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Analysis of latent classes and infuencing factors of frailty in patients with non-Hodgkin's lymphoma during chemotherapy

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Introduction

According to global health statistics, approximately 544,352 new cases of non-Hodgkin lymphoma (NHL) were reported worldwide in 2020. Chemotherapy is the primary treatment method. Although it can significantly improve cure rates, it often leads to frailty due to drug toxicity and immunosuppression, with an incidence rate of 18% to 60%.

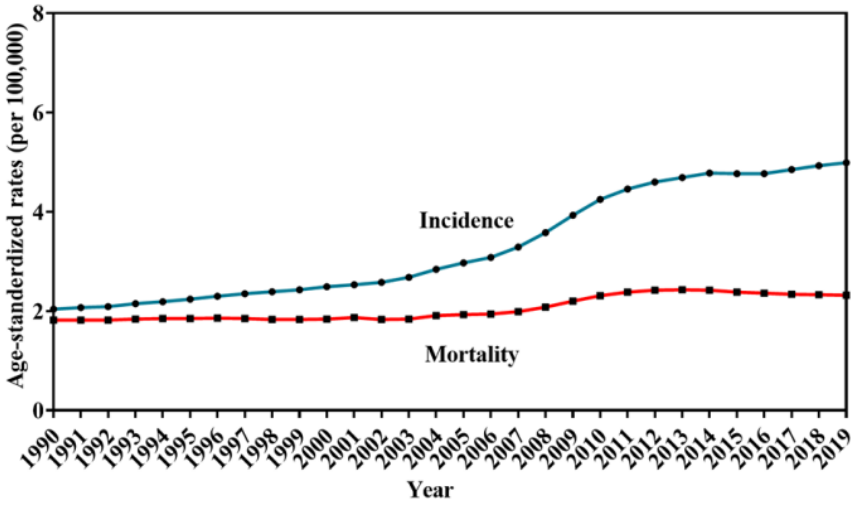

Figure 1. Incidence and mortality rates of NHL in China

Introduction

Frailty refers to a clinical syndrome characterised by a decline in an individual's physiological reserves and resistance, encompassing manifestations such as physical, psychological and social frailty.

Research has found that the rate of chemotherapy discontinuation among patients with NHL who also suffer from frailty is 71.43%, with a mortality rate of 16.8%. Furthermore, frailty symptoms exhibit dynamic changes and significant individual variation.

Aim

To investigate the potential categories and influencing factors of frailty trajectories in NHL patients during chemotherapy, with a view to providing a basis for clinical intervention.

Methods

Study Design

We employed a longitudinal design. Initially, case information, physiological measurements, and questionnaire data were systematically collected from eligible patients across multiple centers in China. The study has been registered in the Chinese Clinical Trial Registry (ChiCTR2500097921).

Methods

Participants and sampling

Inclusion criteria: (1)age of > 18years; (2) confirmed histopathological diagnosis of NHL; (3) treatment with CHOP/R-CHOP chemotherapy regimens; and (4) absence of severe cognitiveimpairment or communication disorders.

Exclusion criteria: (1) previous history of chemotherapy in conjunction with comorbid conditions and (2) history of psychiatric illness or use of psychotropic medications.

Shedding criteria: (1) voluntary withdrawal from the study and (2) chemotherapy-relatedincidents resulting in termination of treatment or death.

Methods

Participants and sampling

Using convenience sampling, the study recruited NHL patients who were admitted to the haematology departments of five public Grade A tertiary hospitals in Henan Province between January and September 2025.

The target sample size was set at a minimum of 250 participants, considering a follow-up loss rate of 20% and meeting the requirement of N ≥ 200 for Bayesian information criterion (BIC) applicability.

Methods

Data Collection

Table 1. Instruments and measurement times

Instrument	before chemotherapy	end of the third cycle of chemotherapy	end of chemotherapy
Sociodemographic questionnaire	√		
Tilburg Frailty Indicator	√	√	√
Montreal Cognitive Assessment-Basic	√	√	√
Short Physical Performance Battery	√	√	√
Chinese Version of the All Aspects of Health Literacy Scale	√	√	√
Generalized Anxiety Disorder Scale	√	√	√
Controlling Nutritional Status Score	√	√	√

Methods

Statistical Analysis

Data were analysed using SPSS 26.0 and Mplus 8.3 software.
Categorical data were described using frequencies and percentages, and comparisons between groups were performed using the χ^2 test; continuous data with a normal distribution were described using means and standard deviations, and comparisons between groups were performed using ANOVA; continuous data with a non-normal distribution were described using medians and quartiles, and comparisons between groups were performed using the Kruskal-Wallis *H* test. Growth mixture model was used to analyse the latent categories of frailty trajectories in NHL patients. Multivariate logistic regression was used to analyse the factors influencing these trajectories.

Results

Characteristics of the Participants

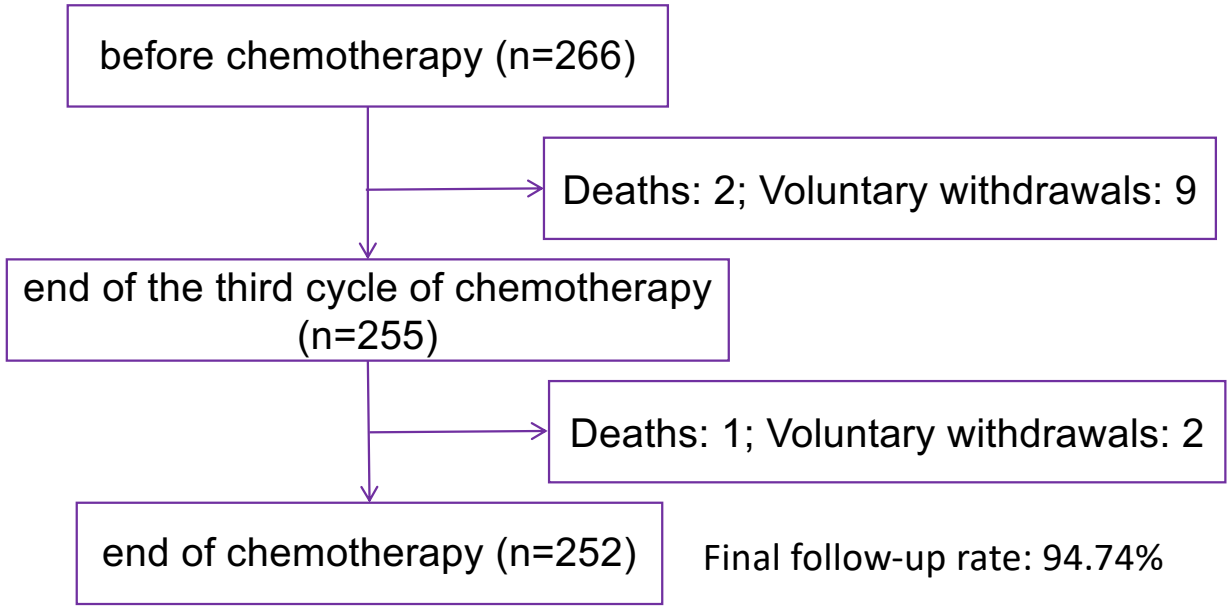

Figure 2. Follow-up Flowchart

Results

Characteristics of the Participants (part)

Table 2. Characteristics of the Participants (part)

Variable	High frailty –slow deterioration (n=30)	Low frailty –stable (n=170)	Low frailty –rapid deterioration (n=14)	Statistic	P-value
Age (years)				χ^2=34.228	<0.001
<60	8 (26.67)	92 (54.12)	6 (42.86)		
60–75	8 (26.67)	65 (38.24)	5 (35.71)		
≥75	14 (46.67)	13 (7.65)	3 (21.43)		
Muscle strength				χ^2=66.298	<0.001
2	1 (3.33)	0	0		
3	3 (10.00)	0	0		
4	17 (56.67)	11 (6.47)	4 (28.57)		
5	9 (30.00)	159 (93.53)	10 (71.43)		
Grip strength(kg)	13.0 (10.0, 16.0)	27.1 (25.5, 28.6)	18.4 (15.0, 21.7)	H=57.846	<0.001
Hemoglobin (g/L)	94.5±20.7	117.7±19.8	101.3±20.9	F=19.966	<0.001
Albumin (g/L)	32.9 (30.8, 35.0)	39.7 (38.9, 40.4)	35.5 (32.0, 39.0)	H=39.584	<0.001
CHLS score	18.7 (17.5, 19.9)	22.3 (21.8, 22.8)	21.4 (19.3, 23.5)	H=30.079	<0.001

Results

Characteristics of the Participants (part)

Continued 2

Variables	Total（n=252）	High frailty-rapid improvement group (n=38)	High frailty-slow deterioration group (n=30)	Low frailty-stable group (n=170)	Low frailty-rapid deterioration group (n=14)	Statistical value	P
BMI	23.14（22.68，23.60）	22.00（20.60，23.40）	21.35（20.18，22.51）	23.83（23.31，24.36）	21.70（19.67，23.72）	20.759[b]	＜0.001
CRP	18.39（14.56，22.23）	19.74（11.80，27.67）	48.59（27.57，69.60）	13.06（9.55，16.58）	14.80（7.32，22.27）	45.040[b]	＜0.001
MoCA-B	27.06（26.51，27.61）	25.74（24.23，27.24）	20.73（19.06，22.40）	28.61（28.16，29.06）	25.36（22.32，28.39）	76.774[b]	＜0.001
SPPB	9.18（8.85，9.52）	7.68（6.86，8.51）	4.73（3.91，5.55）	10.46（10.22，10.70）	7.29（6.43，8.15）	119.329[b]	＜0.001
CONUT	3.46（3.19，3.73）	4.21（3.45，4.97）	5.47（4.64，6.30）	2.86（2.58，3.14）	4.36（3.15，5.57）	44.471[b]	＜0.001
GAD-7	5.31（4.88，5.73）	5.55（4.41，6.69）	9.47（8.05，10.89）	4.51（4.08，4.95）	5.36（3.99，6.73）	41.744[b]	＜0.001

Results

Characteristics of the Participants

Twelve variables differed significantly across the four frailty trajectory groups (all $P < 0.001$):

age, muscle strength, BMI, grip strength, hemoglobin, CRP, albumin,MoCA-B (cognition), SPPB (physical function), CONUT (nutrition),CHLS (health literacy), and GAD-7 (anxiety).

Results

Characteristics of the Participants

The low frailty-stable group consistently had the best profiles (highest hemoglobin, grip strength, SPPB, MoCA-B; lowest CRP, CONUT, GAD-7).

The high frailty-slow deterioration group showed the worst profiles, indicating that persistent frailty is driven by:

- chronic inflammation (high CRP)
- poor nutrition (low albumin, high CONUT)
- functional and cognitive decline
- higher anxiety levels

The other two groups showed intermediate or reversible patterns.

Results

Characteristics of the Participants

Frailty scores (T1–T3):

T1: 4.3 (4.0,4.6) → Frailty rate: 37.30%

T2: 5.2 (4.9,5.5) → Frailty rate: 59.13%

T3: 4.5 (4.2,4.8) → Frailty rate: 46.03%

Results

Potential categories of frailty trajectories

Table 3. Fitting results of latent class models (n = 252)

Classes	AIC	BIC	aBIC	entropy	LMRT（P values）	BLRT（P values）	class probability（%）
1	3277.214	3305.449	3280.088	-	-	-	1.000
2	3231.748	3270.572	3235.700	0.913	0.014	＜0.001	0.151/0.849
3	3222.297	3271.709	3227.327	0.882	0.282	＜0.001	0.075/0.782/0.143
4	**3191.670**	**3251.670**	**3197.778**	**0.878**	**0.045**	**＜0.001**	**0.151/0.120/0.675/0.056**
5	3188.816	3259.404	3196.002	0.838	0.274	0.3750	0.119/0.099/0.643/0.083/0.056

Best model: 4-class solution (BIC smallest, LMRT & BLRT p < 0.05)
Entropy = 0.878

Results

Potential categories of frailty trajectories

Four trajectory classes:

High frailty – rapid improvement (15.08%)

High frailty – slow deterioration (11.90%)

Low frailty – stable (67.46%)

Low frailty – rapid deterioration (5.56%)

Results

Potential categories of frailty trajectories

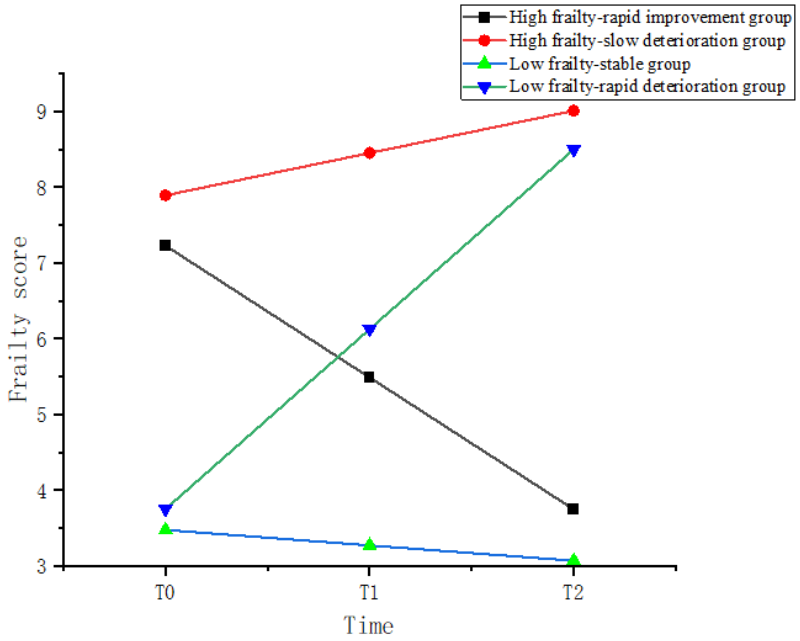

Figure 3. Frailty trajectory chart

Y-axis: Mean frailty score (0–15)

X-axis: T1 (before chemo), T2 (after 3 cycles), T3 (end of chemo)

Lines clearly show four distinct trajectories as listed above.

➔ Significant heterogeneity exists in frailty changes during chemotherapy.

Results

Multivariate logistic regression

- High frailty – rapid improvement group:

  Lower lymphocyte count (OR = 0.838)

  Lower hemoglobin (OR = 0.958)

  Lower SPPB score (OR = 0.427)

- Low frailty – rapid deterioration group:

  Lower SPPB score (OR = 0.380)

Results

Multivariate logistic regression

High frailty – slow deterioration group:

Lower lymphocyte count (OR = 0.744)

Lower hemoglobin (OR = 0.935)

Lower MoCA-B score (OR = 0.694)

Lower SPPB score (OR = 0.273)

Lower monthly income (OR = 42.24–81.66

Note: aThe low frailty-stable group was used as the reference group

Discussion

Four Frailty Trajectories

- Low frailty-stable (67.46%): Maintain good physiological reserve.
  Nursing focus: health promotion, early sign recognition.

- High frailty-rapid improvement (15.08%): Reversible frailty.
  Strengthen nutrition, pain, and psychological support; guide rehabilitation training.

- High frailty-slow deterioration (11.90%): Related to drug toxicity and immunosuppression.
  Monitor nutrition, cognition, physical function; prevent falls.

- Low frailty-rapid deterioration (5.56%): Late-cycle sudden decline.
  Increase symptom assessment frequency; rapid response mechanism.

Discussion

Lymphocyte Count

- Higher lymphocyte count → more likely in low frailty-stable group.
- Lower lymphocyte count → linked to inflammation and poor immune reserve.

➔ Nursing implication: Implement protective isolation, oral/perianal care to prevent infection.

Discussion

Hemoglobin Level

- Higher hemoglobin → more likely in low frailty-stable group.
- Low hemoglobin → tissue hypoxia, impaired energy metabolism.

➔ Nursing implication: Monitor hemoglobin; use RBC transfusion, erythropoietin, iron supplements as needed.

Discussion

Cognitive Function

- Poorer cognitive function (lower MoCA-B) → more likely in high frailty-slow deterioration group.

- Cognitive decline linked to neuroinflammation and muscle atrophy.

➔ Nursing implication: Cognitive training (orientation, memory, executive function); involve caregivers.

Discussion

Physical Function

- Better physical function (higher SPPB score) → more likely in low frailty-stable group.
- Skeletal muscle helps maintain energy and protein reserve during chemotherapy.

➔ Nursing implication: Assess physical function; prescribe moderate aerobic and resistance training.

Discussion

Monthly Household Income

- Lower income → more likely in high frailty-slow deterioration group.

Economic burden limits access to supportive medications and nutrition.

➔ Nursing implication: Provide low-cost nutrition plans; introduce insurance policies and charity support.

Discussion

Classifying the frailty trajectories of NHL patients during chemotherapy can help to implement targeted care measures at key intervention points, thereby delaying or preventing frailty.

Nurses should monitor changes in frailty symptoms among patients with low lymphocyte counts, low haemoglobin levels, low average monthly household income, and impaired cognitive or physical function, and develop targeted intervention measures for them.

Discussion

Limitations

There are few quantitative research indicators of reaction psychology and society. Future research could incorporate relevant variables.

Owing to the limitations of time and labor costs, only patients in central China were investigated, and further multicenter studies with large samples should be carried out.

Conclusion

We identified four frailty trajectories during chemotherapy in NHL patients. The factors influencing these trajectories encompass personal characteristics, psychological and behavioural traits, and social networks.

Medical staff should group and manage patients according to different frailty trajectory types to reduce medical costs.

Thanks!