Post-print: Systematic Review of Cancer Pain Management Guidelines

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Abstract

Background To improve the quality of pain management for cancer patients, clinical guidelines have been published and revised worldwide. However, significant gaps exist in evidence-based resources among various guidelines for cancer pain management, urgently requiring high-quality systematic reviews of guidelines to bridge practice gaps. Objective To analyze the similarities and differences in recommendations across guidelines related to the management of cancer pain patients through systematic review, and to provide evidence-based decision-making references for clinical practice. Methods A systematic search was conducted for guidelines on the management of cancer pain patients in PubMed, Web of Science, Cochrane Library, CNKI, Wanfang Data Knowledge Service Platform, Chinese Biomedical Literature Database, BMJ Best Practice, Scottish Intercollegiate Guidelines Network, National Guideline Clearinghouse, Medlive, as well as relevant academic society and industry organization websites, with the search period from database inception to October 9, 2023. Two researchers screened the literature according to inclusion and exclusion criteria, evaluated guideline quality using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool, and summarized relevant recommendations for cancer pain management across guidelines. Results Seven guidelines were ultimately included, published between 2016 and 2023, including 2 from the United States, 2 from Switzerland, 1 from Canada, 1 from Latin America, and 1 from Japan, all with a recommendation level of A. The relevant recommendations primarily focused on four aspects: cancer pain assessment, pharmacological management, non-pharmacological management, and cancer pain education. Conclusion The recommendations from the seven guidelines can provide new reference evidence for cancer pain management practice in China. It is recommended that clinical practitioners consider the specific conditions of patients and engage in multidisciplinary collaboration and discussion to truly achieve the "5A" goals of cancer pain management.

Full Text

Abstract

Background: To improve the quality of pain management in cancer patients, clinical guidelines have been published and revised worldwide. However, significant gaps exist in evidence-based resources across cancer pain management guidelines, creating an urgent need for high-quality systematic reviews to bridge these practice gaps.

Objective: To systematically review guidelines for the management of cancer pain patients, analyze the similarities and differences in recommendations across guidelines, and provide an evidence-based decision-making reference for clinical practice.

Methods: We systematically searched PubMed, Web of Science, Cochrane Library, CNKI, Wanfang Data, CBM, BMJ Best Practice, SIGN, NGC, Medical Communication, and websites of relevant societies and industry bodies for guidelines on cancer pain management. The search timeframe spanned from database inception to October 9, 2023. Two researchers independently screened literature according to inclusion and exclusion criteria, evaluated guideline quality using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) tool, and summarized recommendations related to cancer pain management in cancer patients.

Results: Seven guidelines were ultimately included, developed between 2016 and 2023, comprising two from the United States, two from Switzerland, one from Canada, one from Latin America, and one from Japan. All guidelines received an A-level recommendation. The recommendations primarily focused on four aspects: cancer pain assessment, pharmacological management, non-pharmacological management, and cancer pain education.

Conclusion: The recommendations from these seven guidelines can provide a new reference for cancer pain management practice in China. It is suggested that clinical practitioners should consider patients'specific conditions and engage in multidisciplinary cooperation to truly achieve the "5A" goals of cancer pain management.

Keywords: Cancer pain; Cancer pain management; Guidelines; Systematic review; Evidence-based medicine

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1. Methods

1.1 Literature Search Strategy

We systematically searched guideline-related databases including PubMed, Web of Science, Cochrane Library, CNKI, Wanfang Data, Chinese Biomedical

Literature Database, BMJ Best Practice, Scottish Intercollegiate Guidelines Network (SIGN), National Guideline Clearinghouse (NGC), Medical Communication, and websites of relevant societies and industry organizations. English search terms included: cancer pain/cancerous pain/the pain of tumor/cancer ache/neoplastic pain/refractory cancer pain/symptom cluster/syndromes/cluster, symptom/clusters, symptom/symptom clusters/management/disease managements/disease management/pain management/pain managements. Chinese search terms included: cancer pain/tumor pain/cancer pain/advanced cancer pain/refractory cancer pain/symptom cluster/symptom cluster/management. The search timeframe was from database inception to October 9, 2023.

Inclusion criteria: Guidelines explicitly addressing pain management in cancer patients; guidelines must be the most recent version; language must be Chinese or English.

Exclusion criteria: Directly translated or duplicate guidelines; guidelines with inaccessible full text; guideline interpretations, abstracts, or policy documents.

Two researchers trained in evidence-based methodology independently conducted the work, strictly following predetermined inclusion and exclusion criteria with cross-checking. Any disagreements were resolved by a third researcher who made final decisions. Extracted content included: (1) Basic guideline characteristics: guideline title, region/country, publishing organization, publication/update year, guideline type, number of authors, page count, target population, and number of references. (2) Quality evaluation indicators: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. (3) Relevant recommendations for cancer pain patient management. This process aimed to ensure accuracy and credibility.

1.4 Guideline Quality Evaluation

All literature was evaluated using AGREE II. The evaluation covered six domains with 23 items: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence. Each item was scored on a 7-point scale, with 1 representing the lowest quality and 7 the highest quality. The calculation method was: standardized score for a domain (%) = (actual score - minimum possible score) / (maximum possible score - minimum possible score) × 100%. Higher scores indicated better completeness in guideline development methodology and reporting. We comprehensively assessed guideline quality and determined recommendation grades using standardized percentages across six domains and scores for each item. Evaluation results were divided into three grades: Grade A: Guidelines scoring $ $70% in four or more domains were considered high quality and strongly recommended for use. Grade B: Guidelines scoring $ $30% in at least three domains but <70% in fewer than four domains required some revision or improvement before rec-

ommendation. Grade C: Guidelines scoring $ $30% in fewer than three domains were not recommended for use and required further improvement.

1.5 Statistical Methods

SPSS 26.0 software was used for statistical analysis. Two reviewers used the intraclass correlation coefficient (ICC) to assess consistency in guideline quality evaluation. ICC ranges from 0 to 1, where ICC <0.40 indicates poor consistency, 0.40-0.75 indicates fair consistency, and >0.75 indicates high consistency.

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2. Results

2.1 Literature Search Results

The initial search retrieved 1,839 documents, including 235 Chinese and 1,604 English articles. After removing 34 duplicates, 347 irrelevant documents were excluded. Reading titles and abstracts yielded 102 potentially relevant articles. After full-text review, 95 documents that did not match the research topic were excluded, resulting in 7 final included guidelines.

2.2 Basic Characteristics of Included Guidelines

The seven included clinical guidelines originated from the United States (2), Canada (1), Switzerland (2), Latin America (1), and Japan (1). Guidelines ranged from 12 to 144 pages, with a maximum of 408 references. One guideline did not list authors. The basic characteristics of included guidelines are shown in Table 1 .

2.4 Guideline Evaluation Consistency Test

In this study, the consistency between two reviewers for all guidelines was >0.75, indicating good consistency in scoring results, as shown in Table 3 .

2.5 Summary of Main Recommendations

Recommendations from cancer pain management guidelines primarily focused on four aspects: cancer pain assessment, pharmacological management, non-pharmacological management, and cancer pain education. Recommendations from different guidelines are shown in Table 4 .

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3. Discussion

3.1 Overall Guideline Quality

This study included seven clinical guidelines, with two from the United States, two from Switzerland, one from Canada, one from Latin America, and one from Japan. Under the AGREE II framework, standardized scores across domains were: scope and purpose 96.03%, stakeholder involvement 91.66%, rigor of development 93.75%, clarity of presentation 91.66%, applicability 90.48%, and editorial independence 92.26%. All seven guidelines received Grade A recommendations.

3.2 Cancer Pain Assessment

Cancer pain assessment is typically the first step in pain management for cancer patients. Currently, the most commonly used pain assessment tools domestically and internationally are unidimensional pain scales, including the Visual Analogue Scale (VAS), Verbal Rating Scale (VRS), and Numerical Rating Scale (NRS). Regarding assessment content, scholars worldwide agree that pain requires more comprehensive and detailed evaluation. Since cancer patients' psychosocial distress may vary and is often difficult to understand deeply, assessment by an interdisciplinary team including psychologists and/or social workers is crucial. Research indicates that cancer pain patients typically experience a range of symptoms including dyspnea, anxiety, and sleep disturbances, so pain assessment should include all symptoms within known symptom clusters. Additionally, healthcare providers should incorporate patients' cultural values during comprehensive pain assessment, as patients may report lower pain scores due to beliefs that pain should be endured, even when facial expressions reflect severe pain.

3.3 Pharmacological Management

Pharmacological intervention is the cornerstone of cancer pain management. Recommendations regarding pharmacological treatment for cancer pain were generally consistent across guidelines, aiming to reduce pain to a level acceptable for patients' quality of life. Oral opioid administration is primary, following the WHO analgesic ladder while advocating individualized dosing. Opioids such as morphine, hydromorphone, and fentanyl are the most commonly used analgesics. Evidence shows they effectively control pain. However, when side effects occur, opioid rotation may be necessary to help relieve uncontrolled pain or treat opioid-induced neurotoxicity. Approximately 30% of cancer patients on opioids will undergo opioid rotation. Since opioids have many adverse effects such as nausea, constipation, and other social issues, seeking new medications for cancer pain is essential. Ji et al. explored Traditional Chinese Medicine-based herbal remedies to alleviate cancer pain, providing a new approach for clinical management.

3.4 Non-pharmacological Analgesia

Non-pharmacological analgesia is an important component of comprehensive care plans. Guidelines showed some variation in non-pharmacological measures for cancer pain management, though providing supportive and culturally appropriate psychological interventions to patients and families/caregivers was a relatively consistent recommendation. Research shows that psychological interventions have small but significant effects on pain severity and pain interference across different cancer stages, particularly for breast cancer patients. Cognitive behavioral therapy, hypnosis, and guided imagery relaxation have proven effective psychological interventions for cancer pain management, though these studies have limitations including small sample sizes and lack of rigorous trial design. Due to technological advances, virtual reality is gaining attention as a future treatment method, though evidence for its use in cancer pain management remains inconclusive. Overall, more research is needed to explore the overall efficacy of non-pharmacological analgesic therapies.

3.5 Cancer Pain Education

Clinical guidelines recommend patient and family/caregiver education as an important component of cancer pain management. Patient education has been shown to improve knowledge about proper use, storage, and disposal of opioids while changing behavior and usage patterns. All patients receiving opioids should receive education about benefits and risks of opioid therapy, alternative options, opioid side effects, and unintended risks of misuse and addiction. Additionally, empowerment strategies beyond knowledge should be taught to enhance patients' confidence in pain management, including providing cancer pain diaries, access to telephone nursing, and personal pain management plans.

3.6 Limitations and Improvement Suggestions for Cancer Pain Management Guidelines

(1) **Insufficient evidence base:** Some guidelines were developed based on limited evidence, resulting in inadequate recommendations. We recommend strengthening clinical trials and research to provide a more solid evidence base. (2) **Insufficient personalized treatment:** Some guidelines do not adequately consider individual patient differences such as age, gender, and disease stage. We recommend developing personalized or precision medicine strategies to accommodate different patient needs. (3) **Implementation difficulty:** Some guidelines are overly theoretical and lack guidance for practical operation. We recommend providing specific implementation strategies and tools to help healthcare providers better apply the guidelines. (4) **Lack of monitoring and evaluation mechanisms:** There is a lack of monitoring and evaluation of guideline implementation effectiveness. We recommend establishing monitoring systems to regularly assess implementation effects and make adjustments based on feedback.

4. Conclusion

The included guidelines are of generally high quality, exploring cancer pain management based on evidence-based medicine. All seven guidelines originated from abroad. In recent years, cancer pain management has received widespread attention in China. Through nationwide initiatives such as establishing standardized cancer pain treatment demonstration wards and publishing the "Cancer Pain Diagnosis and Treatment Standards (2018 Edition)," China has made significant progress in cancer pain management. However, substantial gaps remain in evidence-based medicine research and practice. The evidence-based practice guidelines from this study will provide new references for cancer pain management practice in China. Due to differences in national conditions, cultural values, and demographic characteristics between foreign countries and China, we recommend that clinical practitioners consider patients' specific conditions and engage in multidisciplinary cooperation to truly achieve the "5A" goals of cancer pain management: 1A **Analgesia** (optimize analgesia); 2A **Activities** (optimize daily living activities); 3A **Adverse effects** (minimize adverse events); 4A **Aberrant behavior** (monitor aberrant drug use behavior); and 5A **Affect** (optimize the relationship between cancer pain and emotions).

Author Contributions: He Yuling was responsible for data collection, topic selection, and manuscript writing; Huang Wenting and Jiang Liqin were responsible for data collection and statistical processing guidance; Luo Huiyu and Zhu Hongyu were responsible for conceptualizing the paper' s framework and overall accountability; Lin Meiqun was responsible for reviewing and revising the final version.

Conflict of Interest: The authors declare no conflicts of interest.

References: (References section preserved as in original)

Note: Figure translations are in progress. See original paper for figures.