

Review

Evidence summary on managing radiotherapy-induced oral mucositis in patients with head and neck cancer

Zimo Zhang^a, Li Tian^a, Juan Liu^b, Hua Jiang^{c,*}, Panfeng Wang^{a,*}^a Department of Radiation Oncology, Peking University Third Hospital, Beijing, China^b Beijing Haidian Hospital, Beijing, China^c Peking University Faculty of Nursing, Beijing, China

ARTICLE INFO

Keywords:

Radiotherapy

Oral mucositis

Head and neck cancer

ABSTRACT

Objective: To summarize the best evidence for managing radiotherapy-induced oral mucositis in patients with head and neck cancer, and improve the quality of care.**Methods:** According to the “6S” evidence pyramid model, we searched local and other part of world published clinical guidelines, expert consensus, evidence summary, and systematic review. The literature quality assessment followed the Appraisal of Guidelines for Research and Evaluation (AGREE II). for guidelines, AMSTAR-2 for systematic reviews, and Joanna Briggs Institute (JBI) Evidence-Based Health Care Center's quality evaluation tool for expert opinions and expert consensus articles. The quality of other literature was evaluated according to the type of original literature. If there were any conflicts about the conclusions drawn from different sources of evidence, this study followed the principle of high-quality evidence priority and the latest published authoritative literature priority. The “JBI Evidence Pre-grading and Evidence Recommendation Level System 2014” was adopted for the evidence lacking a grading system. Quality evaluation, evidence extraction, and summary were performed by 2 or more researchers, combined with the advice of the head and neck cancer radiotherapy professionals.**Results:** Finally, a total of ten pieces of literature were included. Twenty-two best evidence items for radiotherapy-induced oral mucositis management were summarized from six aspects, including multidisciplinary management, oral assessment, basic oral care, pain management, nutritional support, and application of honey or propolis.**Conclusions:** This study provides clinical caregivers with the evidence-based measures on managing radiotherapy-induced oral mucositis. Clinical backgrounds, patients' condition, willingness, economy, and cost-effectiveness should be fully considered when promoting evidence transformation. Applying evidence-based approaches with high feasibility, strong appropriateness, clinical significance and high effectiveness could reduce the incidence of severe radiotherapy-induced oral mucositis in patients with head and neck cancer.**Systematic review registration:** This study has been registered on the Fudan University Centre for Evidence-based Nursing. Registration No. is ES20232732.

Introduction

Most head and neck cancers are radiosensitive, radiotherapy is preferred when the tumor cannot be completely resected.¹ However, while radiotherapy kills the tumor cells, it also damages normal tissues, with radiotherapy-induced oral mucositis (RTOM) being a common complication in patients with head and neck cancer.² The incidence of RTOM in patients undergoing conventional radiotherapy for head and

neck cancer is 80% to 100%, with 28% to 80% experiencing severe RTOM.³ OM causes patients oral discomfort, pain, chewing and swallowing difficulties. Moreover, severe OM is a common cause of the interruption or failure of radiotherapy, seriously affecting the patients' quality of life and treatment effects.⁴ At present, many clinical practice guidelines and expert consensus studies on RTOM prevention and treatment have been published locally and abroad, but many related strategies remain controversial. Furthermore, specific and

* Corresponding author.

E-mail addresses: gail_ball@163.com (H. Jiang), liletian180@sina.com (P. Wang).<https://doi.org/10.1016/j.apjon.2024.100386>

Received 4 November 2023; Accepted 24 January 2024

2347-5625/© 2024 The Author(s). Published by Elsevier Inc. on behalf of Asian Oncology Nursing Society. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

comprehensive nursing norms and uniform clinical practices for managing RTOM in patients with head and neck cancer are lacking. Therefore, this study systematically searched, analyzed and summarized the best evidence for the management of RTOM in patients with head and neck cancer.

Methods

Question identification

Evidence-based questions were selected based on the PIPST model.⁵ The formed initial questions were as follows: P (Population): Patients with head and neck cancer managed by radiotherapy. I (Intervention): RTOM preventive management measures, including multidisciplinary management, oral assessment, basic oral care, pain management, nutritional support, and application of honey or propolis. P (Professional): Radiation physicians, nurses, technicians, stomatologists, dietitians, and pharmacists. O (Outcome): Three aspects: the system (presence of a procedure plan for RTOM management and the availability of the relevant tools and environmental conditions for its implementation), nurse (knowledge and practice scores for RTOM management, and the implementation rate of protocol review indicators), and patient (severe RTOM incidence). S (Setting): An oncology radiotherapy clinic. T (Type of evidence): Clinical practice guidelines, best practices, evidence summaries, systematic reviews, and expert consensus.

Retrieval strategy

We followed the “6S” evidence pyramid model⁶ for sequential retrieval of evidence decision systems, including BMJ Best Practice, Up to Date, Clinicalkey; Guideline sites, including Guidelines International Network (GIN), Agency for Health care Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), Australian Clinical Practice Guidelines (ACPG), New Zealand Guideline Group (NZGG), World Health Organization (WHO), National Health Commission of China, and the Chinese Nursing Association; Evidence summary database, including Joanna Briggs Institute (JBI), EBSCO Research Databases.; Systematic review database, including Cochrane Library and JBI Library; Periodical comprehensive database, including PubMed, Medline, CINAHL, Embase, Web of science, SinoMed, CNKI, Wanfang and VIP; Grey literature, including government and professional institutions websites, China's important doctoral/master's thesis full-text database, Baidu academic database, Yi Mai Tong, and Google Scholar. Retrieval time was from database inception to April 30, 2023.

Literature inclusion and exclusion criteria

Inclusion criteria

(1) The head and neck cancer patients were ≥ 18 years old. (2) The latest version of the clinical guidelines, evidence summary, expert consensus, and systematic review literature on managing RTOM. (3) Language was limited to Chinese and English.

Exclusion criteria

(1) Literature with incomplete information content, unobtainable full text or directly translated. (2) It was impossible to determine the evidence's level.

Literature quality evaluation

Literature quality evaluation tools

(1) Guidelines: We used the 2017 Appraisal of Guidelines for Research and Evaluation (AGREE II).⁷ The tool consists of 23 items in six fields, each graded on a 7-point scale, with seven

points for total agreement and one for complete disagreement. The score for each field is equal to the sum of the item scores in that field, standardized as a percentage of the highest possible score for that field. The guidelines were divided into three levels based on their scores: Grade A (can be directly recommended without change), with a score of $\geq 60\%$ in all six fields; Grade B (recommended after some modifications and improvements), with a score of 30% to 60% in ≥ 3 fields; Grade C (not recommended), with a score of $< 30\%$ in ≥ 3 fields.

- (2) Systematic review: We used the 2017 AMSTAR-2.⁸ It comprises 16 items evaluated as a yes, no, or partial yes. The decision on whether to include it was based on the overall quality.
- (3) Expert consensus, evidence summary and clinical decision making: Expert consensus was evaluated by the 2016 JBI expert opinions and expert consensus articles quality evaluation tools.⁹ Evidence summary and clinical decision evaluation were traced back to the original evidence literature, and the quality evaluation was performed according to the original literature type.

The literature quality evaluation process

Literature quality evaluation was conducted independently by two or more researchers with evidence-based nursing training and professional background in head and neck cancer, who selected the appropriate evaluation criteria according to the literature type. Disagreements were resolved by discussion or consultation with a third researcher who made the final decision. In case of conflicts among the conclusions drawn by different evidence sources, this study followed the principle of high-quality evidence priority and the latest published authoritative literature priority.

Evidence level and recommendation level criteria

Evidence lacking a grading system was evaluated using the 2014 JBI Evidence-Based Health Care Center Evidence Pre-grading and Evidence Recommendation Level System.¹⁰ According to the design type of evidence, the evidence Level is divided into 5 levels, Level 1 is at the top and Level 5 is at the bottom in the rank-order. The more rigorous the research design, the higher the evidence level. Level 1 is randomized controlled trials (RCTs) and meta-analyses of RCTs, Level 2 is quasi-experimental study, Level 3 is observational-analytical study, Level 4 is observational-descriptive study, Level 5 is expert opinions and basic research. Subsequently, we invited relevant experts to form a group for discussion (two radiotherapy department doctors, the head nurses of the radiotherapy ward and outpatient department, the deputy director of the nursing department, and two project cadres), evaluating the feasibility, appropriateness, clinical significance and effectiveness of the obtained evidences according to the FAME evaluation principle. We judged each piece of evidence that whether it is clear that desirable effects outweigh undesirable effects of the strategy, whether there is evidence of adequate quality supporting its use, whether there is a benefit or no impact on resource use, and values, preferences and the patient experience have been taken into account. Finally, we recommended the evidences as grade A (strongly recommended) or grade B (weakly recommended).

Results

General characteristics of the included literature

In this study, we initially obtained 1875 literature, of which we excluded 415 duplicates, 1063 after reading the titles and abstracts, and 387 after reading the full texts. Finally, we included 10 literature, including 4 guidelines,^{11–14} 3 expert consensus,^{15–17} 1 evidence summary¹⁸ and 2 systematic reviews.^{19,20} The literature screening flow chart is shown in Fig. 1. The general characteristics of the included literature are shown in Table 1.

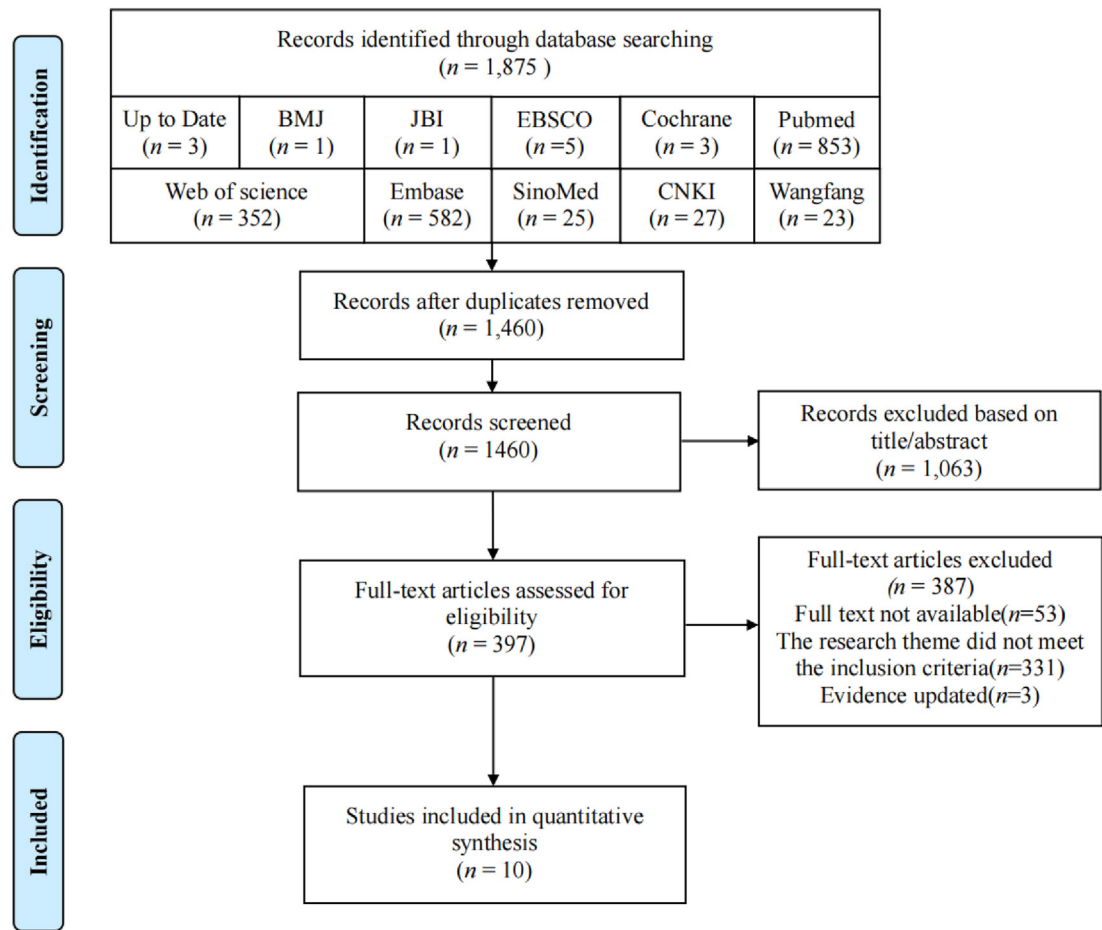


Fig. 1. Screening flow chart for literature.

Quality evaluation of the included literature

Guidelines quality evaluation

Among the four included guidelines,^{11–14} one¹¹ received grade A and three^{12–14} grade B. The quality evaluation results are shown in Table 2.

Expert consensus quality evaluation

The overall quality of three expert consensus reports^{15–17} was good, and all were included. The quality evaluation results are shown in Table 3.

Systematic reviews quality evaluation

The overall quality of two systematic reviews^{19,20} was good, and both were included. The quality evaluation results are shown in Table 4.

Evidence summary quality evaluation

We evaluated the original literature of the included evidence summary,¹⁸ which were comprised of two guidelines^{11,12} in Table 2 and one expert consensus¹⁷ in Table 3. All showed good quality.

Evidence summary and description

Finally, by summarizing the evidence on the management of RTOM in patients with head and neck cancer, a total of 22 pieces of evidence were obtained from six aspects: multidisciplinary management, oral assessment, basic oral care, pain management, nutritional support, and application of honey or propolis, as shown in Table 5.

Discussion

Multidisciplinary management

The first evidence item (Table 5) describes the importance of multidisciplinary team management. In medicine, multidisciplinary team care (MDTC) is a patient-centered collaboration between health care professionals to provide specialized treatment for a variety of conditions that affect patients.²¹ Studies show that MDTC can promote treatment compliance, optimize a complex care plan, improve the quality of life after treatment and prolong survival.²² In European countries, the MDTC approach is standard for cancer care and required for cancer center accreditation by the Organization of European Cancer Institutes.²³ Radiotherapy can damage oral function, resulting in malnutrition and declining physical fitness. Therefore, health care providers should assess each patient's situation and discuss it with MDTC members before and during treatment. When a patient's poor physical condition and difficulty enduring treatment may result in failure to complete treatment, MDTC members should develop a new treatment plan based on individual needs.²⁴

Oral assessment

Evidence items 2–9 describe oral mucosa assessment, including identifying the assessment tools, site, time, frequency, and content. Among the most commonly used clinical oral assessment tools, the WHO grading standard is biased toward assessing eating conditions, while

Table 1
General characteristics of the included literature ($N = 10$).

Included literature	Topic	Year	Source	Type of evidence
Elad et al. ¹¹	MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy	2020	PubMed	Clinical practice guideline
Peterson et al. ¹²	Management of oral and gastrointestinal mucosal injury: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up	2015	PubMed	Clinical practice guideline
Steinmann et al. ¹³	Nursing procedures for the prevention and treatment of mucositis induced by cancer therapies	2021	PubMed	Clinical practice guideline
Ma et al. ¹⁴	Practice guideline for cancer symptom management in China - oral mucositis	2020	CNKI	Clinical practice guideline
Chinese Society for Radiation Oncology ¹⁵	Expert consensus on strategies for prevention and treatment of radiotherapy-induced oral mucositis	2019	Wanfang	Expert consensus
Chinese Society of Clinical Oncology et al. ¹⁶	Expert consensus on diagnosis and prevention of acute oral mucositis caused by antitumor therapy	2021	CNKI	Expert consensus
UKOMIC ¹⁷	Oral care guidance and support in cancer and palliative care	2019	UKOMIC	Expert consensus
Whitehorn et al. ¹⁸	Oral mucositis: Prevention and management principles	2021	JBIC	Evidence summary
An et al. ¹⁹	Role of honey in preventing radiotherapy-induced oral mucositis	2021	PubMed	Systematic review
Tian et al. ²⁰	Impact of honey on radiotherapy-induced oral mucositis in patients with head and neck cancer	2020	PubMed	Systematic review

ESMO, European Society for Medical Oncology; MASCC/ISOO, Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology; UKOMIC, United Kingdom Oral Management in Cancer Group.

Table 2
AGREE II scores of the included guidelines (%) ($N = 4$).

Guidelines	Elad et al. ¹¹	Peterson et al. ¹²	Steinman et al. ¹³	Ma et al. ¹⁴
Scope and purpose	91.67	87.50	95.83	87.50
Involved personnel	72.22	70.83	73.61	75.00
Preciseness of guideline development	82.81	69.79	72.91	69.79
Clarity of presentation	84.72	93.05	59.72	86.11
Applicability	76.04	85.41	56.25	57.29
Independence of writing	87.50	41.67	75.00	8.33
Recommendation level	A	B	B	B
Recommended for use?	Yes	Yes	Yes	Yes

Table 3
Expert consensus quality evaluation ($N = 3$).

Items	Chinese Society for Radiation Oncology ¹⁵	Chinese Society of Clinical Oncology et al. ¹⁶	UKOMIC ¹⁷
1. Is the opinion source clearly identified?	Yes	Yes	Yes
2. Does the opinion source have standing in the field of expertise?	Yes	Yes	Yes
3. Are the relevant population interests the central focus of the opinion?	Yes	Yes	Yes
4. Is the stated position the result of an analytical process, and is there logic in the opinion expressed?	Yes	Yes	Yes
5. Is there reference to the extant literature?	Yes	Yes	Yes
6. Is any incongruence with the literature/sources logically defended?	Yes	Yes	No
Overall evaluation	Included	Included	Included

RTOG and NCI/CTC²⁵ grading standards are biased toward assessing oral pathophysiology. OAG could be a useful tool for detecting early OM.²⁶ The factors in the assessment of RTOM could be classified into two classes: patient-related and treatment-related. Patient-related factors include age, gender, nutritional status, comorbidities, oral hygiene habits, smoking, oral disease history and genetic factors, etc. Treatment-related factors include radiation dose, technique, and site, etc.²⁷ A study²⁸ showed that compared with older patients (> 58 years), higher incidences and severity of OM in head and neck cancer after radiotherapy were observed in young patients (< 45 years). However, Merlano et al.²⁹ found no statistical differences in comparing younger and older patients (age limit 65 years old) with values of grade 3 stomatitis and grade 4 stomatitis. A patient-reported outcome (PRO) assessment is a measurement based on a patient's health condition that comes directly from the patient and cannot be modified or interpreted by the doctor or anyone else. All patients undergoing radiotherapy should

be encouraged to evaluate their mouth and report to clinical caregivers any changes in oral symptoms that they notice or experience.³⁰

Basic oral care

Evidence items 10–14 detail methods of basic oral care. Patients of all ages undergoing radiotherapy should take oral care measures to manage oral mucositis, because effective oral hygiene practices can help reduce the severity of oral mucositis, and reduce the risk of systemic sepsis from oral pathogens.³¹ Previous studies have shown a higher risk of OM in current smokers due to the pro-inflammatory activity of smoking, which could increase the damage to the mucosa.³² Therefore, patients should quit smoking. Furthermore, patients are at increased risk of dental caries following radiotherapy primarily due to hyposalivation. Untreated caries can progress rapidly and require more extensive treatment.³³ Therefore, prevention and early

Table 4
Quality evaluation results of the included systematic reviews (*N* = 2).

Items	An et al. ¹⁹	Tian et al. ²⁰
1. Did the research questions and inclusion criteria for the review include the components of PICO?	Yes	Yes
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	No	No
3. Did the review authors explain their selection of the study designs for inclusion in the review?	No	No
4. Did the review authors use a comprehensive literature search strategy?	Yes	Yes
5. Did the review authors perform study selection in duplicate?	Yes	Yes
6. Did the review authors perform data extraction in duplicate?	Yes	Yes
7. Did the review authors provide a list of excluded studies and justify the exclusions?	Yes	Yes
8. Did the review authors describe the included studies in adequate detail?	Yes	Yes
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes	Yes
10. Did the review authors report on the sources of funding for the studies included in the review?	Yes	No
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?	Yes	Yes
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes	Yes
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?	Yes	Yes
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Yes	Yes
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	Yes	Yes
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Yes	Yes
Overall evaluation	Included	Included

PICO, Population Intervention Comparator Outcome.

detection of mineral loss is essential. Besides, periodontal disease is relevant to the management of the oncology patients as it has been linked to an increased risk of oral mucositis. Extractions of teeth with severely damaged periodontal tissue may be required before tumor treatment begins, especially in areas where high-dose radiotherapy is planned.³⁴ The current recommendation is dental follow-up every 6 months for early detection of caries to maintain oral health. More frequent follow-up may be necessary, depending on the persistence of low salinity and the presence/progression of tooth demineralization, caries, and periodontal conditions.³⁵ Mouthwashes have clinical effectiveness against plaque and gingivitis, clinical caregivers should choose the right mouthwash based on patients' oral pH.³⁶ Sodium bicarbonate rinses have been reported³⁷ to protect inflamed and sensitive mucosa, buffer the intraoral pH, and lubricate and clear the mouth of viscous salivary secretions, even to an extent to decrease the morbidity and severity of RTOM. An RCT³⁸ suggested that saltwater rinses may reduce gingival inflammation following periodontal surgery. Clinicians should advise patients clinically effective and safe mouthwash for management of oral disease.

Pain management

Evidence items 15–17 describe the approach to pain management for patients, including pain scoring and medications use. RTOM can cause pain in the mouth, negatively affecting the patient's physical, emotional, and social comfort and decreasing their quality of life. Reducing pain can increase radiotherapy adherence and avoid treatment interruption.³⁹ Patients with severe oral mucositis with oral pain $\geq$ grade 3, systemic painkillers, such as morphine and fentanyl, can be considered in combination with the specific conditions of the patients.⁴⁰ When using systemic analgesics, the optimal route of administration and dosage should be considered, such as subcutaneous/intravenous analgesia (opioids) or transdermal patches. A study⁴¹ involving nasopharyngeal carcinoma patients showed that treatment with fentanyl transdermal patch could effectively control oropharyngeal pain caused by radiotherapy-induced mucositis, turn moderate or severe pain into mild pain or achieve analgesic effect, and change the phenomenon of less eating and eating difficulty of patients.

Nutritional support

Evidence items 18–20 describe the importance of nutritional support for patients undergoing radiotherapy. Malnutrition reduces immunity and increases the risk of oral mucositis, good nutritional could help defend against local oral infections, maintain the integrity of the mucosa, enhance mucosal tissue repair, and mitigate the deterioration of existing mucositis.⁴² Besides, high-grade mucositis often cause an inadequate food intake, patients can develop serious nutritional deficiency and need parenteral nutrition.⁴³ Study reported⁴⁴ that head and neck cancer patients in treatment with radiotherapy not compliant with individual dietary counseling had a greater incidence of heavy OM. All patients should undergo nutritional assessment to identify factors that might affect their nutritional status, including loss of appetite, taste changes, and dysphagia, and actively enhance nutritional support as appropriate.⁴⁵ Study showed that considering body mass index (BMI) as an indicator of nutritional status, oral cancer patients with BMI > 22 kg/m² had a higher probability of developing OM during radiotherapy treatment if compared with patients with normal BMI.⁴⁶ Furthermore, a prospective study⁴⁷ investigated the nutritional status of nasopharyngeal carcinoma patients during radiotherapy and its association with RTOM, reporting that like body weight and BMI, the change of Nutritional Risk Screening (NRS) 2002 score also revealed the deteriorating nutritional status of patients, which further supported the conclusion that nutritional support and education at the beginning of radiotherapy is very necessary.

Application of honey or propolis

Evidence items 21–22 describe the application of honey or propolis for RTOM. Honey or propolis can be used as an adjunct treatment for OM to relieve associated pain. Propolis is a resinous substance produced by honeybees which is rich in flavonoids and phenolic compounds. It has shown strong antibacterial and anti-inflammatory properties, making it a good choice for oral disease management.⁴⁸ Systematic review⁴⁹ concluded that propolis-based mouthwashes are safe and have potential benefits in reducing plaque and gingival inflammation. Honey has antimicrobial, anti-inflammatory, antioxidant, antimutagenic, and antitumor properties effects. These properties can be attributed to its high acidity

Table 5
Evidence summary on managing radiotherapy-induced oral mucositis in patients with head and neck cancer.

Evidence aspect	Evidence item	Evidence level	Recommendation level
Multidisciplinary management	1. The OM treatment should be performed by a multidisciplinary team, including oncologists, stomatologists, dietitians, nurses, pharmacists, and radiotherapy technicians. Nurses play a key role in the care of oral mucositis. ^{13,16}	Level 5	A
Oral assessment	2. Clinical professionals assessing patients should receive regular specialized training (e.g., on the use of assessment tools). ^{17,18}	Level 5	A
	3. Oral assessment tools: The most used clinical grading criteria for oral mucositis include the WHO, RTOG determined the acute radiation morbidity scoring criteria, OAG, and NCI/CTC. ^{15,17}	Level 5	A
	4. RTOM risk assessment based on the patient and treatment-related factors before radiotherapy, scoring into low, moderate, and high risk. ^{15,16}	Level 1	B
	5. Patients should undergo regular oral assessment examinations before, during and after radiotherapy to dynamically adjust interventions. ^{16,17}	Level 2	A
	6. All patients at risk for OM should have a baseline oral assessment before receiving their first radiotherapy. For patients with moderate or high risk of OM, a dentist could assist in the assessment and preventive treatment. It is recommended to check every 2–3 days. ^{16,17}	Level 5	A
	7. Patients undergoing radiotherapy should continue to receive continuous oral care for up to one month after the end of radiotherapy. Oral evaluations should be conducted every two weeks. ^{16,17}	Level 5	A
	8. All patients undergoing radiotherapy should be encouraged to evaluate their mouth and report any changes in oral symptoms they notice or experience to health care professionals. ^{16,18}	Level 1	A
	9. Health care professionals should guide outpatients with OM to use a self-assessment instrument at home during every clinical visit. ¹⁷	Level 5	A
	10. Good oral hygiene can help to prevent and alleviate oral mucositis. Educate patient to brush the teeth with a soft-bristled toothbrush and fluoride toothpaste after every meal and before going to bed, and change toothbrush monthly or more frequently, depending on the patient's risk of infection. ^{14,17}	Level 5	A
Basic oral care	11. Patients wearing dentures should be guided to properly care for the dentures and reduce the stimulation of oral mucosa. Patients with dental caries should strengthen the cleaning of residual roots. ¹⁴	Level 5	A
	12. Educate patient to avoid food and drink that might aggravate mucosal damage, pain, or discomfort (e.g., overheated, over-acidic, spicy, and coarse food), and quit smoking and drinking. ^{15,16}	Level 5	A
	13. Patients are encouraged to do daily mouth opening, cheek drums, teeth tapping, and other oral function exercises to increase the gas exchange between the oral mucosa and the outside, destroy the living environment of anaerobic bacteria, and prevent secondary infections. ¹⁵	Level 3	B
	14. Mouthwash: Choose the right mouthwash based on the patient's oral pH. Clean the mouth with an alcohol-free saline mouthwash. Gargle first, then drum gargle. Use 15 mL/time, 1 min/time, 4 times/day. Avoid water and food for 30 min after gargling. Patients with ulcers or other problems should gargle frequently (every 2 h while awake). ^{11,12,14}	Level 3	A
Pain management	15. The pain score reflects changes in the patient's mouth and should be part of the oral evaluation. ¹⁷	Level 5	A
	16. Systemic use of strong opioids such as morphine or fentanyl is recommended when severe pain is present. ¹⁵	Level 3	A
	17. Sulfoaluminium (local or systemic) is not recommended for oral mucositis-associated pain prevention in patients undergoing radiotherapy for head and neck cancer. ¹¹	Level 2	B
Nutritional support	18. Nutritional risk assessment should be carried out dynamically in patients with cancer. ¹⁴	Level 5	A
	19. Nutritional intervention should be carried out for patients at risk of malnutrition according to the five-step nutritional intervention model recommended by the professional committee of tumor nutrition and supportive therapy of the Chinese anti-cancer Association. ¹⁴	Level 5	B
	20. Oral nutritional supplements should be given to those able to eat. Enteral nutrition supplements (e.g., by tube feeding) can be given to patients unable to chew or swallow. Parenteral nutrition should be adjusted to achieve the target requirements. ¹⁴	Level 5	A
Application of honey or propolis	21. It is recommended that honey or propolis be used to prevent or reduce the incidence and severity of RTOM in patients undergoing radiotherapy for head and neck cancer. ^{14,19,20}	Level 2	B
	22. Nurses can guide patients 15–20 mL/time honey before the start of each radiotherapy session, and 15 min and 6 h after it ends. Honey should be taken 3 times/day for ≥ 7 days, keeping it in the mouth for 5 min to ensure full contact with the oral mucosa. ¹⁴	Level 5	B

NCI/CTC, National Cancer Institute/Common Terminology Criteria; OAG, Oral assessment guidelines; OM, oral mucositis; RTOG, Radiation Therapy Oncology Group; RTOM, radiotherapy-induced oral mucositis; WHO, World Health Organization.

and osmotic pressure, and contains a glucose oxidase system that inhibits bacterial growth and promotes epithelial cell regrowth.⁵⁰ In a meta-analysis of 19 randomized controlled trials involving 1276 patients, Tzu-Ming Liu et al.⁵¹ observed that the application of honey reduced the degree of oral mucositis induced by radiotherapy. The effect of honey was also observed in the preventive phase. Chao Yang et al.⁵² analyzed 17 randomized studies involving 1265 patients, concluding that pure natural honey is therapeutically superior and decreased the onset time of OM. These evidences support the fact that honey accelerates tissue repair and healing from RTOM lesions. Therefore, honey can be recommended as a first-line adjuvant therapeutic agent in the treatment of OM.

Implications for nursing practice and research

This study provided evidence-based recommendations for clinical caregivers to reduce the incidence of severe RTOM. It is recommended

that the clinical translation process be fully evaluated in the context of different clinical backgrounds, patients' conditions and wishes, economy, and cost-effectiveness, possible obstacles, and other factors to formulate personalized nursing interventions.

Limitations

This evidence summary only included published studies in Chinese and English, and articles in other languages could be included to form a better evidence summary. The search for this study may lack comprehensiveness, as original studies on the management of RTOM were not included. This study included literature from several countries, which may have some bias, considering differences in ethnicity, concepts, values, and regional and cultural differences in medical service systems. Further consideration of the clinical context is needed during the application of the evidence to develop a localized practice plan.

Conclusions

This study summarized the best evidence for managing RTOM in patients with head and neck cancer. It aimed to provide evidence-based recommendations for clinical caregivers to reduce the incidence of severe RTOM, and improve quality of life of patients with head and neck cancer. Future clinical researchers should constantly seek updated evidence and conduct clinical practice reasonably to maximize patient benefits.

Funding

This study was supported by the Peking University evidence-based Nursing Special Research Fund (Grant No. XZJJ-2023-05). The funders had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgments

We would like to extend our gratitude to the Peking University Library for kindly providing databases in this study.

CRediT authorship contribution statement

Zimo Zhang: Formal analysis, Investigation, Data curation, Writing – original draft preparation, Writing – review & Editing. **Li Tian:** Investigation, Data curation. **Juan Liu:** Investigation, Data curation. **Hua Jiang:** Conceptualization, Methodology, Writing – review & Editing, Supervision. **Panfeng Wang:** Conceptualization, Resources, Writing – review & Editing, Project administration. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data availability statement

The data that support the findings of this study are available from the corresponding author, Panfeng Wang, upon reasonable request.

Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

References

- Alterio D, Marvaso G, Ferrari A, Volpe S, Orecchia R, Jereczek-Fossa BA. Modern radiotherapy for head and neck cancer. *Semin Oncol*. 2019;46(3):233–245. <https://doi.org/10.1053/j.seminoncol.2019.07.002>.
- De Meneses AG, Normando AGC, Porto de Toledo I, Reis PED, Guerra ENS. Effects of oral supplementation in the management of oral mucositis in cancer patients: a meta-analysis of randomized clinical trials. *J Oral Pathol Med*. 2020;49(2):117–125. <https://doi.org/10.1111/jop.12901>.
- Villa A, Sonis ST. Pharmacotherapy for the management of cancer regimen-related oral mucositis. *Expert Opin Pharmacother*. 2016;17(13):1801–1807. <https://doi.org/10.1080/14656566.2016.1217993>.
- Wen L, Cui Y, Chen X, Han C, Bai X. Psychosocial adjustment and its influencing factors among head and neck cancer survivors after radiotherapy: a cross-sectional study. *Eur J Oncol Nurs*. 2023;63:102274. <https://doi.org/10.1016/j.ejon.2023.102274>.
- Zhu Z, Hu Y, Xing WJ, et al. The composition of different types of evidence based problems. *J Nurses Training*. 2017;32(21):1991–1994. <https://doi.org/10.16821/j.cnki.hsxx.2017.21.025>. Chinese.
- Dicenso A, Bayley L, Haynes RB. Accessing pre-appraised evidence: fine-tuning the 5S model into a 6S model. *Evid Base Nurs*. 2009;12(4):99–101. <https://doi.org/10.1136/ebn.12.4.99-b>.
- AGREEII-users Manual and 23-item Instrument; 2017. <https://www.agreetrust.org/about-the-agreetrust/introduction-to-agree-ii/>. Accessed March 5, 2023.
- Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017;358:j4008. <https://doi.org/10.1136/bmj.j4008>, 2017 Sep 21.
- Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P. Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. *Int J Evid Base Healthc*. 2015;13(3):132–140. <https://doi.org/10.1097/XEB.0000000000000055>.
- The Joanna Briggs Institute. The Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party. Supporting Document for the Joanna Briggs Institute Levels of Evidence and Grades of Recommendation. <http://joannabriggs.org/jbi-approach.html#tabbed-nav=Levels-of-Evidence>; 2014. Accessed March 5, 2023.
- Elad S, Cheng KKF, Lalla RV, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2020;126(19):4423–4431. <https://doi.org/10.1002/cnrc.33100>.
- Peterson DE, Boers-Doets CB, Bensadoun RJ, Herrstedt J, ESMO Guidelines Committee. Management of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. *Ann Oncol*. 2015;26(suppl 5):v139–v151. <https://doi.org/10.1093/annonc/mdv202>.
- Steinmann D, Babadağ Savaş B, Felber S, et al. Nursing procedures for the prevention and treatment of mucositis induced by cancer therapies: clinical practice guideline based on an interdisciplinary consensus process and a systematic literature search. *Integr Cancer Ther*. 2021;20:1534735420940412. <https://doi.org/10.1177/1534735420940412>.
- Ma TT, Wu Q, Ouyang J, et al. Chinese practice guide for cancer symptom management - oral mucositis. *J Adv Nurs*. 2020;35(20):1871–1878. <https://doi.org/10.16821/j.cnki.hsxx.2020.25.028>. Chinese.
- Society of Radiation Oncology, Chinese Medical Association. Expert consensus on prevention and treatment strategies for radiation oral mucositis. *Chin J Radiat Oncol*. 2019;28(9):641–647. <https://doi.org/10.3760/cma.j.issn.1004-4221.2019.09.001>. Chinese.
- Chinese Society of Clinical Oncology anti-tumor drug Safety Management Expert Committee, Chinese Society of Clinical Oncology Cancer support and rehabilitation treatment expert committee. Expert consensus on diagnosis and prevention of acute oral mucositis induced by antitumor therapy. *J Clin Oncol*. 2021;26(5):449–459. <https://doi.org/10.3969/j.issn.1009-0460.2021.05.011>. Chinese.
- UK Oral Management in Cancer Care Group. Oral care guidance and support in cancer and palliative care. <http://ukomic.co.uk/guidelines.html>; 2019. Accessed March 14, 2023.
- Whitehorn A, Ombech E. Evidence summary. Oral mucositis: prevention and management principles. The JBI EBP database. <https://ovidweb.dcl.ovid.com/ovid-a/ovidweb.cgi>; 2021. Accessed May 6, 2023.
- An W, Li S, Qin L. Role of honey in preventing radiation-induced oral mucositis: a meta-analysis of randomized controlled trials. *Food Funct*. 2021;12(8):3352–3365. <https://doi.org/10.1039/d0fo02808h>.
- Tian X, Xu L, Liu X, et al. Impact of honey on radiotherapy-induced oral mucositis in patients with head and neck cancer: a systematic review and meta-analysis. *Ann Palliat Med*. 2020;9(4):1431–1441. <https://doi.org/10.21037/apm-20-44>.
- Rosell L, Alexandersson N, Hagberg O, Nilbert M. Benefits, barriers and opinions on multidisciplinary team meetings: a survey in Swedish cancer care. *BMC Health Serv Res*. 2018;18(1):249. <https://doi.org/10.1186/s12913-018-2990-4>, 2018 Apr 5.
- Chang YL, Lee SC, Liao CT, Wang CH, Lin YF, Chen SC. Factors impacting on discordance with treatment plan in head and neck cancer patients: a retrospective, population-based cohort study. *Support Care Cancer*. 2020;28(2):951–958. <https://doi.org/10.1007/s00520-019-04904-z>.
- Borras JM, Albrecht T, Audisio R, et al. Policy statement on multidisciplinary cancer care. *Eur J Cancer*. 2014;50(3):475–480. <https://doi.org/10.1016/j.ejca.2013.11.012>.
- Chang YL, Lin CY, Kang CJ, et al. Association between multidisciplinary team care and the completion of treatment for oral squamous cell carcinoma: a cohort population-based study. *Eur J Cancer Care (Engl)*. 2021;30(2):e13367. <https://doi.org/10.1111/ccc.13367>.
- National Cancer Institute. Common Terminology criteria for adverse events (CTCAE). <https://biportal.bioontology.org/ontologies/CTCAE>; 2017. Accessed September 15, 2023.
- Maria OM, Eliopoulos N, Muanza T. Radiation-induced oral mucositis. *Front Oncol*. 2017;7:89. <https://doi.org/10.3389/fonc.2017.00089>, 2017 May 22.
- Lorini L, Perri F, Vecchio S, et al. Confounding factors in the assessment of oral mucositis in head and neck cancer. *Support Care Cancer*. 2022;30(10):8455–8463. <https://doi.org/10.1007/s00520-022-07128-w>.
- Morais-Faria K, Palmier NR, de Lima Correia J, et al. Young head and neck cancer patients are at increased risk of developing oral mucositis and trismus. *Support Care Cancer*. 2020;28(9):4345–4352. <https://doi.org/10.1007/s00520-019-05241-x>.
- Merlano MC, Monteverde M, Colantonio I, et al. Impact of age on acute toxicity induced by bio- or chemo-radiotherapy in patients with head and neck cancer. *Oral Oncol*. 2012;48(10):1051–1057. <https://doi.org/10.1016/j.oraloncology.2012.05.001>.
- Lee CT, Galloway TJ. Pathogenesis and amelioration of radiation-induced oral mucositis. *Curr Treat Options Oncol*. 2022;23(3):311–324. <https://doi.org/10.1007/s11864-022-00959-z>.
- Lalla RV, Brennan MT, Gordon SM, Sonis ST, Rosenthal DI, Keefe DM. Oral mucositis due to high-dose chemotherapy and/or head and neck radiation therapy. *J Natl*

- Cancer Inst Monogr.* 2019;2019(53):lgz011. <https://doi.org/10.1093/jncimonographs/lgz011>.
32. Tao Z, Gao J, Qian L, et al. Factors associated with acute oral mucosal reaction induced by radiotherapy in head and neck squamous cell carcinoma: a retrospective single-center experience. *Medicine (Baltim)*. 2017;96(50):e8446. <https://doi.org/10.1097/MD.00000000000008446>.
 33. Escoda-Francolí J, Rodríguez-Rodríguez A, Pérez-García S, Gargallo-Albiol J, Gay-Escoda C. Dental implications in oral cancer patients. *Med Oral Patol Oral Cir Bucal*. 2011;16(4):e508–e513. <https://doi.org/10.4317/medoral.16.e508>, 2011 Jul 1.
 34. Khaw A, Logan R, Keefe D, Bartold M. Radiation-induced oral mucositis and periodontitis - proposal for an inter-relationship. *Oral Dis*. 2014;20(3):e7–e18. <https://doi.org/10.1111/odi.12199>.
 35. Sroussi HY, Epstein JB, Bensadoun RJ, et al. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med*. 2017;6(12):2918–2931. <https://doi.org/10.1002/cam4.1221>.
 36. Brookes Z, Teoh L, Cieplik F, Kumar P. Mouthwash effects on the oral microbiome: are they good, bad, or balanced? *Int Dent J*. 2023;73(suppl 2):S74–S81. <https://doi.org/10.1016/j.identj.2023.08.010>. Suppl 2.
 37. Madeswaran S, Jayachandran S. Sodium bicarbonate: a review and its uses in dentistry. *Indian J Dent Res*. 2018;29(5):672–677. https://doi.org/10.4103/ijdr.IJDR_30_17.
 38. Collins JR, Veras K, Hernández M, Hou W, Hong H, Romanos GE. Anti-inflammatory effect of salt water and chlorhexidine 0.12% mouthrinse after periodontal surgery: a randomized prospective clinical study. *Clin Oral Invest*. 2021;25(7):4349–4357. <https://doi.org/10.1007/s00784-020-03748-w>.
 39. Kusiak A, Jereczek-Fossa BA, Cichońska D, Alterio D. Oncological-Therapy related oral mucositis as an interdisciplinary problem-literature review. *Int J Environ Res Publ Health*. 2020;17(7):2464. <https://doi.org/10.3390/ijerph17072464>. Published 2020 Apr 3.
 40. Chinese Society of Lung Cancer. Chinese anti-cancer association. EGFR-TKI ADR management Chinese expert consensus. *Zhongguo Fei Ai Za Zhi*. 2019 Feb 20;22(2):57–81. <https://doi.org/10.3779/j.issn.1009-3419.2019.02.01>. Chinese.
 41. Feng HX, Xiong JY, Chen L, et al. Clinical observation and nursing of fentanyl transdermal patch in the treatment of oral mucositis pain caused by radiotherapy for nasopharyngeal carcinoma. *Chin J Surg Oncol*. 2016;8(4):273–275. <https://doi.org/10.3969/j.issn.1674-4136.2016.04.016>. Chinese.
 42. Citak E, Tulek Z, Uzel O. Nutritional status in patients with head and neck cancer undergoing radiotherapy: a longitudinal study. *Support Care Cancer*. 2019;27(1):239–247. <https://doi.org/10.1007/s00520-018-4319-6>.
 43. Pulito C, Cristaudo A, Porta C, et al. Oral mucositis: the hidden side of cancer therapy. *J Exp Clin Cancer Res*. 2020;39(1):210. <https://doi.org/10.1186/s13046-020-01715-7>, 2020 Oct 7.
 44. Hopanci Bicakli D, Ozkaya Akagunduz O, Meseri Dalak R, Esassolak M, Uslu R, Uyar M. The effects of compliance with nutritional counselling on body composition parameters in head and neck cancer patients under radiotherapy. *J Nutr Metab*. 2017;2017:8631945. <https://doi.org/10.1155/2017/8631945>.
 45. Talwar B, Donnelly R, Skelly R, Donaldson M. Nutritional management in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol*. 2016;130(S2):S32–S40. <https://doi.org/10.1017/S002225116000402>.
 46. Saito N, Imai Y, Muto T, Sairenchi T. Low body mass index as a risk factor of moderate to severe oral mucositis in oral cancer patients with radiotherapy. *Support Care Cancer*. 2012;20(12):3373–3377. <https://doi.org/10.1007/s00520-012-1620-7>.
 47. Shu Z, Zeng Z, Yu B, et al. Nutritional status and its association with radiation-induced oral mucositis in patients with nasopharyngeal carcinoma during radiotherapy: a prospective study. *Front Oncol*. 2020;10:594687. <https://doi.org/10.3389/fonc.2020.594687>. Published 2020 Nov 6.
 48. Zulhendri F, Felitti R, Fearnley J, Ravalía M. The use of propolis in dentistry, oral health, and medicine: a review. *J Oral Biosci*. 2021;63(1):23–34. <https://doi.org/10.1016/j.job.2021.01.001>.
 49. Halboub E, Al-Maweri SA, Al-Wesabi M, et al. Efficacy of propolis-based mouthwashes on dental plaque and gingival inflammation: a systematic review. *BMC Oral Health*. 2020;20(1):198. <https://doi.org/10.1186/s12903-020-01185-5>, 2020 Jul 10.
 50. Jicman Stan D, Sărbu MI, Fotea S, et al. Oral mucositis induced by chemoradiotherapy in head and neck cancer-A short review about the therapeutic management and the benefits of bee honey. *Medicina (Kaunas)*. 2022;58(6):751. <https://doi.org/10.3390/medicina58060751>, 2022 May 31.
 51. Liu TM, Luo YW, Tam KW, Lin CC, Huang TW. Prophylactic and therapeutic effects of honey on radiochemotherapy-induced mucositis: a meta-analysis of randomized controlled trials. *Support Care Cancer*. 2019;27(7):2361–2370. <https://doi.org/10.1007/s00520-019-04722-3>.
 52. Yang C, Gong G, Jin E, et al. Topical application of honey in the management of chemo/radiotherapy-induced oral mucositis: a systematic review and network meta-analysis. *Int J Nurs Stud*. 2019;89:80–87. <https://doi.org/10.1016/j.ijnurstu.2018.08.007>.