Risk Factors of Frailty in People with Hematologic Malignancies: A Systematic Review and Meta-Analysis

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Abstract: Due to the burden of diseases and adverse reactions to treatment, people with hematologic malignancies usually experience frailty. This study determined the risk factors associated with frailty in people with hematologic malignancies. A thorough examination of the literature was conducted across nine databases following the PRISMA guidelines, including PubMed, Web of Science Core Collection, Embase, CINAHL, CNKI, Wanfang Data, CBM, VIP Database, and SinoMed, covering the period from 2001 to July 26, 2024. The Newcastle-Ottawa Scale was used to assess the quality of the included studies, in conjunction with evaluation tools from the Agency for Healthcare Research and Quality.

The analysis included 23 studies, encompassing 13,849 participants. A high prevalence of frailty was observed in this study, affecting 27.1% of the participants involved. Several risk factors for frailty were identified, including demographic traits (gender, age), clinical features (hand grip strength, physical activity, comorbidities, advanced disease stages, neurological symptoms), biochemical markers (albumin levels, interleukin-6), and mental state (anaemia, depressive symptoms). Our analysis suggests that frailty is common among people with hematologic malignancies. Nurses should pay attention to individuals who exhibit the above-mentioned influencing factors in clinical practice, prevent the occurrence and progression of frailty, and engage in multidisciplinary collaboration and multi-targeted interventions to better manage individuals with frailty.

Keywords: Frailty, Hematologic malignancies, Meta-analysis, Prevalence, Risk factors, Systematic review

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Introduction

Hematological malignancies are highly aggressive and require complex treatment approaches, often resulting in a poor prognosis. These treatments could cause serious complications such as myelosuppression and graft-versus-host disease due to the impaired efficacy of immune and hematopoietic functions. A biological syndrome of increasing concern is frailty. Frailty is characterized by reduced systemic reserves

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and lowered threshold to tolerate stressors, significantly increasing vulnerability to adverse outcomes.[1] These outcomes include prolonged hospitalizations, decreased mobility, incidence of disabilities, increased mortality rate, and adverse medication reactions.[2] Current epidemiological data indicate that frailty affects 18%-64% of people with hematological malignancies,[3,4] which makes the identification of risk factors difficult and often yields inconsistent and sometimes contradictory results.

Several studies have underscored the association between frailty and adverse health outcomes.[5-6] However, recognizing the risk factors associated with frailty in people with hematologic malignancies is essential for the early identification of those at increased risk and for developing targeted intervention strategies. Despite the importance of this issue, there has been a lack of comprehensive studies addressing these risk factors. In clinical practice, nurses should pay attention to frailty indicators, incorporate them into routine nursing work, evaluate and monitor the high-risk population of frailty in a timely manner, and formulate precise interventions to improve frailty.

Literature Review

People with hematological malignancies bear a significant burden of illness. Frailty is recognized as a significant negative prognostic factor.[7] Hematological malignancies are often experienced with various adverse health outcomes linked to frailty, including an elevated risk of falls, increased susceptibility to infections, a greater likelihood of myelosuppression, disruption in the execution of the initial treatment plan, a reduced overall survival duration, and higher all-cause mortality rates.[2] Identifying modifiable risk factors is crucial for preventing and managing frailty early, and plays a vital role in enhancing outcomes and facilitating precision care.

Previous studies have indicated that the influencing factors of frailty include comorbidities, chemotherapy, anxiety, social support, etc.,[3] which have certain guiding significance. However, there are key limitations, including a limited sample size and regional variations. More seriously, some research results are controversial, for example, while Atakul et al.[8] highlighted gender as a potential risk factor, Arora et al.[9] disputed its association with frailty. The possible reason is that the two used different assessment tools for evaluating frailty, which affects the comparability of the research results.

Meanwhile, most studies focus on the relationship between frailty and adverse outcomes, including mortality rate, chemotherapy toxicity, and hospitalization.[5-6] This is important, but there is a lack of comprehensive, systematic and high-quality integrated evidence on the risk factors themselves. The existing studies are mostly single-center, small-sample, and highly heterogeneous observational studies, which cannot provide reliable conclusions regarding the intensity, consistency and relative importance of the risk factors.

This study was specifically designed to address these critical evidence gaps. By conducting a comprehensive and unbiased literature search and employing standardized tools to assess the risk of bias within included studies, our methodology ensures a robust synthesis of existing evidence. Crucially, this systematic review and meta-analysis will provide quantitative estimates of risk factor effect sizes, including confidence intervals (CIs) and systematically explore potential sources of heterogeneity. Distinct frailty models employ divergent conceptual frameworks and assessment tools. The phenotypic model, restricted to the physiological domain, yields lower estimates of frailty prevalence and predominantly identifies physiologically oriented risk factors. Conversely, the cumulative deficit model encompasses multidimensional determinants, including physiological, psychological, and social dimensions, resulting in higher detection rates and more comprehensive risk factor profiles. Consequently, this study conducted subgroup analyses stratified by frailty diagnostic criteria.

This work will generate higher-level evidence to inform clinical practice and guideline development more reliably. The findings are anticipated to facilitate the selection of appropriate frailty assessment tools and the development of validated risk prediction models. Furthermore, the result will guide clinical nursing decisions and resource allocation, while identifying potential modifiable intervention targets to underpin the formulation of effective prevention and early detection strategies for frailty.

Study Aim and Research Question

This systematic review and meta-analysis aimed to assess the risk factors associated with frailty in people with hematologic malignancies. The research question was "*What are the risk factors associated with frailty in people with hematologic malignancies?*"

Methods

Design: To ensure the correct execution of this meta-analysis, it adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Under the identifier CRD 42024566837, the study protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO).

Selection criteria: Inclusion criteria: 1) people with clinically confirmed hematologic malignancies such as leukemia, multiple myeloma, lymphoma; 2) clearly defined diagnostic criteria for frailty; 3) research identifying risk factors for frailty within this population; and 4) observational studies, including cross-sectional studies and prospective/retrospective cohort studies. Exclusion criteria encompassed: 1) studies with incomplete datasets; 2) the language of the publication was other than English or Chinese; 3) commentaries, conference abstracts, case reports, narrative reviews, and 4) duplicated studies retrieved from different databases.

Data sources and search strategy: A comprehensive search was performed on July 26, 2024 across several databases including International databases (PubMed, Web of Science Core Collection, Embase, the CINAHL), Chinese databases (the CNKI, Wanfang Data, CBM, VIP Database, and SinoMed) and supplementary sources (gray literature was screened via clinical trial registries, citation tracking) from 2001 to July 26, 2024. We employed the search strategies combining MeSH terms and free words: Neoplasms, Neoplasm, neoplas,* neoplas,* tumor*, malignanc,* carcinoma, oncology, CA; frailty, frail,* debilit,* weakness; risk factors, influence factor,* influencing factor,* impact factor,* contributing factor,* dangerous factor,* risk factor,* relevant factor,* relative factor,* correlative factor,* associated factor,* predictive factor.* Corresponding terms in Chinese were utilized for searches in Chinese databases. Additional studies were identified by reviewing references from retrieved articles (**Appendix, Table A1**).

Study selection: To eliminate duplication in the Endnote X9, two reviewers (The first author and the second author) separately checked each study's title and abstract for eligibility. Then, the full texts were read and further screened to determine if they report the relevant data of the research results. A third reviewer was appointed to resolve any conflicts (the second corresponding author).

Data extraction: The following information was extracted by two researchers working independently: author, publication year, country of study, participant demographics, study design, sample size, age range, frailty assessment tools used, prevalence of frailty, and risk factors associated with it. A standardized data extraction form was developed to collect the above information (see **Appendix, Table A2**). Consensus discussions were held to address discrepancies, facilitate an initial reconciliation attempt between the two reviewers, and adjudicate unresolved items by a third reviewer (the co-first author).

Quality assessment: Two independent reviewers evaluated study quality using the Agency for Healthcare Research and Quality (AHRQ) tool for cross-sectional studies and the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies.[10,11] The AHRQ tool comprises 11 criteria designed to evaluate the overall quality of a study, classifying them into three categories: low (0-3), moderate (4-7), and high quality (8-11). The NOS employs a nine-point scale, with studies scoring 0-4 classified as having low quality and those scoring 5-9 as having high quality. For example, Smeland et al.[12] (AHRQ): 9/11 (Unreported: confounding control, missing data handling). Eissa et al.[13] (NOS): 6/9 (Selection: 4; Comparability: 0; Outcome: 2). Discrepancies were resolved through consensus.

Data analysis: Data concerning the prevalence and primary outcome were collated using Microsoft Excel and analyzed using Stata software, version 18.0. Frailty prevalence proportions were extracted from all studies to calculate the pooled estimate. This pooled frailty prevalence (95%CI) was derived using a random-effects model if $I^2 > 50\%$; otherwise, a fixed-effects model was applied.[14] Odds ratios (ORs) with 95%CIs quantified risk factors, with statistical significance ($p < 0.05$) assessed via Z-test.

Subgroup analyses and meta-regression were performed to explore heterogeneity sources due to disease type (hematopoietic stem cell transplantation, lymphoma, leukemia and hematologic malignancies), geographic region (North America, Asia and Europe), study design (cross-sectional study, retrospective cohort study and case-control study), diagnosed criteria (Fried Frailty Phenotypic vs. Other assessments). Sensitivity analyses alternated between fixed and random effects models to ensure the robustness of the meta-analytic results. We employed funnel plot visualization and Egger's statistical test to evaluate publication bias.

Results

Search results

A comprehensive search yielded 13,818 articles from various databases, including PubMed (n = 3650), Embase (n = 1921), Web of Sciences Core Collection (n = 4572), CINAHL (n = 3448), CNKI (n = 84), Wanfang (n = 62), VIP (n = 42), and SinoMed (n = 39), supplemented by an additional article from gray literature sources. After deduplication, 8,767 articles underwent title and abstract screening, from which 53 were deemed relevant. Subsequent full-text assessments refined this to 23 studies that satisfied the meta-analysis inclusion criteria. Systematic literature screening is schematically represented in the PRISMA-compliant flow diagram (**Figure 1**).

Characteristics of the included studies

The meta-analysis comprised 23 studies involving 13,849 participants, spanning the period from 2007 to 2024. The studies comprised nineteen cross-sectional,[8,12,16-31] three retrospective cohort,[9,13,32] and one case-control study.[33] The investigations covered various conditions, with seven studies on lymphoma,[12,15,20,28-31] three on acute lymphoblastic leukemia,[16-17,32] two on multiple myeloma,[25,33] and five on hematopoietic cells or bone marrow transplantation.[9,13,21-22,26] The investigations covered various methodological qualities (risk of bias) assessed by standardized tools (NOS and AHRQ), with six high quality,[9,13,17-18,22-23,30] 17 medium quality.[8,13,15,16,19-21,24-29,31-33] The age range of participants varied from 5.3 to 79.2 years. Eight studies employed the Fried frailty phenotype,[9,13,16-17,21-22,24,26] with frailty prevalence ranging from 7.1% to 71.8% **(Appendix, Table A2).**

Prevalence of frailty in hematologic malignancies

Nineteen studies reported frailty prevalence, calculating a combined prevalence of 27.1% (95%CI = 0.204-0.344). Notable heterogeneity was present ($I^2 = 98.113\%$, $p < 0.001$) **(Figure 2).**

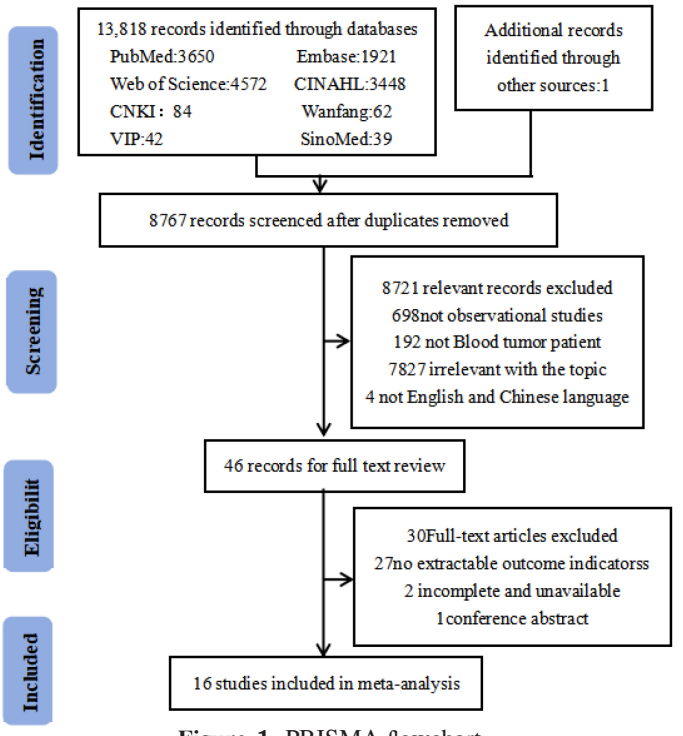

Figure 1. PRISMA flowchart

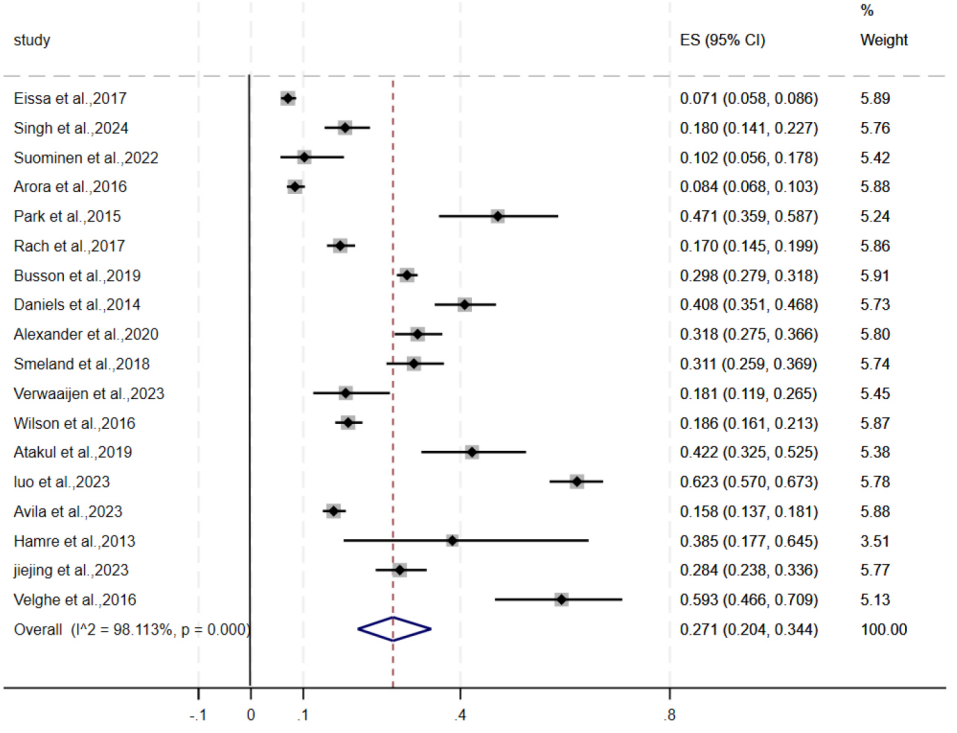

Figure 2. Forest plots of the effects of frailty on hematologic malignancies

Subgroup analyses and meta-regression analysis

Subgroup analysis was conducted to explore heterogeneity between studies (**Table 1**). Studies with different disease types, geographic regions, study designs, and diagnostic criteria were grouped and analyzed separately. Although subgroup analyses failed to substantially reduce heterogeneity, lymphoma consistently demonstrated higher frailty prevalence (31.8%, 95%CI = 24.7-39.3%) than other disease types. Regional analyses revealed substantial variation in frailty prevalence: Asia reported 44.9% (26.7-63.8%) and Europe 30.6% (24.2-37.5%), though both exhibited significant heterogeneity. North America demonstrated notably lower prevalence (13.7%, 95%CI = 9.5-18.5%) than other regions, despite considerable heterogeneity. Furthermore, studies employing the Fried Frailty Phenotype reported lower frailty prevalence (14.8%, 95%CI = 9.4-21.3%) compared to alternative assessment instruments (36.5%, 95%CI = 20.4-45.8%).

Table 1. Summary of meta-analysis for the prevalence of frailty

Subgroup	Studies (n)	Sample size	I^2 (%)	OR (95%CI)	p-value
Disease type					
Hematopoietic cell transplantation	4	2614	89.43	10.4% (6.6-14.8)	< 0.0 V01
Lymphoma	6	3780	94.44	31.8% (24.7-39.3)	< 0.001
Leukemia	2	967	-	18.4% (16-20.9)	-
Hematologic malignancies	6	1798	98.3	40.2% (21.1-61)	< 0.001
Geographic region					
Asia	4	829	96.3	44.9% (26.7-63.8)	< 0.001
Europe	8	3234	89.7	30.6% (24.2-37.5)	< 0.001
North America	6	5186	95.5	13.7% (9.5-18.5)	< 0.001
Study design					
Cross-sectional study	16	7033	96.7	30.2% (23.9-36.9)	< 0.001
Retrospective cohort study	2	1084	-	7.7% (6.6-8.8)	-
Diagnosed criteria					
Fried Frailty Phenotypic	7	3908	95.9	14.8% (9.4-21.3)	< 0.001
Other assessments	11	5341	97.4	36.5% (20.4-45.8)	< 0.001

Univariate and multivariate meta-regression analyses were used to evaluate the associations between frailty prevalence and key study characteristics, including disease type, geographic region, study design, and diagnostic criteria. In the multivariate meta-regression model, frailty diagnosis criteria (β = 0.11, 95%CI = 0.00-0.22, p = 0.049) and geographic region (β=-0.12, 95%CI = -0.19--0.15, p = 0.002) were related to the prevalence of frailty, yielding a model that explained 80.61% of the variance between studies. The remaining factors were not significantly associated with the prevalence of frailty.

Associations between frailty and hematologic malignancy

In the fixed-effects model, the pooled estimate showed that frailty risk was significantly elevated in people with hematologic malignancy relative to non-cancer populations (OR = 2.29, 95%CI = 1.25-4.19, p = 0.007), with a low degree of statistical heterogeneity (I^2 = 22.8%, Q = 1.30, p = 0.255).

Sensitivity analysis

Examinations of model stability, alternating between fixed and random effects, verified the consistency of the influential factors—complications,

hand grip strength, activity, gender, albumin, anaemia, depression, age, disease severity (stages 3-4), neurological signs, and interleukin-6. The robustness of these results is illustrated in **Table 2.**

Publication bias

The funnel plot analysis revealed an asymmetric pattern, and the Egger test result (t = 2.17, p = 0.046) indicated potential publication bias **(Figure 3).**

Table 2. Sensitivity analysis in hematologic malignancies

Risk factors	fixed		Random	
	OR	95%CI	OR	95%CI
Complication	2.11	1.66-2.69	3.04	1.49-6.22
Handgrip	0.82	0.78-0.86	0.81	0.68-0.96
Activity	0.99	0.97-1.00	2.04	1.09-3.79
Gender	1.24	1.07-1.42	1.78	1.08-2.94
Albumin	0.93	0.88-0.98	0.93	0.88-0.98
Anxiety	1.33	1.27-1.39	1.37	1.15-1.62
Depression	1.34	1.28-1.40	1.28	1.14-1.44
Age	1.54	1.24-1.92	1.59	1.01-2.50
Disease severity 3-4	1.73	1.43-2.10	1.73	1.43-2.1
Neurological sign	1.52	1.30-1.78	1.29	1.01-1.65
Interleukin-6	2.48	1.58-3.87	1.77	1.03-3.05
Emotion	1.09	1.03-1.15	2.91	0.39-21.85
Hematopoietic cell transplantation	1.43	0.83-2.46	2.29	0.37-14.34
Obesity	5.38	2.16-13.35	252.87	0.03-1997690.97
Education	1.96	1.19-3.22	1.97	0.24-16.18
Hemoglobin	0.99	0.97-1.00	0.61	0.22-1.74
Profession	3.15	1.39-7.14	17.83	0.1-3322.32
Course of disease	0.95	0.91-0.98	1.055	0.786-1.416
Height	0.69	0.46-1.06	0.391	0.074-2.059
Graft-versus-host disease	1.31	1.03-1.68	1.61	0.8-3.24

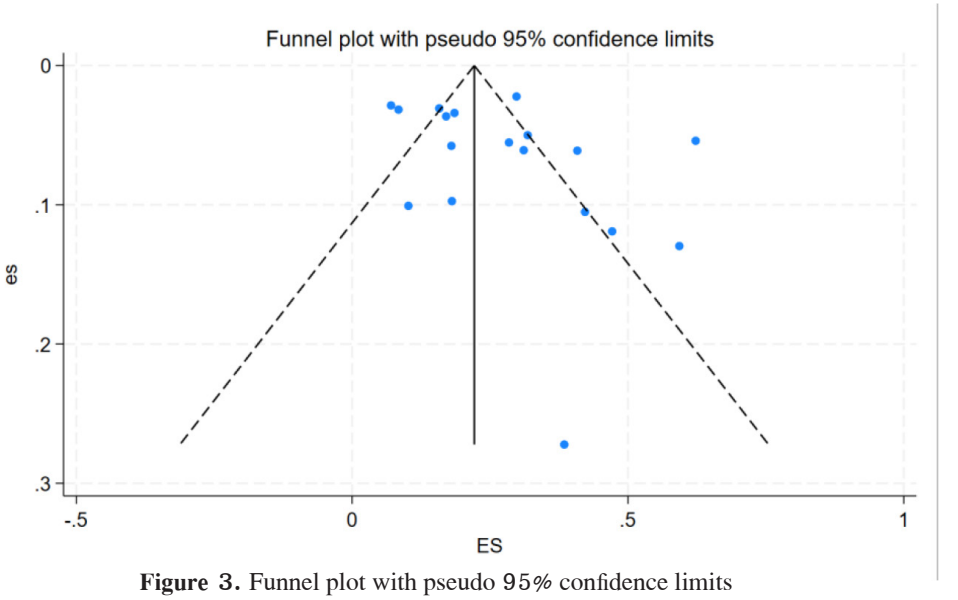

Figure 3. Funnel plot with pseudo 95% confidence limits

Risk factors

The analysis identified eleven risk factors associated with frailty among people with hematologic malignancy: gender, age, hand grip strength, activity, complications, disease severity (stages 3-4), neurological signs, albumin, interleukin-6, anaemia, and depression. The consolidated findings for these risk factors are presented in **Table 3.**

Table 3. Pooled risk factors for frailty in hematologic malignancies

Number	Risk factor	Number of included studies	Pooled effects			Statistical method	Heterogeneity	
			OR	95CI%	p-value		I2	p-value
1	Gender	9	1.78	1.08-2.94	0.024	IV, Random	85.10%	< 0.001
2	Age	3	1.59	1.01-2.50	0.043	IV, Random	61%	0.077
3	Handgrip	3	0.81	0.68-0.96	0.014	IV, Random	80.60%	0.006
4	Activity	5	2.04	1.09-3.79	0.025	IV, Random	96%	< 0.001
5	Complication	4	3.04	1.49-6.22	0.002	IV, Random	81.10%	0.001
6	Disease severity 3-4	2	1.73	1.43-2.10	< 0.001	M-H-Fixed	0.00%	0.574
7	Neurological sign	3	1.83	1.29-2.60	0.001	IV, Random	76.80%	0.013
8	Albumin	2	0.93	0.88-0.98	0.005	M-H-Fixed	0.00%	0.551
9	Interleukin-6	3	1.71	1.06-2.75	0.027	M-H-Fixed	42.30%	0.177
10	Anxiety	4	1.37	1.15-1.62	< 0.001	IV, Random	75.90%	0.006
11	Depression	6	1.43	1.19-1.72	< 0.001	IV, Random	77.80%	0.004
12	Social support	4	1.23	0.56-2.67	0.608	IV, Random	88.80%	< 0.001
13	Emotion	2	2.91	0.39-21.85	0.299	IV, Random	97.20%	< 0.001
14	Hematopoietic cell transplantation	2	2.29	0.37-14.34	0.377	IV, Random	87%	0.006
15	Obesity	2	252.87	0.03-1,997,690.97	0.227	IV, Random	95.40%	< 0.001
16	Education	3	1.97	0.24-16.18	0.527	IV, Random	84.90%	0.001
17	Hemoglobin	2	0.61	0.22-1.74	0.360	IV, Random	88.40%	0.003
18	Multiple myeloma	2	0.36	0.00-127.12	0.734	IV, Random	90.90%	< 0.001
19	Profession	2	17.83	0.1-3,322.32	0.280	IV, Random	62.30%	0.103
20	Smoke	2	1.94	0.79-4.73	0.147	IV, Random	84.70%	0.011
21	Course of disease	3	1.055	0.786-1.416	0.724	IV, Random	87.80%	< 0.001
22	Height	2	0.391	0.074-2.059	0.268	IV, Random	77.70%	95.60%
23	Graft-versus-host disease	2	1.61	0.8-3.24	0.18	IV, Random	59.70%	0.115

Discussion

Through a thorough analysis, we found that there is a high incidence of frailty among people with hematologic malignancies. Our analysis further suggested that this high frailty incidence is closely related to 11 risk factors, i.e., gender, age, hand grip strength, activity, complications, disease severity, neurological signs, albumin level, interleukin-6 expression, anaemia, and depression.

Overall prevalence and comparison with other populations

Firstly, we analyzed the data from 13,849 participants, derived from 23 studies, and found that the aggregate prevalence of frailty was approximately 27.1%. This is very close to the 27% frailty incidence

recorded in people with general tumors.[34] The elevated prevalence in people with hematologic malignancy may be attributed to cytokine dysregulation, which is one of the significant advent effects of cancer treatment. As is known, a high level of cytokine expression is negatively related to central nervous system symptoms, such as IL-6 and TNF-α.[35]

Subgroup and meta-regression

After analysing the overall incidence, we further investigated the frailty incidence in different disease types, geographic regions, study designs and diagnostic criteria. As shown in **Table 1**, we found that different types of malignancies indeed exhibited very different incidence rates, with lymphoma recording the highest incidence at 31.8%, and hematopoietic stem cell transplantation demonstrating the lowest frequency at 10.4%. The high incidence of frailty in lymphoma is likely linked to the disease's characteristic distribution of lymph nodes throughout the body, especially when it invades the central nervous system and bone marrow. Moreover, chemotherapy's toxic effects and the recurrence of the disease also amplify the risks of frailty in lymphoma. Subgroup analysis and meta-regression revealed that diversity in geographic region and diagnostic criteria could account for the wide range of frailty prevalence in the literature and the heterogeneity between studies. On the one hand, this may stem from ethnic differences, dietary patterns, and exercise regimens. On the other hand, it could reflect varying diagnostic accuracy across assessment tools. These findings highlight the critical need for diligent frailty assessment and prevention in people with hematologic malignancy, particularly those with lymphoma. Current recommendations emphasize aligning frailty instruments with study objectives, advocating combined or sequential implementation for optimal assessment in hematologic malignancies.

Key risk factors, and biological and psychosocial mechanisms

Then, individual influence factors associated with frailty prevalence were analysed. Gender analysis showed that frailty was more common in women than men with hematologic malignancies (OR = 1.78, 95%CI = 1.08-2.94), which was consistent with previous studies. Women exhibit reduced lean body mass and diminished muscular strength, resulting in lower muscle mass compared to men and an increased risk of frailty. Additionally, frailty was notably more prevalent in older individuals (OR = 1.59, 95%CI = 1.01-2.50), similar to findings from some previous research.[34] Previous studies systematically illustrate the relationship between frailty, old age and inflammation biomarkers consisting of CXCL10 (C-X-C motif chemokine ligand 10), IL-6 (interleukin 6), CX3CL1 (C-X3-C motif chemokine ligand 1), and found that older people tended to develop frailty than their younger counterparts, and generally recorded high levels of these cytokins.[35] In clinical practice, nurses should perform dynamic frailty assessments for older adults and females, implement personalized exercise plans such as chair-stand exercises with elastic band resistance training, administer targeted nutrition support, such as 30 g whey protein in divided doses daily for older adults. Additionally, nurses should coordinate interdisciplinary frailty management pathways: pre-treatment, collaborate with physicians/nutritionists on care planning; during treatment, conduct serial frailty screenings and monitoring; post-treatment, supervise execution of rehabilitation exercise protocols.

Hand grip strength is recognized as a contributing factor to frailty in individuals with hematologic malignancies. The close relationship between frailty and hand grip strength stems from the direct association of frailty with the deterioration of skeletal muscle metabolic quality. Frailty can contribute to the attenuation and loss of skeletal muscle components, leading to sarcopenia development. Our research aligns with previous studies, showing that decreased activity levels correlate with heightened frailty in people with hematologic malignancies (OR = 2.04, 95%CI = 1.09-3.79), similar to findings that associate sedentary lifestyles with increased frailty risk (OR = 2.26,

95%CI = 1.57–3.27).[36] Variables such as hand grip strength, sarcopenia, and mobility may independently or interactively influence frailty, while some variables may act as intermediate factors affecting frailty, necessitating further investigation. In the further, researchers should explore the pathogenesis of frailty and the biological markers of muscle mass. Medical staff can develop comprehensive exercise rehabilitation programs for people with hematological tumors. Following the principles of safety, staged progression, and symptom adaptation, they can use low-intensity aerobic exercises, progressive resistance training, and functional training to improve frailty, enhance their quality of life, and reduce the risk of complications.

We also found that frailty in people with hematologic malignancies occurs more frequently in populations with multiple complications, aligning with earlier studies.[37] This is because the simultaneous presence of various chronic conditions potentially synergistically degrades immune function, compromises the body's homeostatic capabilities, reduces resilience to external pressures, and expedites the development of frailty. Moreover, people who are both frail and have additional complications are likely to encounter unfavorable risk-benefit ratios concerning pharmaceutical treatments, suggesting potential adverse effects of polypharmacy.[38] Therefore, it is recommended to adopt a multidisciplinary collaborative diagnosis and treatment model for comprehensive management.

This study further discovered that enhanced frailty is related to progressed disease stages, particularly stages III and IV. Such individuals are significantly weakened, with disrupted homeostasis and diminished resistance to external challenges. Additionally, neurological symptoms, notably pain, are distinctly linked with frailty. The presence of neuropathic traits can induce central sensitization and may be associated with nociplastic processes.[39] Nurses should implement specialized nutritional support to augment physiological resilience against stressors. For those reporting elevated pain scores, non-pharmacological intervention—including attentional diversion techniques and evidence-based music therapy—should be prioritized. When pharmacological management is clinically indicated, nurses must administer analgesics in strict accordance with physician prescriptions aligned with the WHO's three-step analgesic ladder framework. Continuous reassessment of analgesic efficacy through validated pain scales is essential for therapeutic optimization.

A substantial correlation exists between frailty and the levels of albumin (ALB) and interleukin-6 (OR = 0.93, 95%CI = 0.88–0.93 and OR =1.71, 95%CI = 1.06–2.75, respectively), which are key indicators of the nutritional status of people. Both serum ALB and hemoglobin levels show inverse associations with frailty and sarcopenia. Albumin has been investigated as a potential biomarker for frailty in other studies.[35] People with hematologic malignancies typically endure prolonged chronic inflammation, which heightens capillary permeability and accelerates serum ALB loss, increasing frailty risk. Interleukin-6 is particularly linked with sarcopenia and frailty in those over the age of 75. Currently, whether other inflammatory cytokines are associated with frailty in individuals with hematologic tumors remains to be further explored. These insights highlight the imperative for healthcare providers to closely monitor and address the nutritional and inflammatory statuses of people with hematologic malignancies to avert frailty at an early stage.

The occurrence of hematologic malignancies is elevated in groups experiencing anemia and depression. The reciprocal relationship between frailty and depression is grounded in shared risk factors and underlying pathophysiological mechanisms, such as chronic inflammation and dysregulation of the hypothalamic-pituitary-adrenal axis.[40] Healthcare providers should prioritize psychological support for people with hematologic malignancies, ensuring effective communication and guidance, fostering social involvement, and reinforcing family connections.

The aforementioned factors lay the foundation for the investigation of the mechanisms of frailty and

the correlations between frailty and other variables. Researchers should conduct further verification and exploration based on diverse research objectives. Additionally, the predictive factors in the study design are of paramount importance for ensuring the predictive validity of a predictive model research. These objective factors mentioned above can serve as excellent references. However, further exploration is needed to determine whether the influence of these factors on frailty varies over time in different disease stages and populations.

Strength and Limitations

This study showcases several strengths; it can be used to serve as the pioneering global meta-analysis to evaluate both the prevalence and risk factors associated with frailty in people with hematologic malignancy. The approach was methodologically sound, adhering to PRISMA guidelines and effectively synthesizing data concerning prevalence and risk factors. The results demonstrated considerable reliability. Nevertheless, the study faced certain limitations. Primarily, there was notable heterogeneity in the reported prevalence of frailty. Despite conducting subgroup analyses, the origins of this heterogeneity could not be definitively ascertained. Additionally, there is a potential for publication bias, likely owing to the exclusion of non-Chinese and non-English studies, which further increases the selection bias, necessitating the inclusion of more high-quality studies to solidify these conclusions.

Conclusion and Implications for Nursing Practice

This study established that the prevalence of frailty in people with hematologic malignancies stands at 27.1%. Influential factors contributing to heightened frailty risk include demographic traits, clinical features, biochemical markers, mental state. To prevent the advancement of frailty, medical personnel must quickly identify and screen individuals at high risk, advising on risk reduction strategies, with special attention to the elderly and female patients. Promising interventions involve suitable physical activities, managing multiple medications, addressing pain, augmenting nutritional support, and providing psychological support to prevent or reduce further degradation. Future investigations should develop appropriate frailty assessment tools and validated risk prediction models. In clinical practice, nurses should timely evaluate and monitor the high-risk population of frailty, and formulate precise interventions to improve frailty.

Author Contributions

Conceptualization: Y.Z., R.D., H.Y., X.Z.
Writing original draft: Y.Z.
Formal analysis, Y.Z., R.D., Y.D., H.Y.
Method, Software, Visualization: Y.Z., R.D.
Investigation, Data curation, Review and editing: Y.Z, Y.L.

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Appendix

Table A1. Search strategy

Step	Search content
#1	"Neoplasms"[MeSH Terms] OR "Neoplasm"[All Fields] OR "neoplas*"[All Fields] OR "cancer*"[All Fields] OR "tumor*"[All Fields] OR "malignanc*"[All Fields] OR "carcinoma"[All Fields] OR "oncology"[All Fields] OR "CA"[All Fields]
#2	"frailty"[MeSH Terms] OR "frailty"[All Fields] OR "frail*"[All Fields] OR "debilit*"[All Fields] OR "weakness*"[All Fields]
#3	"risk factors"[MeSH Terms] OR "influence factor*"[All Fields] OR "influencing factor*"[All Fields] OR "impact factor*"[All Fields] OR "contributing factor*"[All Fields] OR "dangerous factor*"[All Fields] OR "risk factor*"[All Fields] OR "relevant factor*"[All Fields] OR "relative factor*"[All Fields] OR "correlative factor*"[All Fields] OR "associated factor*"[All Fields] OR "predictive factor*"[All Fields]
#4	#1 AND #2 AND #3

Table A2. Characteristics of the studies included in this meta-analysis

Number	Author, Year	Country	Participant	Study design	Sample size	Age	Frailty tool
1	Eissa et al., 2017	USA	HSCT	Rcs	1218	28.4 ± 5.9	FFP
2	Park et al., 2015	Korea	NHL	C-ss	70	73.5	GFI
3	Verwaaijen et al., 2023	Netherlands	ALL	C-ss	105	5.3	FFP
4	Atakul et al., 2019	Turkey	Hematologic malignancies	C-ss	90	none	EFS
5	Wilson et al., 2016	USA	ALL	C-ss	862	31.3	FFP
6	luo et al., 2023	China	Hematologic malignancies	C-ss	342	50.02±15.07	TFI
7	Avila et al., 2023	USA	Hematologic malignancies	C-ss	1057	79.2	CDP/GS
8	Rach et al., 2017	USA	HL	C-ss	751	none	FACIT-F
9	Singh et al., 2024	USA	pre-HCT	C-ss	300	63	FFP
10	Suominen et al., 2022	Finland	HSCT	C-ss	98male	28.7	FFP
11	Ging et al. 2021	China	MM	C-cs	78	66.27 ± 4.39	TFI
12	Arora et al., 2016	USA	HCT	Rcs	998	42.5	FFP
			Missingat footnote				
13	Smeland et al., 2018	Norway	Lymphoma	C-ss	270	none	CFS
14	Hamre et al., 2013	Norway	ALL and lymphoma	C-ss	232	29.7	CFQ
15	jiejing et al., 2023	China	Hematologic malignancies	C-ss	18	none	FFP
16	lee et al., 2021	Korea	MM	C-ss	728	70.7	none
17	Nora et al., 2024	USA	BMT	C-ss	3346	57	FFP
18	Velghe et al., 2016	Belgium	Hematologic malignancies	C-ss	59	77.3 ± 4.8	G8
19	Busson et al., 2019	France	HL	C-ss	2023	47.8	MFI
20	Daniels et al., 2014	UK	HL	C-ss	267	46	FAS
21	Steur et al., 2019	Netherlands	ALL	R-cs	113	none	MFS
22	Majhail et al., 2007	USA	HL	C-ss	425	44	BMT-SS
23	Alexander et al., 2020	Norway	Lymphoma	C-ss	399	none	FQ

Number	Author, Year	Frailty prevalence	Risk factors	Study quality score
1	Eissa et al., 2017	7.10%	Pulmonary disease; Complication	6
2	Park et al., 2015	47.14%	Multi-agent chemotherapy	7
3	Verwaaijen et al., 2023	17.70%	Weight; maintenance week; appendicular skeletal muscle mass; dominant handgrip strength; Time Up and Go test; physical activity, minutes per day; Gender	6
4	Atakul et al., 2019	42.20%	Gender; MM; employment	6

Number	Author, Year	Frailty prevalence	Risk factors	Study quality score
5	Wilson et al., 2016	18.60%	Growth hormone; smoke; alcohol consumption	8
6	Luo et al., 2023	62.30%	Disease duration of 6-12 months; Disease duration exceeding 12 months; Complication; Prealbumin levels; hemoglobin levels; generalized Anxiety Disorder-7 (GAD-7) scores; Patient Health Questionnaire-9 (PHQ-9) scores; age	9
7	Avila et al., 2023	15.80%	Widow; female widower; gender	6
8	Rach et al., 2017	17%	Emotional distress; pain; physical functioning limitation; female; no employed	4
9	Singh et al., 2024	18%	Older age; AlloHCT; PHQ-9 ≥ 10	4
10	Suominen et al., 2022	10%	Chronic graft-versus-host disease; shorter stature; higher body fat mass; hazardous drinking	8
11	Ging et al., 2021	71.80%	Depression; anxiety; age; social support	6
12	Arora et al., 2016	8.40%	Low annual household; less than college education; grades 3 to 4 chronic health conditions; MM; resolved chronic GvHD; active chronic GvHD; gender; age	8
13	Smeland et al., 2018	31.00%	Neuroticism score; IL-6	9
14	Hamre et al., 2013	28.00%	Interleukin-6	8
15	Jiejing et al., 2023	27.80%	Gender; handgrip; arm circumference; albumin	6
16	Lee et al., 2021	none	Age; CCI; ECOG; LDH	5
17	Nora et al., 2024	none	Lack of exercise; smoking; grade 3-4chronic health conditions; female; anxiety; pre-BMT radiation	5
18	Velghe et al., 2016	59%	Hand grip strength	5
19	Busson et al., 2019	29.80%	Age; female; low education level; not living with partner; obesity; health disorders	6
20	Daniels et al.,2014	41%	Education level; height; course of disease; anxiety; depressed; age; gender; social support; disease duration	6
21	Steur et al.,2019	none	Active	6
22	Majhail et al., 2007	none	Female	7
23	Alexander et al., 2020	32%	Neurological symptoms; obesity; IL-6	6

Note. Object: HSCT = Hematopoietic stem cell transplantation; HCT = Hematopoietic cell transplantation; HL = Hodgkin lymphoma; NHL = non-Hodgkin lymphoma; ALL = Acute lymphoblastic leukemia; MM = Multiple myeloma; MPN = Myeloproliferative neoplasms; BMT = Bone or marrow transplantation; AML = Acute myeloid leukemia. **Study design:** Rcs = Retrospective cohort study; C-ss = Cross-sectional study; C-cs = Case-control study. **Frailty tool:** TFI = Tilburg Frailty Indicator; FFP = Fried Frailty Phenotypic; GFI = Groningen Frailty Index; EFS = Edmonton Frailty Scale; FACIT-F = Functional Assessment of Chronic Illness Therapy-Fatigue scale; mFI = McIsaac frailty index; ACG-F = the Johns Hopkins Adjusted Clinical Groups frailty indicator; CDP = cumulative deficit phenotype; GS = Geriatric screen; CFS = Clinical Frailty Scale; CFQ = Chalder's Fatigue questionnaire; MFI = Multidimensional Fatigue Inventory FAS = Fatigue Assessment Scale; MFS = Multidimensional Fatigue Scale; BMT-SS = Bone Marrow Transplant Survivor Study Questionnaire; FS-C = Fatigue Scale-Child; FS = Frailty Scale; FQ = Fatigue Questionnaire; FA = Frailty algorithm.

ปัจจัยเสี่ยงของภาวะเปราะบางในผู้ป่วยมะเร็งทางโลหิตวิทยา : การทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์อภิมาน

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บทคัดย่อ : เนื่องจากภาระจากโรคและอาการไม่พึงประสงค์จากการรักษา ผู้ป่วยโรคมะเร็งทางโลหิตวิทยาจึงมักเผชิญกับภาวะเปราะบาง การศึกษานี้มีวัตถุประสงค์เพื่อระบุปัจจัยเสี่ยงที่สัมพันธ์กับภาวะเปราะบางในผู้ป่วยกลุ่มโรคมะเร็งทางโลหิตวิทยา โดยทำการทบทวนวรรณกรรมอย่างเป็นระบบตามแนวทางปฏิบัติของ PRISMA จากฐานข้อมูลทั้งหมด 9 แห่ง ได้แก่ PubMed, Web of Science Core Collection, Embase, CINAHL, CNKI, Wanfang Data, CBM, VIP Database และ SinoMed ซึ่งครอบคลุมงานวิจัยตั้งแต่ปี พ.ศ. 2544 ถึงวันที่ 26 กรกฎาคม พ.ศ. 2567 ประเมินคุณภาพของงานวิจัยที่คัดเลือกเข้ามาโดยใช้เครื่องมือประเมินคุณภาพนิวคาสเซิล-ออตตาวา ร่วมกับเครื่องมือประเมินของสำนักงานเพื่อการวิจัยและคุณภาพบริการสุขภาพ

การวิเคราะห์นี้มีจำนวนการศึกษาทั้งหมด 23 ฉบับ ซึ่งมีผู้เข้าร่วมการวิจัยทั้งสิ้น 13,849 ราย ผลการศึกษาพบความชุกของภาวะเปราะบางสูง โดยพบถึงร้อยละ 27.1 โดยพบปัจจัยเสี่ยงของภาวะเปราะบางหลายประการ ได้แก่ ลักษณะทางประชากรศาสตร์ (เพศ อายุ) ลักษณะทางคลินิก (แรงบีบมือ การมีกิจกรรมทางกาย โรคร่วม ระยะของโรคที่ลุกลาม และ อาการทางระบบประสาท) ตัวชี้วัดทางชีวเคมี (ระดับอัลบูมิน อินเตอร์ลิวคิน-6) ภาวะโลหิตจาง และภาวะทางจิตใจ (อาการซึมเศร้า) ผลการวิเคราะห์นี้ชี้ให้เห็นว่า ภาวะเปราะบางเป็นภาวะที่พบได้บ่อยในกลุ่มผู้ป่วยโรคมะเร็งทางโลหิตวิทยา ในการปฏิบัติงานทางคลินิก พยาบาลควรให้ความสำคัญกับผู้ป่วยที่มีปัจจัยเสี่ยงดังกล่าวเพื่อป้องกันการเกิดและอาการเลวลงของภาวะเปราะบาง และควรทำงานร่วมกับทีมสหสาขาวิชาชีพโดยใช้แนวทางการช่วยเหลือที่มุ่งเป้าหลายด้านเพื่อจัดการดูแลผู้ป่วยที่มีภาวะเปราะบางให้ดียิ่งขึ้น

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