Instruments on symptom clusters in adult patients with hematological malignancies: A scoping review

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Abstract

Background

Patients diagnosed with hematological malignancies usually experience multiple symptoms. Assessment is the key point of symptom management. Therefore, an applicable and feasible instrument is vital.

Methods

A search was performed in these databases: PubMed, CINAHL complete, Web of Science, China HowNet Periodical Databank, WanFang Data. All identified citations were uploaded into EndNote X9 software and duplicates removed. Data extracted from the included studies were mapped. Results were reported in consistent with PRISMA-ScR guidelines.

Results

Of the 410 articles searched through, 58 met the inclusion criteria. A total of 13 instruments of symptom clusters-related hematological malignancy were identified, including seven generic instruments and six specific-disease instruments. Majority instruments did not have theoretical framework. Besides, emotional and cognitive components were absent from several instruments. There was a lack of the large-scale psychometric tests on most instruments.

Conclusions

It is vital to select an available instrument to measure symptom clusters. However, a paucity of the large-scale psychometric tests and theoretical framework create the challenges in choosing amongst the tools available.

1. Background

Cancer greatly menaces mankind’s health, it not only causes heavy burden on human life, but also interferes with prevention and treatment. Hematological malignancies, defined as a highly heterogeneous set of diseases of hemopoietic system, including leukemia, lymphoma, myeloma and so on, account for 1.2 million new cases per year over the world in 2020 [1]. Influenced by environmental exposure, family heredity, abnormal immunological function. The incidence rate of hematological malignancies recently has been rising rapidly. An epidemiological investigation in China reported that there were about 4.4 million newly diagnosed cancer cases in 2019, of which around 200,000 people were diagnosed with hematological malignancies, accounting for 4.5% of all domestic cancer cases [2]. Therefore, a prompt clinical nursing method has become imminent as the disease condition worsened.

Patients diagnosed with hematological malignancies often experience a wide range of symptoms from multiple systems both at the phase of treatment and deterioration [3]. The symptoms can exert adverse synergy effect on physical and psychological health of patients via interaction and catalyzation with each other. According to these symptoms with common characteristics, Dodd first coined “symptom cluster” and defined it as three or more concurrence symptoms related to each other [4]. Furthermore, Kim et al. perfected the definition of symptom cluster [5]. Aktas deemed that the concept of “symptom cluster” should be extended, that was, two signs could also form an aggregate [6]. Enormous clusters have been proposed since the concept of symptom cluster was ascertained. Yang et al. investigated a group of 130 patients with acute myeloma leukemia (AML) who were treated with induction remission therapy and clustered four colonies, namely psychological cluster, nutritional cluster, neurological cluster and pain-sweating cluster [7], and Baggot et al. refined three clusters (chemotherapy sequelae, emotional distress and neuropsychological cluster) from children with acute leukemia [8]. Due to the stack effect yielded by different symptoms, adults patients with blood tumor are more likely suffering from the worse quality of life [9], which is in line with the argument of the Theory of Unpleasant Symptoms (TOUS) [10].

As far as clinical nursing, there is no doubt that the overall management of the concurrent symptoms advances nursing quality and optimizes the medical resources allocation. The key to determine whether symptom management is carried out smoothly is symptom assessment. As NIH Symptom Science Model (NIH-SSM), proposed by National Institute of Nursing Research (NINR), specified that symptom recognition was the first step of semiology [11]. So important is the assessment for nurses that it has been a vital proposition to conduct. Based on the status quo, an applicable and feasible measure plays a crucial role in nursing evaluation. At present, various measures assessing symptom clusters have been developed. For instance, the MD Anderson Symptom Inventory (MDASI) [12], Memorial Symptom Assessment Scale (MSAS) [13], Edmonton Symptom Assessment Scale (ESAS) [14], Therapy-Related Symptom Checklist for Adults (TRSC) [15], Functional Assessment of Cancer Therapy-Lymphoma Symptom Index-18 (FLymSI-18) [16], etc. Still, vast majority instruments are patients-rated rather than objective, and they are short of a comprehensive understanding of the symptoms experienced
by the blood tumor patients, the clusters and composition naturally are disturbed by instruments. Hence, there is an urgent need for providing the validated and specific-disease tools to measure hematological symptoms to achieve best nursing practice in clinical.

Despite the existence of these tools, little is known about their practicability (e.g., reliability, validity), structure (e.g., number of items, dimensions) and administration (e.g., patient-reported, nurse-reported) in the context of hematological malignancy. The aim of this scoping review is therefore to synthesize the range of tools available to measure symptom clusters that pertain to the hematological malignancy in clinical and academic setting. Given that scoping review can partially deal with the data as well as supplement the evidence-based knowledge that cannot be handled in the systematic review [17], and it is conducive to offer clarity and definition to a research field that is nebulous. Scoping review is chosen due to the variability between the large number of instruments in the literature, as outlined above.

The primary purpose of this review is to integrate exiting symptom assessment instruments associated with leukemia, myeloma and lymphoma, and further to analyze the aims, structure, psychometric testing and applicable populations of these instruments for the sake of providing an available instrument for the following studies on symptom clusters.

2. Methods

2.1 Inclusion and exclusion criteria

Type of Studies

This scoping review concerned on primary research studies, dissertations employing qualitative, quantitative or mixed methods. The present review included studies that illustrated reliability and validity of an instrument and/or administered an instrument in a sample of patients with hematological malignancy.

Type of Participants

Scoping review meeting the following criteria were eligible: (a) adult patients with leukemia / myeloma / lymphoma; (b) measuring symptom clusters related to hematological malignancy; and (c) published in English and Chinese. Exclusion criteria were as follow: study protocols, conference abstracts, duplicated publication and full texts unable to get.

2.2 Search strategy

The search was conducted between January 2023 and March 2023. In keeping with the JBI approach, a three-step search strategy were undertaken, the initial search was limited to two databases: PubMed and CINAHL complete using a combination of MeSH terms and free-text terms: measure, assessment, evaluat*, scale, tool, instrument, questionnaire, leukemia, hematologic malignancies, myeloma, lymphoma, symptom cluster*. Second, a search was performed in all databases: PubMed; CINAHL complete; Web of Science; China HowNet Periodical Databank, WanFang Data. Third, the reference lists were manually searched to find additional studies. All identified citations were uploaded into EndNote X9.

2.3 Study selection and data extraction

Following the search, all identified citations were uploaded into EndNote X9 software and duplicates removed. The citations were assessed independently by two reviewers (C.Y. and Y.J.L.) in three steps: (a) title and abstract screening; (b) full-text review; and (c) extraction in Endnote X9. Studies that appeared to meet the inclusion criteria were retrieved in full. Any discrepancies during the processing were resolved by discussion with project members to reach an agreement. Studies that did not meet the inclusion criteria were excluded and reasons for exclusion were provided in the PRISMA flow diagram. Consistent with the JBI approach for scoping reviews, critical appraisal of included studies was not undertaken.

2.4 Analysis

Data extracted from the included studies were recorded in Excel using a charting table. The following data from each study were separately extracted by the same reviewers: developer, themes of the instrument, aims of the instruments, number of items, number of included studies using the tool, hematological diseases in which the tool has been used. Results were reported in consistent with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping reviews (PRISMA-ScR) guideline [18].

3. Results
3.1 Description of the studies in the review

Our three-stage searching identified 410 papers and 274 proceeded for screening process after all duplicates were removed. Finally, fifty-eight studies were identified, as is shown in Fig. 1. The number of papers over the years showed an overall upward trend from 2005 to 2023, particularly during the period of 2020–2021. The trend of publication is shown in Fig. 2. The selected studies with characteristics are presented in Table 1. All told, 13 measurements were used in the studies that examined the symptom clusters of adults with hematological tumors in different cultures and countries. Studies included data obtained from China (n = 17), USA (n = 14), UK (n = 6), Canada (n = 4), Germany (n = 3), Australia (n = 2), Brazil (n = 2), Denmark (n = 2), Turkey (n = 2) and one paper for the rest of countries. Figure 3 represents the number of publications in different countries.
<table>
<thead>
<tr>
<th>Instrument/Developer (s)</th>
<th>Themes/subscales of the items of the instrument</th>
<th>What the tool measures</th>
<th>Number of the items</th>
<th>Administration</th>
<th>Number of included studies using the tool</th>
<th>Hematological diseases in which the tool has been used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memorial Symptom Assessment Scale (MSAS), Portenoy et al. (1994)</td>
<td>Part 1: Physical symptom subscale Part 2: Psychological symptom subscale Part 3: Global Distress Index</td>
<td>The occurrence, severity and distress of the symptoms in the past one week</td>
<td>32</td>
<td>Patient-reported</td>
<td>13</td>
<td>Acute leukemia; Multiple myeloma; Non-Hodgkin's lymphoma</td>
</tr>
<tr>
<td>MD Anderson Symptom Inventory (MDASI), Cleeland et al. (2000)</td>
<td>Part 1: Core list of symptoms (13 items) Part 2: Symptom interference (6 items)</td>
<td>The severity of 13 common symptoms of cancer in the past 24 hours and the degree of distress on daily life</td>
<td>19</td>
<td>Patient-reported</td>
<td>3</td>
<td>Acute leukemia; Non-Hodgkin's lymphoma; Multiple myeloma</td>
</tr>
<tr>
<td>The Chemotherapy Symptom Assessment Scale (C-SAS), Brown et al. (2001)</td>
<td>Physical Symptom subscale (23 items)</td>
<td>The incidence, severity and distress of symptoms</td>
<td>23</td>
<td>Patient-reported</td>
<td>1</td>
<td>Lymphoma with cytotoxic chemotherapy</td>
</tr>
<tr>
<td>Stem Cell Transplantation Symptom Assessment Scale (SCT-SAS), Jarden et al. (2009)</td>
<td>Part 1: Physical-related symptoms Part 2: Affective-related symptoms Part 3: Cognitive-related symptoms</td>
<td>The symptom (s) that most distressed patients during the past week.</td>
<td>24</td>
<td>Patient-reported</td>
<td>1</td>
<td>Acute/chronic myelogenous leukemia; Acute lymphoblastic leukemia; Aplastic anemia; myelofibrosis; myelodysplasia</td>
</tr>
<tr>
<td>Instrument/Developer (s)</td>
<td>Themes/subscales of the items of the instrument</td>
<td>What the tool measures</td>
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<tr>
<td>Therapy-Related Symptom Checklist for Adults (TRSC), Williams et al. (1997)</td>
<td>Part 1: Physical symptom (23 item) Part 2: Psychological symptom (2 items)</td>
<td>Symptoms and severity of the patient since the last treatment cycle and after.</td>
<td>25</td>
<td>Patient/physician/nurse-reported</td>
<td>1</td>
<td>Cancer patients undergoing chemotherapy, radiation, or combined therapies</td>
</tr>
<tr>
<td>Lymphoma Symptom Assessment Scale for Adults (LSASA), Qiu et al. (2020)</td>
<td>Part 1: Physical symptom burden (32 item) Part 2: Psychological symptom burden (6 items)</td>
<td>The severity, frequency and distress of symptoms from the last treatment to the current admission</td>
<td>38</td>
<td>Patient-reported</td>
<td>2</td>
<td>B-cell lymphoma; Non-Hodgkin's lymphoma</td>
</tr>
<tr>
<td>The Functional Assessment of Cancer Therapy-lymphoma (FACT-Lym), Cellad et al. (2005)</td>
<td>Part 1: FACT-General (27 items): Physical well-being, social/family well-being, emotional well-being, functional well-being Part 2: LymS (15 items): Common lymphoma disease and/or treatment-related symptoms</td>
<td>Quality of life concerns that are relevant to NHL</td>
<td>42</td>
<td>Patient-reported</td>
<td>11</td>
<td>Non-Hodgkin's lymphoma; Relapsed/refractory diffuse Large B-cell lymphoma; Mantle cell lymphoma; Chronic lymphocytic leukemia; Myelofibrosis;</td>
</tr>
</tbody>
</table>
### 3.2 Frequency of utilization of tools

Table 1 shows the characteristics of 13 instruments. Among identified tools, Memorial Symptom Assessment Scale was used most frequently \((n = 13)\), followed by The Functional Assessment of Cancer Therapy-Lymphoma \((n = 11)\), Edmonton Symptom Assessment Scale \((n = 8)\), The Functional Assessment of Cancer Therapy-MM \((n = 7)\), The Myeloma Patient Outcome Scale \((n = 6)\), The MD Anderson Symptom Inventory \((n = 3)\), European Organization for Research and Treatment of Cancer Quality of Life Questionnaire \((n = 3)\), Lymphoma Symptom Assessment Scale \((n = 2)\), Lymphoma Symptom Assessment Scale for Adults \((n = 2)\), and the rest were used in only one study.

### 3.3 Methods of tool development

More than half \((n = 7)\) instruments were generic scales for the evaluation of symptom burden of patient with hematological tumor, and six of thirteen measurements were developed specifically for lymphoma or myeloma patients. In addition, TRSC was employed to investigate the manifestations associated with chemotherapy and radiotherapy, and SCT-SAS focused on a core set of symptoms experienced by patients undergoing allo-HSCT.

We found that the items for inclusion in the most of instruments were generated from interviews with healthcare providers and published papers. MyPOS was a module from the Palliative Care Outcome Scale (POS), extended by myeloma-specific concerns. Moreover, item pool of TRSC was drawn from Eastern Cooperative Oncology Group (ECOG) documents and the clinical experiences of the authors, and the development of the C-SAS item pool took the Worthing Chemotherapy Questionnaire (WCQ) pool as a starting point for item selection. SCT-SAS was modeled on the Cancer Therapy Evaluation Program where common toxicity criteria were used.

### 3.4 Content of symptom clusters assessed in the included instruments

All instruments almost consisted of psychological and physical symptoms, including gastrointestinal reactions (nausea, vomiting, anorexia), pain, dyspnea, sleeping problems, numbness of limbs, fatigue, depression and anxiety. In an attempt to harmonize disease- or condition-specific signs, several special items were designed. FACT-Lym, developed to address the disease-specific QoL issues of NHL, contained lymphoma-specific items-B symptoms (e.g., fever, night sweat, weight gain and pruritus). Also, MyPOS, a disease-specific measure of quality of life and palliative care concerns in multiple myeloma, collected the bone-related items (tingling in hands / feet, poor mobility, etc). One of the most prominent points differentiating from other tools was that MyPOS had the module of healthcare support.

### 3.5 Psychometric properties of the instruments

The psychometric properties of the instruments in adult patients with hematological malignancies were reported from thirteen instruments. Construct validity was reported from three instruments (LSAS, LSASA and MyPOS); content validity only evaluated in two instruments (LSAS and LSASA) with 0.900. Concurrent validity was provided from two instruments (MyPOS and FACT-Lym), the total scores of FACT-Lym were positively associated with physical subscale \((r = 0.62)\) and mental subscale \((r = 0.47)\) of the SF-36 scale. Also, MyPOS total scores were correlated positively with MY20 Disease Symptoms \((r = 0.65)\) and Side Effects of Treatment \((r = 0.74)\). Reliability was mainly expressed in internal consistency reliability with Cronbach's \(\alpha\) coefficients for eight instruments (MSAS, MDASI, C-SAS, TRSC, LSAS, LSASA, FACT-Lym and MyPOS), which both reached to ideal value. Test-retest reliability for MyPOS was reported as 0.840, 0.850 and 0.900 by Hlubocky et al. (2013), Cella et al. (2005) and Ramsenthaler et al. (2017), respectively. Item-total correlations for MyPOS was between 0.250 and 0.660.

### 4. Discussion
We conducted this review to scope the development, psychometric properties, pros and cons of instruments that were used to assess frontline symptom relating to vicious hematological tumors. This review presented the following findings about the instruments that were performed to evaluate the symptoms of blood tumor: (a) a total of 13 instruments were designed to assess symptom clusters; (b) majority instruments were lack of theoretical framework; (c) physical aspects was a major dimension in the symptom assessment scales, but emotional and cognitive aspects were absent from several instruments; (d) most instruments were self-assessment; (e) a lack of all-round psychometric properties of most instruments.

The first question raised from this review was the paucity of theoretical framework for instruments. Retrospectively reviewed the origins and development of the instruments, we found that a large proportion of these instruments were compiled on the basis of other tools or literature to construct item pool. For instance, items of TRSC were mainly obtained from Eastern Cooperative Oncology Group (ECOG) documents [15]; items for inclusion in the lymphoma subscale for LSSA were generated from interviews with healthcare providers and MSAS [13]. Quite many instruments for assessing the symptom clustering can be found, but surprisingly, hardly ever described was theoretical frameworks for these measurements. Despite its recognized importance, the demand for theoretical basis of symptom instruments is still neglected by developers.

Fast as evaluation tools for symptom clusters developed, specific-disease scales, like LSAS, LSASA and MyPOS, have been examined for internal consistency, construct validity, content validity, test-retest reliability and criterion-related validity, which were both confirmed as good. As universal tools, MSAS, MDASI and ESAS are also employed in people with blood tumors. Several specific modules of MSAS and MDASI were further designed, such as FACT-MM. However, for the most tools, either reliability and validity or item discrimination and homogeneity barely were rated. The psychometric testing of these instruments on the population of hematological malignancy also were not extensive. This ambiguity emphasized a main issue that can results in the incorrect application in the studies, such as MSAS, MDASI, and FACT, have multiple derivatives without explanation as to the psychometric traits. The future use of these instruments may require the rigorous investigations on the reliability and validity.

Moreover, some instruments pay more attention to physical problems rather than social function and mental health in the present study. It is undoubtedly vital to make no exception in the physical-psychological-social dimension. With the emergence of biopsychosocial medical mode, it attache great importance to construct a three-dimensional integration in the occurrence and development of diseases. Regarding the psychological-physical-social traits as the core of symptom evaluation are highly needed.

Symptoms experienced by patients varied from person to person. Nakaguchi pointed out that compared with psychological symptoms and support demands, physical symptoms were prone to be discerned by medical staff [19]. Almost identified instruments are self-reported without impersonal indicators in this review. Self-reported outcomes contribute to directly reflect patients’ real experience, the key role of self-reported measures in gaining the subjective negative feelings is also emphasized [20], but subjective outcomes hamper the observation of the subtle physiological changes. Personally speaking, the best way to strengthen the symptoms management is to combine the self-assessment questionnaires with clinical biomarkers and nurse- or clinician-reported measures, establishing a scientific, roundly and effective measurement system.

The severity and distress of symptoms are in dynamic change in the course of treatment. The emergence, deterioration, duration and alleviation of the symptoms are closely associated with the therapies and metabolism. Taking chemotherapy as an example, fatigue, sleep disturbance, nausea and vomiting increased within 48 hours after treatments and reach to peak within 96 hours [21]. According to the trajectory changes of symptoms, assessment nodes and time frame have a major significance in spotting sickness. In agreement with Barsevick’s view, a feasible instrument was able to comprehensively measure the accurate condition, in other words, to capture all discomfarts of patients as soon as possible in the most effective way within an acceptable range [22]. Still, there is an inconsistent use of assessment nodes and setting across studies. For example, Hess et al. collected the FACT-Lym at the beginning of clinic visits prior to any procedures [23], this differed from the assessment node presented in Maziarz et al.’s study, in which FACT-Lym was performed at baseline and months 3, 6, 12 and 18 [24]. Additionally, the time range of MSAS-in the past week-was considered inappropriate for comprehensively grasping the symptoms of patients with hematological tumors during chemotherapy. Furthermore, there is an ambiguity about research site. Ramsenthaler et al. conducted a multi-center cross-sectional study using MyPOS completed either during clinic visit or at home [25], whilst participants were given the options of completing the MyPOS at the time of consent or taking it home in Osborne et al.’s investigation [26]. Given the difference across studies on the time frame and setting, researchers can summarize the trajectory of symptom through longitudinal studies at hospital or home to further revise the application range of the symptom evaluation tools.

The final issue around measurement is the instrument update. As the revolution of clinical procedures, a variety of treatment-related symptoms initially emerge from patients, in this circumstance, items cannot be reflective of the real and accurate symptoms. It is known
that Chimeric Antigen Receptor T-cell (CAR-T) Therapy currently are proved to have a marked therapeutic effect on hematological diseases, but this brand-new therapy is also accompanied with serious complications, mainly neurotoxicity [27] and cytokine release syndrome (CRS) [28] that cause unique manifestations, such as disorientation, hypotension, hypoxemia, etc. Evidently, some earlier versions of symptom scale are not fit for the symptoms correlated with CAR-T treatment. In short, the items for symptom measures must keep up with frontiers.

4.1 Limitations

In this scoping review, some limitations should be considered. First, guide websites were not retrieved, which could result in the incomplete inclusion of symptom assessment tools. Second, some instruments had multiple revised versions applied in the people with blood cancers, this review only included the one with widely utilization and good validity and reliability. In addition, limited to the scoping review, no critical appraisal was conducted, there was no information on the methodology quality of the articles.

5. Conclusion

Several instruments have been compiled to measure symptom cluster of patients with hematological malignancies, it is undeniable that a validated tool with well psychometric properties is instrumental in strengthen nursing management in population with hematological tumor. Of course, there are some weaknesses in these instruments, therefore, the large, multi-center tests on reliability and validity should be further conducted.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Shuyi Ding and Aiyun Jin critically revised the manuscript and supervised the inception process. Yin Cheng was responsible for the literature review, and manuscript writing. Jiali Yan contributed to literature searching. Qiong Cheng and Xiaoyu Zhou were responsible for the literature review. All authors contributed to the article and approved of the submitted version.

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References


Figures
Figure 1

PRISMA flowchart of literature review
Figure 2

The trend of publication from 2005 to 2023

Figure 3

The number of publications in different countries