Review Article

GAVIN PUBLISHERS

Identification of the Core Symptom Clusters among Head and Neck Cancer Patients at Different Treatment Stages: A Systematic Review

Dan Duan[1], Yijing Wan[2], Xiaofeng Luo[2*], Wenting Xing[3]

[1]School of Nursing, Lanzhou University, Lanzhou City 730000, Gansu Province, China

[2]School of Public Health, Lanzhou University, Lanzhou City 730000, Gansu Province, China

[3]Department of Rehabilitation, The First Hospital of Lanzhou University, Lanzhou City 730030, Gansu Province, China

*Corresponding author: Xiaofeng Luo, School of Public Health, Lanzhou University, Lanzhou City 730000, Gansu Province, China

Abstract

Background: Head and Neck Cancer (HNC) is a devastating group of diseases with limited treatment options. More than 60% of HNC are diagnosed in advanced stages and often have severe symptoms, making symptom management paramount, yet the symptom clusters of HNC patients are not well understood. **Objective:** The purpose of this systematic review is to synthesize the current evidence regarding the symptom clusters of HNC patients during and after cancer treatment. **Methods:** A search was conducted using six databases for studies which reporting symptom clusters among HNC patients. **Results:** Fifteen studies met the inclusion criteria. All studies used a quantitative approach. The number of symptom clusters ranged from two to five, and the number of symptoms in a cluster ranged from 2 to 11. Despite names and composition of symptom clusters were variable, the conclusion revealed three prominent symptom clusters: "oropharyngeal SC", "fatigue-sleep SC" and "gastrointestinal SC". Further, the composition of symptom clusters tended to change across different stages of cancer treatment. **Conclusion:** Clinical workers should pay more attention to these three core symptom clusters and take preventive measures in advance to reduce the burden of symptoms. More studies would examine the symptom clusters which occurring among HNC patients at a particular treatment stage, and use the standardized instruments to assess symptoms. Further research would effectively identify the biological pathways associating with various symptom clusters, and it could inform the development of effective and efficient symptom management strategies

Introduction

Head and Neck Cancer (HNC), as a general name for several types of cancer, includes malignancies that arise in the paranasal sinuses, nasal cavity, oral cavity, pharynx, and larynx [1]. HNC is the seventh most common malignancy worldwide [2] and caused more than 0.9 million new cases and 0.4 million deaths in 2020 [3]. HNC and its different treatment modalities are prone to cause numerous adverse symptoms to patients, and the severity of symptoms affects the quality of life of HNC patients [4-6].

With the development of diverse theories about symptom management, many researchers define a stable cluster of two or more related symptoms that occur simultaneously as a symptom cluster [7]. Studies have shown that patients with HNC are prone to persistent moderate to severe symptoms, such as mucositis, fatigue and sleep disruption, which often in the form of symptom clusters (SCs) [8-15]. Compared with symptoms in isolation, the impact of SCs on Quality of Life (QOL) tends to be greater due to synergistic action [16].

It is known that SCs occurrence and severity can change during treatment trajectory [17]. This has caused problems for health care providers in developing symptom management strategies for patients with HNC. We can intervene or prevent the problems by exploring the changing regularity of symptoms in the symptom cluster, intervening in the core SCs of HNC and using the interactions between SCs [18]. In recent years, many studies by scholars were related to the fields for SCs of HNC [19], yet, there is no summary of longitudinal changes in SCs of HNC at different treatment stages and core symptom clusters. Therefore, the purposes of this review are to summarize the evolution of SCs in HNC patients during different treatments and explore the core SCs, and to provide a reference for health care providers on symptom management strategies for HNC. The research question in this review is as follows: (1) What SCs occur before, during and after cancer treatment; and (2) Do the compositions of the SCs change during cancer treatment?

Methods

This review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [20] and the Cooper's prescriptions for research syntheses, Garrard's structured review method [21, 22].

Search Strategy

The initial search was undertaken on October 31, 2022. Six databases were used in the search, including PubMed, Embase, Cochrane library, and CNKI, CBM, Wan Fang databases. We used a combination of Medical Subject Headings with Entry Terms, EMTREE with keywords or Subject Terms as follows: neoplasms, malignant neoplasm, neoplasm, cancer, symptom cluster, symptom constellations and so on. Furthermore, a manual search was also conducted to identify further eligible studies to ensure a comprehensive data collection.

Eligibility Criteria

We included studies regarding the SCs for HNC. We had no restrictions on gender, age, drug dosage, duration and severity of HNC.

Studies must meet the following inclusion criteria:

1. Clinically definite diagnosis of HNC;
2. Original studies of any study design;
3. Chinese or English language;
4. Identifying SCs.

The exclusion criteria included: republished literature, qualitative study and studies without available data or full text.

Study selection and data extraction

Two investigators reviewed independently all titles and abstracts for relevant articles, in case of discrepancies, consensus was achieved by discussion. Two investigators independently extracted data and resolved differences by discussion. If consensus could not be reached, a third reviewer was consulted.

Initially, all titles and abstracts were screened for potentially relevant studies after automatically removing duplicates and manually deleting duplicates simultaneously. Further, full-text articles were reviewed and selected relevant studies according to eligibility criteria.

The basic characteristics were extracted from the included articles including the first author, publication year, country, study settings, study design, sample size, the SCs identified, the symptoms in each cluster, and so on. The corresponding author of the study was contacted via email to obtain the unclear or missing information.

Quality assessment

The quality of included studies was using the Joanna Briggs Institute's (JBI) critical appraisal tool for risk of bias assessment [23] and the Newcastle-Ottawa Scale (NOS) [24]. Some of the items from the two checklists were not applicable to the studies focused on symptom-cluster identification. Five of these articles were longitudinal studies, and the 'exposure-outcome' approach of the appraisal tool was not applicable. One article was a secondary analysis and did not report on key methodological aspects. The reporting quality was first assessed by one reviewer, and the

assessment results were then independently verified by a second reviewer. Any disagreement in the assessment results was resolved through discussion.

Each item on the JBI tools was answered against "Yes", "No", "Unclear", or "Not Applicable". The risk of bias was categorized as high if a study scored ≤49% on the JBI tool, moderate for a JBI score between 50% and 69%, and low for a score more than 70%. This categorization was based on previous use of the tools by other systematic review authors and in consensus with the authors of this review. The NOS with a maximum of 9 points, including three parts: "selection" (four elements) "comparability" (one element) and "outcome" (three elements). The NOS score <6 was considered of moderate or low quality [24]. Risk of bias and quality assessment information were considered in interpretation of findings.

Results

Search results

A total of 4 462 articles were initially identified through the literature search of the six databases and manual search. After removing duplicates (n=1 690), the remaining 2 772 articles were screened by titles and abstracts. Then 21 articles were retained for full-text review, six of these studies were excluded due to the absence of SCs or the identification of SCs based on patient classification. Finally, 15 articles [25-39] met the inclusion criteria for this review. Figure 1 provides the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram that presenting the results of the literature search.
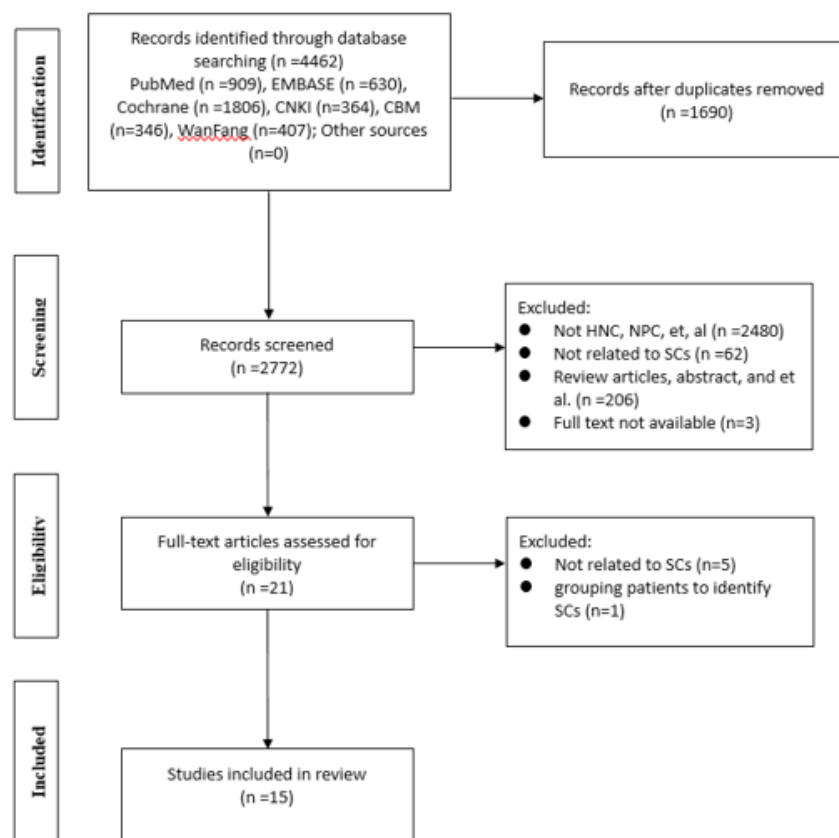
PRISMA 2009 Flow Diagram

Figure 1: A flow diagram of study screening and selection procedures is illustrate.

Study Characteristics

The characteristics of the 15 included studies are presented in Table 1. The included articles contained six English language literatures [25,35-39] and nine Chinese language literatures [26-34]. 9 articles were cross-sectional studies, 5 were longitudinal studies and one was a secondary data analysis study. All articles were published between 2013 and 2021, including two articles from USA [25,39] and 13 from China [26-38]. Of the 15 studies, seven assessed patients with specific HNC: NPC and OC; one assessed HNC patients with ETT. A total of 3 526 participants with HNC were enrolled in these 15 studies. The age of HNC patients ranged from 18 to 70.2 years old. Male patients (78.94%) were predominant in the all studies. And the HNC patients were at different time points of treatment. The details of the time points were summarized in Table 2.

Study Quality

The quality of studies was listed in Table 3. Two studies in this review were rated as low quality, and the others all were high or moderate quality. Overall, all the studies had clearly specified their sample and objectives, and used standardized measures to assess symptoms and other variables of interest. However, the confounding variables were not clear in studies using factor analysis or cluster analysis.

SCs in HNC

Analysis of the study findings revealed that patients with HNC had multiple related and coexisted symptoms. The number of identified SCs ranged from two to five, and the number of symptoms in a cluster ranged from 2 to 11. The review demonstrated that SCs and cluster components differed by symptom measurement and statistical methods. Even among those, using the same tools, the names and composition of the SCs varied, and the same symptoms might appear in different clusters. The details of SCs were showed in Table 2.

Identified SCs among HNC who were undergoing treatment

Ten studies [25,26,28-31,34,35,37,38] investigated the SCs reported by HNC who were undergoing cancer treatment. Five of these studies reported SCs at different time points during the cancer treatment [25,28,31,35, 37]. Furthermore, seven studies [26,27,30,34,35,37,38] reported SCs for these aspects of symptom severity, symptom interference and symptom occurrence. The number of identified SCs ranged from two to four, and the number of symptoms in a cluster ranged from 2 to 11. "Gastrointestinal (GI) SC", "HNC/RT-specific SC" and "sickness SC" were the most commonly reported clusters.

"GI SC" was reported in all ten studies with HNC undergoing cancer treatment, and all reported nausea and vomiting. Chen YQ et al. demonstrated that the "GI SC" included emotional symptoms (feeling of being distressed and feeling sad) [30]. Furthermore, the "GI SC" also included lack of appetite, feeling full, taste change, dehydration, and numbness, shortness of breath, difficulty remembering and constipation. "HNC/RT-specific SC" was observed in 33.3% of the studies [25, 26, 29, 35, 37], and dry mouth was reported in all of them. These studies all showed difficulty swallowing/chewing were associated with the "HNC/RT-specific SC" (excepting one article [25]). And only two studies [26,35] demonstrated that fatigue was involved in "HNC/RT-specific SC". Other symptoms were mostly about adverse radiotherapy reaction. As for "sickness SC", it was reported in three studies [27-30] during the cancer treatment. Problem with remembering things was the common symptom in "sickness SC". Wu WY et al. demonstrated that, before receiving the RT but during receiving CT, problem with remembering things did not exist in the "sickness SC". Furthermore, the "sickness SC" also included feeling drowsy, numbness or tingling, shortness of breath and disturbed sleep.

Identified SCs among HNC who had completed treatment

Among the included studies, seven [27,28,31-33,36,39] examined the SCs by patients who had completed cancer treatment. Three of the studies reported that the time point of symptom assessment was after surgery, one was at the end of treatment, one was 1 month after the end of treatment, and one was 5 years after discharge. The number of identified SCs ranged from two to five, and the number of symptoms in a cluster ranged from 2 to 7. One of the studies [33] did not make a detailed description of symptoms in SCs. The SCs in other six studies were named differently. Qiu LY et al. demonstrated that the five SCs were in chronic clinical phase, and the SCs all named "chronic SC"[27]. Li YY et al. examined the five SCs by patients with Endotracheal Tube (ETT) [36]. And David IR et al. [39] found the two SCs ("the local SC" and "systemic SC"). The "digestive tract SC" and "fatigue SC" were the most commonly reported clusters. Lack of appetite, constipation, nausea, feeling drowsy, and problem with tasting food were included in "digestive tract SC". Fatigue, disturbed sleep and sleepy were the common symptoms in "fatigue SC", and feeling of being distressed, feeling sad were associated with this SC.

In summary, a number of SCs were identified among HNC patients during and after cancer treatment. However, no SCs was identified before cancer treatment in the included articles. Despite the heterogeneity in the nomenclature of these SCs, three of them, namely "oropharyngeal SC", "fatigue-sleep SC" and "GI SC", were commonly identified by multiple studies. In addition, multiple studies reported the "fatigue-sleep SC" and the "GI SC" were respectively associated with the psychological symptoms (feeling of being distressed and feeling sad). Although the three SCs co-occurred in patients at the two treatment stages, the more

frequent and severe of symptoms were during cancer treatment. The identified SCs with specific symptoms at different stages of cancer treatment were shown in Figure 2.
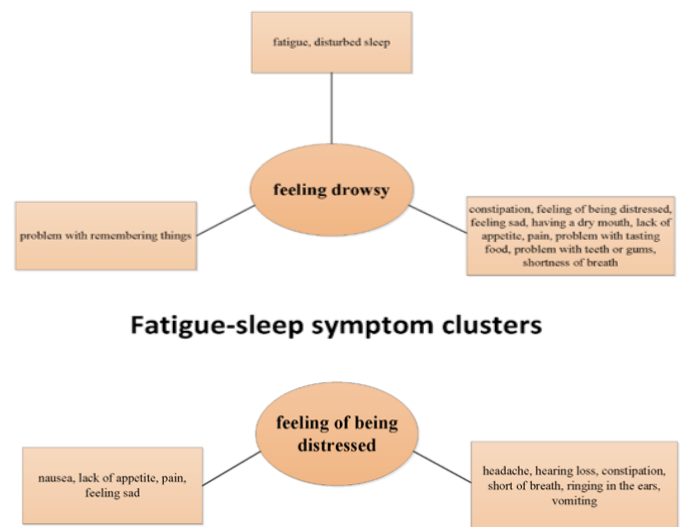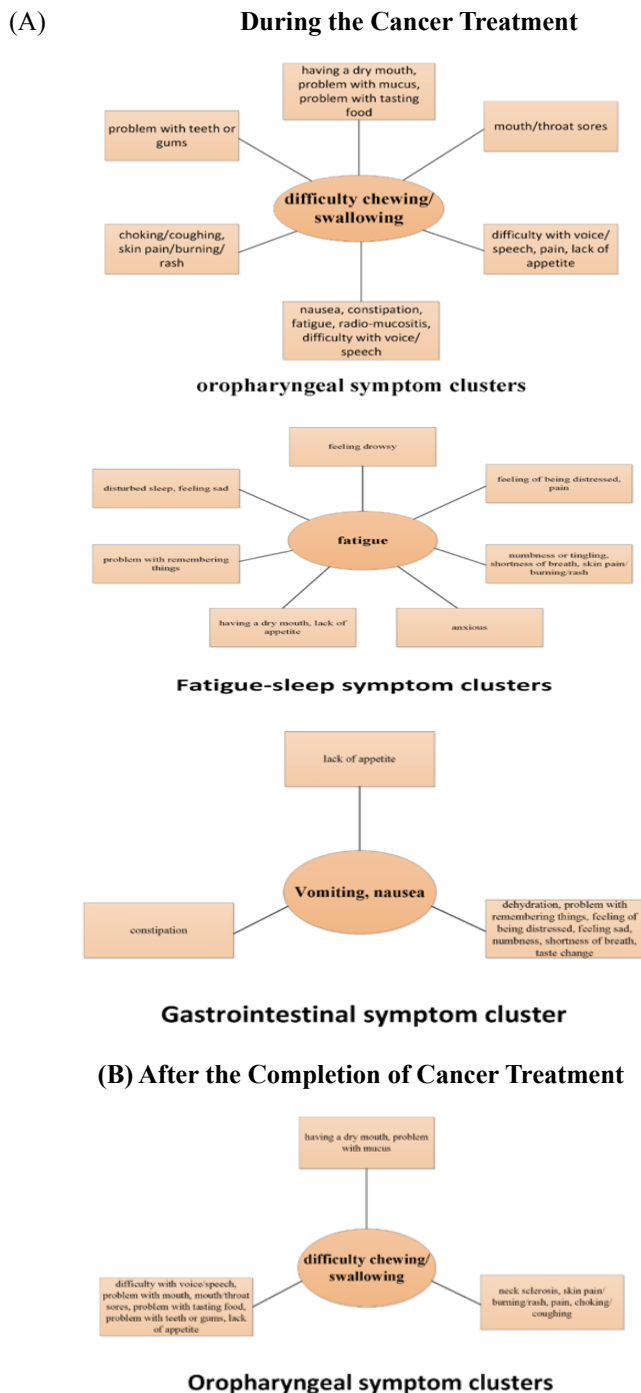
(A)   **During the Cancer Treatment**

oropharyngeal symptom clusters

Fatigue-sleep symptom clusters

Gastrointestinal symptom cluster

(B) After the Completion of Cancer Treatment

Oropharyngeal symptom clusters

Fatigue-sleep symptom clusters

Gastrointestinal symptom clusters

Figure 2: (A) During the cancer treatment (B) After the completion of cancer treatment, 2A schematic diagram depicting the symptoms associated with the identified symptom clusters among HNC patients during cancer treatment (A) and after the completion of their cancer treatment (B).

The longitudinal changes of the composition of SCs

Three of the included studies [28,31,37] assessed changes in the composition of SCs over time. Most studies demonstrated that SCs with a low level of stability, because the number of symptoms and symptoms varied at different treatment stages. Wu WY et al. [28] reported that the "GI SC" comprising the symptom of lack of appetite, which disappeared after patients, started receiving RT. In addition, the symptom of feeling drowsy in "sickness SC" disappeared after patients started receiving RT. During the RT treatment, the "sickness SC" increased the symptoms of shortness of breath, problem with remembering things, and the "somatic SC" increased the symptoms of having a dry mouth. Changes in the composition of the SCs after RT treatment were the same as described above. Zhang N et al. [31] demonstrated the identified SCs at four stages (RT week 2, week 4, week 6, and 1 month after the end of RT) of cancer treatment. Week 2 after starting RT, the number of identified SCs was two, and week 4 and week 6 increased to four SCs, then decreased to three at 1 month after the end of RT. The "oral mucosal SC" including the symptom of nausea disappeared at week 4, week 6, and 1 month after the end of RT. Nevertheless, the nausea symptom combined with vomiting and constipation to form another new SC "GI SC" at week 4 and week 6. In addition, the pain symptom was initially associated with the "fatigue-sleep-emotion SC", yet, this symptom was found to form another cluster "vocal-dysphagia SC" at week 4, and week

6. The symptoms of shortness of breath and choking/coughing initially appeared at week 6. In addition, the symptom of mouth/throat sores appearing at week 4 and week 6 which disappeared at 1 month after the end of RT. Although two studies showed that the composition of SCs was generally unstable over time, Chiang SH [42] indicated that the two identified SCs were relatively stable from weeks 1-6 of postoperative RT. The "HNC-specific SC" comprised the symptoms of pain, dry mouth, lack of appetite, sleep disturbance, fatigue, drowsiness, distress, and sadness. The "GI SC" included nausea, vomiting, numbness, shortness of breath, and difficulty remembering.

Discussion

The field of research about SCs has become increasingly important, particularly within HNC patients. The SCs identified in current studies play influential roles in improving HNC patient's care and symptom management [19]. Yet, the existing studies has not summarized the exact core SCs experienced by HNC patients and the longitudinal changes in SCs at different treatment stages, which is not beneficial for health care providers to directly use in clinical practice. This systematic review focused on summarizing the core SCs, as well as the longitudinal changes of the composition of SCs in HNC patients, and analyzing the quality of selected studies to provide ideas for formulators of clinical symptom management strategies.

This review found the number of SCs ranged from two to five, and the number of symptoms in a cluster ranged from 2 to 11. The results were same as the articles conducted by Asha Mathew et al [19]. Due to no study reported the SCs among HNC patients prior to treatment, this review only showed changes during and after cancer treatment. This review showed that "oropharyngeal SC", "fatigue-sleep SC" and "GI SC" were the most common SCs identified, and these SCs were present throughout the course of cancer treatment, and had been reported even at the end of cancer treatment. The findings indicated that these SCs might be caused by the cancer itself and the adverse effects of its treatment, and this was consistent with previous findings [40]. Another notable finding of this review was that the composition of SCs among HNC patients appeared to change over time. Yet, the variability did not always appear; Chiang SH et al. [37] found that the composition of the identified SCs remained in the same clusters throughout the course of radiotherapy. Because the 13 symptoms of the tool (MDASIT) were the most typical symptoms of HNC patients undergoing radiotherapy, these symptoms might be the core symptoms of their corresponding clusters. In addition, this might explain the apparent stability SCs [41]. We found that the temporal instability of SCs was consistent with a review on SCs in patients with advanced cancer [42]. Health care providers should be aware that different symptoms clustered to form a cluster at different stages of treatment, so they should take targeted care measures when caring for patients. To promote precision care, more longitudinal studies are necessary to delineate changes in SC structure over time. Although it was difficult to draw general conclusions because of the variations in the identified clusters with temporal changes, "core" symptoms (lack of appetite and pain) consistently persisted in some clusters. Some studies have defined the symptoms that persist or occur most frequently over time within SCs as "core" symptoms and have suggested that SCs can be assessed and managed by "core" symptoms [43,44]. In addition, the symptoms in clusters might cause by common biological pathways, and the symptoms might be managed simultaneously with a single intervention. Thus, it is vital to catch these "core" symptoms. For example, the toxicity of chemotherapeutic substances to normal tissues caused salivary glands and taste bud injury, leading to dryness of the mouth and cavity of the patient, taste perception changes, to lower the appetite [45]; and lack of appetite increased the risk of depression [46]. This suggests that health care providers should identify signs of lack of appetite early and explain the causes to patients, and protect the oral mucosa to improve all symptoms in the SCs, rather than focusing on measures such as improving nutritional intake only. In addition, implementing pain management strategies can help reduce the patients' level of many other symptoms, such as fatigue, anxiety and depression levels [46,47]. In addition, studies have shown that managing pain as a "core" symptom can alleviate multiple symptoms simultaneously [48]. Mastering these core SCs gives health care providers a deeper understanding and awareness of a single symptom, which can help assess holistically and intervene in advance to prevent or mitigate other related symptoms within the same core SCs in HNC patients, thus improving clinical efficiency. Therefore, clinical workers should pay more attention to these three core SCs and take preventive measures in advance to reduce the burden of symptoms.

Limitations

This review has several limitations. Firstly, although a comprehensive systematic search was conducted, we possibly ignored the unpublished studies, which lead to a potential publication bias. Secondly, there is a high degree of heterogeneity in the methodology used for symptom assessment of patients and symptom cluster identification among the included studies. Thirdly, the number of included studies is small, and the conclusions need to be further verified by more and better studies. Finally, only Chinese and English studies were included, which could have led to language bias. Therefore, caution is required for the interpretation of the findings of this review.

Conclusions

With growing evidence that cancer-related symptoms often co-occur and these symptoms can mutually influence their occurrence

and severity, more studies have aimed to identify cancer-related SCs. Our review provides an overview of the identified SCs among HNC patients, and reveals that "oropharyngeal SC", "fatigue-sleep SC" and "GI SC" are three of the most commonly reported SCs. In addition, some of these identified SCs show a considerable degree of longitudinal instability. Clinical workers should pay more attention to these three core symptom clusters and take preventive measures in advance to reduce the burden of symptoms. Sufficiently powered studies are needed to identify clinically relevant SCs in the future to elucidate the core SCs in HNC patients. Further research could promote the development of effective and efficient symptom management strategies.

Authors' Contributions

DD and WYJ planned and designed the study. All authors contributed to the eligibility assessment and creation of the data tables. DD and WYJ performed the statistical analysis. DD wrote the first draft. XFL revised the draft.

References

1. Gurushekar PR, Isiah R, John S, Sebastian T, Varghese L (2020) Effects of radiotherapy on olfaction and nasal function in head and neck cancer patients. Am J Otolaryngol 41: 102537.

2. Chow LQM (2020) Head and Neck Cancer. N Engl J Med 382: 60-72.

3. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, et al. (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clinc 71: 209-49.

4. Cleeland CS (2007) Symptom burden: multiple symptoms and their impact as patient-reported outcomes. J Natl Cancer Inst Monogr 37:16-21.

5. Allen-Ayodabo CO, Eskander A, Davis LE, Zhao H, Mahar AL, et al. (2019) Symptom burden among head and neck cancer patients in the first year after diagnosis: Association with primary treatment modality. Oral Oncol 99:104434.

6. Bubis LD, Davis L, Mahar A, Barbera L, Li Q, et al. (2018) Symptom Burden in the First Year After Cancer Diagnosis: An Analysis of Patient-Reported Outcomes. J Clin Oncol 36: 1103-1111.

7. Kim HJ, McGuire DB, Tulman L, Barsevick AM (2005) Symptom clusters: concept analysis and clinical implications for cancer nursing. Cancer Nurs 28: 270-82.

8. Townes TG, Navuluri S, Pytynia KB, Kamal MJ, Joseph LM, et al. (2020) Assessing patient-reported symptom burden of long-term head and neck cancer survivors at annual surveillance in survivorship clinic. Head Neck. 42: 1919-1927.

9. Bressan V, Stevanin S, Bianchi M, Aleo G, Bagnasco A, et al. (2016) The effects of swallowing disorders, dysgeusia, oral mucositis and xerostomia on nutritional status, oral intake and weight loss in head and neck cancer patients: A systematic review. Cancer Treat Rev 45: 105-119.

10. Shi Q, Mendoza TR, Gunn GB, Wang XS, Rosenthal DI, et al. (2013) Using group-based trajectory modeling to examine heterogeneity of symptom burden in patients with head and neck cancer undergoing aggressive non-surgical therapy. Qual Life Res 22: 2331-2339.

11. Gunn GB, Mendoza TR, Fuller CD, Gning I, Frank SJ, et al. (2013) High symptom burden prior to radiation therapy for head and neck cancer: a patient-reported outcomes study. Head Neck. 35: 1490-1498.

12. Wulff-Burchfield E, Dietrich MS, Ridner S, Murphy BA (2019) Late systemic symptoms in head and neck cancer survivors. Supportive Care Cancer. 27: 2893-2902.

13. Hanna EY, Mendoza TR, Rosenthal DI, Gunn GB, Sehra P, et al. (2015) The symptom burden of treatment-naive patients with head and neck cancer. Cancer. 121: 766-773.

14. Paiar F, Cristaudo A, Gonnelli A, Giannini N, Cocuzza P, et al. (2020) Radiation-induced nausea and vomiting in head and neck cancer: Is it something worth considering in the intensity modulated radiotherapy era? "A narrative review". Head Neck. 42: 131-137.

15. Stinson J, Chan K, Lee J, Chow R, Cheon P, et al. (2017) Managing chemotherapy-induced nausea and vomiting in head and neck cancer patients receiving cisplatin chemotherapy with concurrent radiation. Ann Palliat Med 6: S13-S20.

16. Williams LA (2007) Clinical management of symptom clusters. Seminars in oncology nursing. 23: 113-120.

17. Tantoy IY, Cooper BA, Dhruva A, Cataldo J, Paul SM, et al. (2018) Changes in the Occurrence, Severity, and Distress of Symptoms in Patients With Gastrointestinal Cancers Receiving Chemotherapy. J Pain Symptom Manage 55: 808-834.

18. Hamash KI, Umberger W, Aktas A, Walsh D, Cheruvu VK (2018) The Effect of the Pain Symptom Cluster on Performance in Women Diagnosed with Advanced Breast Cancer: The Mediating Role of the Psychoneurological Symptom Cluster. Pain Manag Nurs 19:627-636.

19. Mathew A, Tirkey AJ, Li H, Steffen A, Lockwood MB, et al. (2021) Symptom Clusters in Head and Neck Cancer: A Systematic Review and Conceptual Model. Semin Oncol Nurs 37: 151215.

20. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, et al. (2015) Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 350: g7647.

21. Tomasic D (2011) Health Sciences Literature Review Made Easy: The Matrix Method, 3rd Edition. 23.

22. Cooper HM (2010) Research synthesis and meta-analysis: a step-by-step approach.

23. Zhou Y, Ying G, Yan H, et al. (2018) The joanna briggs institute critical appraisal tools for use in systematic review:Prevalence study and analytical cross sectional study.

24. Stang A (2010) Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 25: 603-605.

25. Xiao C, Hanlon A, Zhang Q, Ang K, Rosenthal DI, et al. (2013) Symptom clusters in patients with head and neck cancer receiving concurrent chemoradiotherapy. Oral Oncol 49: 360-366.

26. Shen Y, Qiang WM (2017) Investigation on symptom group of nasopharyngeal carcinoma patients during concurrent chemoradiotherapy. Nursing Research. 31: 3962-3966.

27. Qiu LY, Yang L, Liu TT (2021) Correlation between symptom group and quality of life in patients with nasopharyngeal carcinoma 5 years after discharge. Journal of Nursing. 36: 38-41.

28. Wu WY, Yang F Y, Wu Y (2016) Longitudinal study of symptom group changes in patients with nasopharyngeal carcinoma during radiotherapy [J]. Chinese Journal of Modern Nursing. 22: 1804-1808.

29. Shen Y, Qiang W M, Li Z (2017) Late chemoradiation in patients with symptoms of nasopharyngeal carcinoma (NPC) and its influencing factors analysis. Journal of Nursing Education. 32: 1279-84.

30. Chen YQ, Zhou JR, Yang J (2014) Symptom group and influencing factors in patients with nasopharyngeal carcinoma during concurrent chemoradiotherapy. Journal of Chongqing Medical University. 39: 1830-1834.

31. Zhang N, Song JX, Wang HQ (2019) Longitudinal study of symptom group in patients with nasopharyngeal carcinoma undergoing concurrent chemoradiotherapy. Chinese Journal of Nursing. 26: 6-10.

32. Peng CE, Li Z, Lv CL, Wang K, Zhou B, et al. (2020) Investigation and analysis of Postoperative symptoms in patients with oral cancer. Chinese Journal of Practical Nursing. 36: 2209-2215.

33. Peng CE, Li Z, Zhou B, et al. Correlation between symptom group and quality of life in patients with oral cancer after surgery [J]. Chinese Journal of Modern Nursing. 08: 1038-43.

34. Deng W, Zhou JR, Liu DD, Duan X (2015) Symptom cluster of patients with head and neck cancer. Chinese Journal of Practical Nursing. 36: 426-429.

35. Wang Y, Lu Q, Zhang L, Zhuang B, Zhang T, et al. (2021) Nutrition Impact Symptom Clusters in Patients With Head and Neck Cancer Receiving Concurrent Chemoradiotherapy. J Pain Symptom Manage 62: 277-285.

36. Li Y, Li X, Mao C, Lv G, Xie Z, et al. (2020) Symptom clusters in head and neck cancer patients with endotracheal tube: Which symptom clusters are independently associated with health-related quality of life?. Eur J Oncol Nurs 48: 101819.

37. Chiang Sh, Ho Ky, Wang Sy, Lin CC (2018) Change in symptom clusters in head and neck cancer patients undergoing postoperative radiotherapy: A longitudinal study. Eur J Oncology Nur 35: 62-66.

38. Xiao W, Chan CWH, Fan Y, Leung DYP, Xia W, et al. (2017) Symptom clusters in patients with nasopharyngeal carcinoma during radiotherapy. Eur J Oncol Nurs 28: 7-13.

39. Rosenthal DI, Mendoza TR, Fuller CD, Hutcheson KA, Wang XS, et al. (2014) Patterns of symptom burden during radiotherapy or concurrent chemoradiotherapy for head and neck cancer: a prospective analysis using the University of Texas MD Anderson Cancer Center Symptom Inventory-Head and Neck Module. Cancer. 120: 1975-1984.

40. Kwekkeboom KL, Cherwin CH, Lee JW, Wanta B (2010) Mind-body treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer. J Pain Symptom Manage 39: 126-138.

41. So WKW, LAW BMH, Ng MSN, He X, Chan DNS, et al. (2021) Symptom clusters experienced by breast cancer patients at various treatment stages: A systematic review. Cancer Med 10: 2531-2565.

42. Dong ST, Butow PN, Costa DS, Lovell MR, Agar M (2014) Symptoms clusters in patients with advanced cancer: a systematic review of observational studies. J Pain Symptom Manage 48: 411-450.

43. Brown JK, Cooley ME, Chernecky C, Sarna L (2011) A symptom cluster and sentinel symptom experienced by women with lung cancer. Oncol Nurs Forum 38: E425-435.

44. Aktas A (2013) Cancer symptom clusters: current concepts and controversies. Curr Opin Support Palliat Care 7: 38-44.

45. Mitchell EP (2006) Gastrointestinal toxicity of chemotherapeutic agents. Semin Oncol 33: 106-1020.

46. Oh HS, Seo WS (2011) Systematic review and meta-analysis of the correlates of cancer-related fatigue. Worldviews Evid Based Nurs 8: 191-201.

47. Miller-Matero LR, Chipungu K, Martinez S, Eshelman A, Eisenstein D (2017) How do I cope with pain? Let me count the ways: awareness of pain coping behaviors and relationships with depression and anxiety. Psychol Health Med 22:19-27.

48. Kwekkeboom KL, Wanta B, Bumpus M (2008) Individual difference variables and the effects of progressive muscle relaxation and analgesic imagery interventions on cancer pain. J Pain Symptom Manage 36: 604-615.