literacy gaps to maximize long-term adherence? Finally, how can standardized frameworks be developed for biological functional and patient-reported outcomes? What barriers hinder resilience enhancement and inflammation control in precision care? Rigorous clinical research addressing these questions is essential to improve oral cancer outcomes.

CONCLUSION

In this review, evidence on stress–inflammation–resilience triad in patients with OSCC undergoing multimodal therapy is synthesized. Stress and systemic inflammation, exacerbated by betel quid chewing, drive tumor progression and cardiovascular risk, and resilience mitigates these effects, improving functional recovery and survival. Interventions, including psychosocial support, lifestyle modifications, nonopioid analgesia, nutritional counseling, and rehabilitation, target this triad effectively. However, gaps in real-time biomarker monitoring, resilience-stratified trials, and cardio-oncology surveillance persist. Bridging digital literacy gaps through

Table 3: Summary of evidence-based interventions and their effect on inflammatory markers, psychological stress, and quality of life

Intervention	Inflammatory markers	Psychological stress	Quality of life	References
Smoking/Betel quid cessation	Reduction	Indirect improvement	Consistent improvement	[66,67]
CBT	Significant reduction	Marked improvement	Consistent improvement	[60]
MBIs	Reduction	Improvement	Consistent improvement	[95]
HRV-BFB	Reduction	Marked improvement	Consistent improvement	[65]
Exercise (aerobic and/or resistance)	Reduction	Improvement	Consistent improvement	[78,93]
Nutrition (omega-3-rich and/or Mediterranean diet)	Reduction	Indirect improvement	Consistent improvement	[82,86]
Acupuncture/acupressure	Reduction	Improvement	Consistent improvement	[77]
Beta-blockers	Mixed or inconclusive findings	No significant effect	No clear benefit	[97,98]

CBT: Cognitive-behavioral therapy, HRV-BFB: Heart rate variability-Biofeedback, MBIs: Mindfulness-based interventions

innovative platforms and hybrid education models remains essential. Future research should focus on optimizing integrative protocols, developing predictive biomarkers, and implementing precision supportive care models to enhance clinical outcomes and QoL for this population.

Data availability statement

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Conflicts of interest

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REFERENCES

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-49.
- Filho AM, Warnakulasuriya S. Epidemiology of oral cancer in South and South-East Asia: Incidence and mortality. *Oral Dis* 2024;30:4847-54.
- Health Promotion Administration, Ministry of Health and Welfare (Taiwan). Introduction to oral cancer screening. Taipei: Division of Cancer Prevention and Control; 2024. Available from: <https://www.hpa.gov.tw/Pages/Detail.aspx?nodeid=622&pid=1139>. [Last accessed on 2025 May 12].
- National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 2. 2025. Fort Washington (PA): NCCN; 2025. Available from: <https://www.nccn.org>. [Last accessed on 2025 May 14].
- MacDonald C, Theurer JA, Fung K, Yoo J, Doyle PC. Resilience: An essential element in head and neck cancer survivorship and quality of life. *Support Care Cancer* 2021;29:3725-33.
- Eckerling A, Ricon-Becker I, Sorski L, Sandbank E, Ben-Eliyahu S. Stress and cancer: Mechanisms, significance and future directions. *Nat Rev Cancer* 2021;21:767-85.
- Henry M, Rosberger Z, Bertrand L, Klassen C, Hier M, Zeitouni A, et al. Prevalence and risk factors of suicidal ideation among patients with head and neck cancer: Longitudinal study. *Otolaryngol Head Neck Surg* 2018;159:843-52.
- Snijders RA, Brom L, Theunissen M, van den Beuken-van Everdingen MH. Update on prevalence of pain in patients with cancer 2022: A systematic literature review and meta-analysis. *Cancers (Basel)* 2023;15:591.
- George T, Shah F, Tiwari A, Gutierrez E, Ji J, Kuchel GA, et al.

- Resilience in older adults with cancer: A scoping literature review. *J Geriatr Oncol* 2023;14:101349.
- Ahuja SK, Manoharan MS, Lee GC, McKinnon LR, Meunier JA, Steri M, et al. Immune resilience despite inflammatory stress promotes longevity and favorable health outcomes including resistance to infection. *Nat Commun* 2023;14:3286.
- Mravec B, Tibensky M, Horvathova L. Stress and cancer. Part I: Mechanisms mediating the effect of stressors on cancer. *J Neuroimmunol* 2020;346:577311.
- Antoni MH, Dhabhar FS. The impact of psychosocial stress and stress management on immune responses in patients with cancer. *Cancer* 2019;125:1417-31.
- Irwin MR, Opp MR. Sleep health: Reciprocal regulation of sleep and innate immunity. *Neuropsychopharmacology* 2017;42:129-55.
- Huang YC, Geng JH, Wu PY, Huang JC, Chen SC, Chang JM, et al. Betel nut chewing increases the risk of metabolic syndrome and its components in a large taiwanese population follow-up study category: Original investigation. *Nutrients* 2022;14:1018.
- Malik NH, Maganti M, McQuestion M, Tjong MC, Keilty D, Monteiro E, et al. Pre-treatment psychoeducational intervention and outcomes in head and neck cancer patients undergoing radiotherapy. *Support Care Cancer* 2021;29:1643-52.
- Ifitkhar A, Islam M, Shepherd S, Jones S, Ellis I. Cancer and stress: Does it make a difference to the patient when these two challenges collide? *Cancers (Basel)* 2021;13:163.
- Homan E, Kwakkenbos L, Deuning Smit E, Jansen F, Verdonck de Leeuw IM, Takes RP, et al. Three year trajectories and associated factors of fear of cancer recurrence in newly diagnosed head and neck cancer patients: A longitudinal study. *J Cancer Surviv* 2024. doi:10.1007/s11764-024-01731-y.
- Mäkitie AA, Alabi RO, Pulkki-Råback L, Almangush A, Beitler JJ, Saba NF, et al. Psychological factors related to treatment outcomes in head and neck cancer. *Adv Ther* 2024;41:3489-519.
- Labaig PJ, Aymerich C, Rullan A, Llop S, Brana I, Cacicedo J, et al. Mapping the mental health correlates of head and neck cancer: A systemic review and meta-analysis. *J Clin Oncol* 2024;42(Suppl 16):6077.
- Ivascu R, Torsin LI, Hostiu L, Nitipir C, Corneci D, Dutu M. The surgical stress response and anesthesia: A narrative review. *J Clin Med* 2024;13:3017.
- Li R, Ye JJ, Gan L, Zhang M, Sun D, Li Y, et al. Traumatic inflammatory response: Pathophysiological role and clinical value of cytokines. *Eur J Trauma Emerg Surg* 2024;50:1313-30.
- Wang Y, Wang M, Tang Y, Sun B, Wang K, Zhu F. Perioperative mortality of head and neck cancers. *BMC Cancer* 2021;21:256.
- Iocca O, Copelli C, Ramieri G, Zocchi J, Savo M, Di Maio P. Antibiotic prophylaxis in head and neck cancer surgery: Systematic review and Bayesian network meta-analysis. *Head Neck* 2022;44:254-61.
- Brook I. Late side effects of radiation treatment for head and neck cancer. *Radiat Oncol J* 2020;38:84-92.

25. Van Cleave J, Brooks C, Zahriah E, Riccobene A, Most A, Liang E, et al. Pain prevalence in head and neck cancer. *J Pain* 2022;23:29.
26. Nasir KS, Hafeez H, Hussain R, Jamshed A. P20-10 Chemical neurolysis for refractory head and neck cancer-related pain. *Ann Oncol* 2021;32:S340.
27. Mardelle U, Bretaud N, Daher C, Feuillet V. From pain to tumor immunity: Influence of peripheral sensory neurons in cancer. *Front Immunol* 2024;15:1335387.
28. Kouri M, Vadalouca A, Kouloulis V, Papadopoulou E, Vardas E, Kyrodimos E, et al. Oral complications of head and neck cancer therapy. *Forum Clin Oncol* 2021;12:52-66.
29. Samim F, Epstein JB, Osagie R. Oral pain in the cancer patient. *Curr Opin Support Palliat Care* 2022;16:174-9.
30. Almeida KA, Rocha AP, Carvas N, Pinto AC. Rehabilitation interventions for shoulder dysfunction in patients with head and neck cancer: Systematic review and meta-analysis. *Phys Ther* 2020;100:1997-2008.
31. Oliveira CB, Maher CG, Franco MR, Kamper SJ, Williams CM, Silva FG, et al. Co-occurrence of chronic musculoskeletal pain and cardiovascular diseases: A systematic review with meta-analysis. *Pain Med* 2020;21:1106-21.
32. Lyman GH, Carrier M, Ay C, Di Nisio M, Hicks LK, Khorana AA, et al. American Society of Hematology 2021 guidelines for management of venous thromboembolism: Prevention and treatment in patients with cancer. *Blood Adv* 2021;5:927-74.
33. Huang CH, Lue KH, Chen PR, Hsieh TC, Chou YF. Association between sarcopenia and immediate complications and mortality in patients with oral cavity squamous cell carcinoma undergoing surgery. *Cancers (Basel)* 2022;14:785.
34. Liang X, Chen X, Wang G, Wang Y, Shi D, Zhao M, et al. Intraoperative hypotension, oliguria and operation time are associated with pulmonary embolism after radical resection of head and neck cancers: A case control study. *BMC Anesthesiol* 2021;21:304.
35. Albertsen IE, Lyhne NM, Larsen TB, Nielsen PB. Incidence of venous thromboembolism following head and neck surgery. *Eur Arch Otorhinolaryngol* 2023;280:5081-9.
36. Zarifa A, Albittar A, Kim PY, Hassan S, Palaskas N, Iliescu C, et al. Cardiac toxicities of anticancer treatments: Chemotherapy, targeted therapy and immunotherapy. *Curr Opin Cardiol* 2019;34:441-50.
37. Sara JD, Kaur J, Khodadadi R, Rehman M, Lobo R, Chakrabarti S, et al. 5-fluorouracil and cardiotoxicity: A review. *Ther Adv Med Oncol* 2018;10:1758835918780140.
38. Riba MB, Donovan KA, Andersen B, Braun I, Breitbart WS, Brewer BW, et al. Distress management, version 3.2019, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2019;17:1229-49.
39. Kumar K, Kumar S, Mehrotra D, Tiwari SC, Kumar V, Khandpur S, et al. Prospective evaluation of psychological burden in patients with oral cancer. *Br J Oral Maxillofac Surg* 2018;56:918-24.
40. EORTC. Head & Neck Cancer (update of QLQ-H&N35). Brussels: European Organisation for Research and Treatment of Cancer. Available from: <https://qol.eortc.org/questionnaire/qlq-hn43/>. [Last accessed on 2025 May 12].
41. Hoene G, von Hahn N, Sievers D, Schuffelen L, Wolfer S, Goldstein K, et al. Improvement of quality of life after surgical treatment of patients with MRONJ: A prospective analysis using the SF-12 and OHIP-14 questionnaires. *Int J Dent* 2024;2024:4435791.
42. Leonard JA, Hayden JA, Tripuraneni PS, Maxwell JH, Giurintano JP. Malnutrition universal screening tool predicts postoperative complications following major head and neck cancer surgery. *Head Neck* 2023;45:604-11.
43. Elma Ö, Brain K, Dong HJ. The importance of nutrition as a lifestyle factor in chronic pain management: A narrative review. *J Clin Med* 2022;11:5950.
44. Aman MM, Mahmoud A, Deer T, Sayed D, Hagedorn JM, Brogan SE, et al. The American Society of Pain and Neuroscience (ASPN) best practices and guidelines for the interventional management of cancer-associated pain. *J Pain Res* 2021;14:2139-64.
45. Dineshkumar T, Anandan N, Rajkumar K. Understanding the properties and functional role of neutrophils in oral squamous cell carcinoma – A systematic review. *Oral Oncol Rep* 2024;10:100440.
46. Feng J, Lu X, Li H, Wang S. High neutrophil-to-lymphocyte ratio is a significant predictor of depressive symptoms in maintenance hemodialysis patients: A cross-sectional study. *BMC Psychiatry* 2022;22:313.
47. McIntosh RC, Lobo J, Pappozzi J, Goodman Z, Kornfeld S, Nomi J. Neutrophil to lymphocyte ratio is a transdiagnostic biomarker of depression and structural and functional brain alterations in older adults. *J Neuroimmunol* 2022;365:577831.
48. Diao Y, Liu Z, Chen L, Zhang W, Sun D. The relationship between cancer and functional and structural markers of subclinical atherosclerosis: A systematic review and meta-analysis. *Front Cardiovasc Med* 2022;9:849538.
49. Smith J, Margalit D, Golledge J, Nastasi D, Nohria A, McDowell L. Carotid artery stenosis and ischemic stroke in patients with head and neck cancer treated with radiation therapy: A critical review. *Int J Radiat Oncol Biol Phys* 2024;119:1437-54.
50. Randolph W, Dains JE. Ultrasound evaluation of carotid artery intima-media thickness: Effective early marker of carotid artery disease in adult head and neck cancer patients after neck radiation? *J Adv Pract Oncol* 2022;13:683-94.
51. Kloter E, Barrueto K, Klein SD, Scholkmann F, Wolf U. Heart rate variability as a prognostic factor for cancer survival – A systematic review. *Front Physiol* 2018;9:623.
52. Huang CC, Lai YR, Chiu WC, Fang FM, Hsieh DY, Lien CY, et al. Concurrent chemoradiation therapy is associated with an accelerated risk of cardiovascular autonomic dysfunction in patients with nasopharyngeal carcinoma: A 9-year prospective follow-up study. *Radiother Oncol* 2022;170:129-35.
53. Wagnild GM, Young HM. Development and psychometric evaluation of the resilience scale. *J Nurs Meas* 1993;1:165-78.
54. Wagnild GM. The Resilience Scale user's Guide: For the US English Version of the Resilience Scale and the 14-item Resilience Scale (RS-14): Resilience Center; 2011.
55. Chen W, Xie E, Tian X, Zhang G. Psychometric properties of the Chinese version of the Resilience Scale (RS-14): Preliminary results. *PLoS One* 2020;15:e0241606.
56. Gao Y, Yuan L, Pan B, Wang L. Resilience and associated factors among Chinese patients diagnosed with oral cancer. *BMC Cancer* 2019;19:447.
57. Graboyes EM, Maurer S, Balliet W, Li H, Williams AM, Osazuwa-Peters N, et al. Efficacy of a brief tele-cognitive behavioral treatment versus attention control for head and neck cancer survivors with body image distress: A pilot randomized clinical trial. *JAMA Otolaryngol Head Neck Surg* 2023;149:54-62.
58. Bonanno GA. The resilience paradox. *Eur J Psychotraumatol* 2021;12:1942642.
59. Alvord MK, Rich BA, Berghorst LH. Resilience interventions. In: Norcross JC, VandenBos GR, Freedheim DK, editors. *APA Handbook of Clinical Psychology: Psychopathology and Health*. Vol. 4. Washington (DC): American Psychological Association; 2016, p. 505-19.
60. Ma H, Xu J, Li R, McIntyre RS, Teopiz KM, Cao B, et al. The impact of cognitive behavioral therapy on peripheral interleukin-6 levels in depression: A systematic review and meta-analysis. *Front Psychiatry* 2022;13:844176.
61. Richardson AE, Morton R, Broadbent E. Psychological support needs of patients with head and neck cancer and their caregivers: A qualitative study. *Psychol Health* 2015;30:1288-305.
62. Fu WW, Popovic M, Agarwal A, Milakovic M, Fu TS, McDonald R, et al. The impact of psychosocial intervention on survival in cancer: A meta-analysis. *Ann Palliat Med* 2016;5:93-106.
63. Seth I, Bulloch G, Qin KR, Xie Y, Sebastian B, Liew H, et al.

- Pre-rehabilitation interventions for patients with head and neck cancers: A systematic review and meta-analysis. *Head Neck* 2024;46:86-117.
64. Beck JS, Fleming S. A brief history of Aaron T. Beck, MD, and cognitive behavior therapy. *Clin Psychol Eur* 2021;3:e6701.
 65. Spada GE, Masiero M, Pizzoli SFM, Pravettoni G. Heart rate variability biofeedback in cancer patients: A scoping review. *Behav Sci (Basel)* 2022;12:389.
 66. Gupta R, Mariano LC, Nethan ST, Kedar A, Sinha DN, Warnakulasuriya S, et al. Risk reversal of oral, Pharyngeal and oesophageal cancers after cessation of betel quid users: A systematic review and meta-analysis. *Ann Glob Health* 2022;88:5.
 67. Silva CC, Presseau J, van Allen Z, Schenk PM, Moreto M, Dinsmore J, et al. Effectiveness of interventions for changing more than one behavior at a time to manage chronic conditions: A systematic review and meta-analysis. *Ann Behav Med* 2024;58:432-44.
 68. Shepherd SJ, Creber N, Mansour K, Wiesenfeld D, Iseli TA, Amott D. Relationship between age, comorbidities and complications in head and neck cancer patients undergoing curative surgery. *ANZ J Surg* 2020;90:851-5.
 69. Gilchrist SC, Barac A, Ades PA, Alfano CM, Franklin BA, Jones LW, et al. Cardio-oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: A scientific statement from the American Heart Association. *Circulation* 2019;139:e997-1012.
 70. Matsuda Y, Jayasinghe RD, Zhong H, Arakawa S, Kanno T. Oral health management and rehabilitation for patients with oral cancer: A narrative review. *Healthcare (Basel)* 2022;10:960.
 71. Gent DG, Rebecca D. The 2022 European Society of Cardiology Cardio-oncology guidelines in focus. *Eur Cardiol* 2023;18:e16.
 72. Lyon AR, Dent S, Stanway S, Earl H, Brezden-Masley C, Cohen-Solal A, et al. Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: A position statement and new risk assessment tools from the Cardio-Oncology Study Group of the Heart Failure Association of the European Society of Cardiology in collaboration with the International Cardio-Oncology Society. *Eur J Heart Fail* 2020;22:1945-60.
 73. Rosen R, Bodnar M, Randolph J, Bailey CJ, Nickel C, Katsoulakis E, et al. Risk, prevention, screening and management of carotid artery stenosis in head & neck cancer patients-An evidence based review. *Oral Oncol* 2024;156:106876.
 74. Mangolian Shahrabaki P, Farokhzadian J, Ahmadi F, Khabbazzadeh F. Persistence of pain and suffering in cancer patients: Challenges of pain management from the perspective of nurses. *Front Pain Res (Lausanne)* 2024;5:1425036.
 75. Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of Transcutaneous Electrical Nerve Stimulation (TENS) for acute and chronic pain in adults: A systematic review and meta-analysis of 381 studies (the meta-TENS study). *BMJ Open* 2022;12:e051073.
 76. Cai DC, Chen CY, Lo TY. Foot reflexology: Recent research trends and prospects. *Healthcare (Basel)* 2022;11:9.
 77. He Y, Guo X, May BH, Zhang AL, Liu Y, Lu C, et al. Clinical evidence for association of acupuncture and acupressure with improved cancer pain: A systematic review and meta-analysis. *JAMA Oncol* 2020;6:271-8.
 78. Austin PD, Lee W, Costa DS, Ritchie A, Lovell MR. Efficacy of aerobic and resistance exercises on cancer pain: A meta-analysis of randomised controlled trials. *Heliyon* 2024;10:e29193.
 79. Feng B, Hu X, Lu WW, Wang Y, Ip WY. Are mindfulness treatments effective for pain in cancer patients? A systematic review and meta-analysis. *Eur J Pain* 2022;26:61-76.
 80. Preti K, D'Aouost R, Beeber AS, Baker DJ. Multimodal interprofessional adult cancer pain management: An integrative review. *Oncol Nurs Forum* 2024;52:41-50.
 81. Cook F, Rodriguez JM, McCaul LK. Malnutrition, nutrition support and dietary intervention: The role of the dietitian supporting patients with head and neck cancer. *Br Dent J* 2022;233:757-64.
 82. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, et al. ESPEN practical guideline: Clinical nutrition in cancer. *Clin Nutr* 2021;40:2898-913.
 83. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN practical guideline: Clinical nutrition in surgery. *Clin Nutr* 2021;40:4745-61.
 84. de van der Schueren MA, Laviano A, Blanchard H, Jourdan M, Arends J, Baracos VE. Systematic review and meta-analysis of the evidence for oral nutritional intervention on nutritional and clinical outcomes during chemo (radio) therapy: Current evidence and guidance for design of future trials. *Ann Oncol* 2018;29:1141-53.
 85. Ueshima J, Nagano A, Maeda K, Enomoto Y, Kumagai K, Tsutsumi R, et al. Nutritional counseling for patients with incurable cancer: Systematic review and meta-analysis. *Clin Nutr* 2023;42:227-34.
 86. Lu S, Sun X, Zhang W, Li X, Zhou Z, Xiao R, et al. Effects of the Mediterranean diet on metabolic indices and quality of life in cancer patients: A systematic review and meta-analysis of randomized controlled trials. *J Funct Foods* 2024;114:106074.
 87. Wang Y, Wang M, Hou L, Xiang F, Zhao X, Qian M. Incidence and risk factors of surgical site infection in patients with head and neck cancer: A meta-analysis. *Head Neck* 2023;45:2925-44.
 88. Gillis C, Gill M, Gramlich L, Culos-Reed SN, Nelson G, Ljungqvist O, et al. Patients' perspectives of prehabilitation as an extension of enhanced recovery after surgery protocols. *Can J Surg* 2021;64:E578-87.
 89. Chorath K, Go B, Shinn JR, Mady LJ, Poonia S, Newman J, et al. Enhanced recovery after surgery for head and neck free flap reconstruction: A systematic review and meta-analysis. *Oral Oncol* 2021;113:105117.
 90. Duckett KA, Kassir MF, Nguyen SA, Brennan EA, Chera BS, Sterba KR, et al. Delays starting postoperative radiotherapy among head and neck cancer patients: A systematic review and meta-analysis. *Otolaryngol Head Neck Surg* 2024;170:320-34.
 91. Ferreira AS, Macedo C, Silva AM, Delerue-Matos C, Costa P, Rodrigues F. Natural Products for the prevention and treatment of oral mucositis-a review. *Int J Mol Sci* 2022;23:4385.
 92. Hajdú SF, Wessel I, Dalton SO, Eskildsen SJ, Johansen C. Swallowing exercise during head and neck cancer treatment: Results of a randomized trial. *Dysphagia* 2022;37:749-62.
 93. Batalik L, Chamradova K, Winnige P, Dosbaba F, Batalikova K, Vlazna D, et al. Effect of exercise-based cancer rehabilitation via telehealth: A systematic review and meta-analysis. *BMC Cancer* 2024;24:600.
 94. Mali SB. Role of telemedicine in head neck cancer. *Oral Oncol* 2024;151:106746.
 95. Matiz A, Scaggiante B, Conversano C, Gemignani A, Pascoletti G, Fabbro F, et al. The effect of mindfulness-based interventions on biomarkers in cancer patients and survivors: A systematic review. *Stress Health* 2024;40:e3375.
 96. Lopes-Santos G, Bernabé DG, Miyahara GI, Tjioe KC. Beta-adrenergic pathway activation enhances aggressiveness and inhibits stemness in head and neck cancer. *Transl Oncol* 2021;14:101117.
 97. Kim MS, Han KD, Kwon SY. Pre-diagnostic beta-blocker use and head- and neck cancer risk: A nationwide population-based case-control study. *Medicine (Baltimore)* 2019;98:e16047.
 98. Chen HY, Zhao W, Na'ara S, Gleber-Netto FO, Xie T, Ali S, et al. Beta-blocker use is associated with worse relapse-free survival in patients with head and neck cancer. *JCO Precis Oncol* 2023;7:e2200490.
 99. de la Cour CD, Dehlendorff C, von Buchwald C, Garset-Zamani M, Grønhoj C, Carlander AF, et al. Non-aspirin NSAIDs and head and neck cancer mortality in a Danish nationwide cohort study. *Cancer Epidemiol* 2022;77:102121.