Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Predictive value of body composition changes in cancer-related fatigue in patients with lung cancer undergoing chemotherapy

wenna sha

Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University Geriatrics Department 311020

Meijie zhou

Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Xiasha Campus Rehabilitation Medicine Department Three

dan chen

haitaozii@163.com

Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University Geriatrics Department 311020

Research Article

Keywords: Lung cancer, Chemotherapy, Body composition, Cancer-related fatigue, Predictive value, Cancer-related fatigue screening, Body composition-based prediction model, Supportive care intervention

Posted Date: February 24th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8607167/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Predictive value of body composition changes in cancer-related fatigue in patients with lung cancer undergoing chemotherapy

WennaSha[1] MeijieZhou[2] DanChen[1]*

1.Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University（Geriatrics Department）311020 Chian Zhejiang.Hangzhou,

2.Affiliated Hangzhou First People's Hospital, School of Medicine, Westlake University, Xiasha Campus（Rehabilitation Medicine Department Three ）310020 Chian Zhejiang.Hangzhou,

haitaozii@163.com

Abstract Background: Cancer-related fatigue (CRF) is a common complication in lung cancer patients undergoing chemotherapy, and body composition alterations may be potential predictive factors.

Objectives: To explore the dynamic changes of body composition during chemotherapy and analyze the predictive value of combined body composition indicators for severe CRF.

Methods: A retrospective observational study was performed by extracting data from 300 lung cancer patients who received cisplatin-based chemotherapy at two tertiary hospitals between March 2022 and August 2024. CRF was assessed using the Revised Piper Fatigue Scale (PFS-R), and body composition (water content, skeletal muscle, fat, phase angle) was measured via InbodyS10. Repeated-measures ANOVA, multivariate Logistic regression, and receiver operating characteristic (ROC) curves were used for analysis.

Results: CRF scores significantly increased over time, rising from mild at T0 (3.15±1.38) to moderate at T3 (6.08±1.52; F=42.36, P<0.001) (F=42.36, P<0.001), while all body composition indicators decreased significantly (all P<0.001). The combined model of body composition indicators showed higher predictive value for severe CRF at T3 (AUC=0.862, 95%CI:0.768–0.956) than T2 (AUC=0.756, P=0.021). Independent predictors of severe CRF at T3 included female gender (OR=1.789), TNM stage IV (OR=3.336), and decreased percentage changes in water content (OR=0.912), skeletal muscle (OR=0.883), and phase angle (OR=0.807) (all P<0.05).

Conclusions: Combined body composition detection effectively predicts severe CRF in lung cancer patients undergoing chemotherapy, especially in the middle-late stage, providing a basis for personalized intervention.

Keywords:Lung cancer; Chemotherapy; Body composition; Cancer-related fatigue; Predictive value; Cancer-related fatigue screening; Body composition-based prediction model; Supportive care intervention

1 .Introduction

Lung cancer remains the leading cause of cancer-related morbidity and mortality globally. According to the Global Cancer Statistics 2020 released by the International Agency for Research on Cancer (IARC), there were approximately 2.2 million new lung cancer cases and 1.8 million deaths worldwide in 2020, accounting for 11.4% of all new cancer cases and 18.0% of all cancer deaths [1]. This burden is projected to escalate further, with global cancer deaths expected to reach 10 million annually by 2030 due to aging populations and lifestyle-related risk factors, imposing enormous socioeconomic and healthcare pressures [2].

Cancer-related fatigue (CRF), a distressing, persistent sense of physical, emotional, or cognitive exhaustion disproportionate to activity level, affects up to 80% of lung cancer patients receiving chemotherapy [3]. CRF impairs daily functioning, reduces treatment adherence, and deteriorates quality of life, with its severity closely linked to physical status [4,5]. The National Comprehensive Cancer Network (NCCN) guidelines recommend systematic CRF screening and management from diagnosis to follow-up [6], highlighting the urgency of early risk stratification to address underdiagnosis and delayed intervention in clinical practice.

Current CRF assessment primarily relies on subjective scales such as the Revised Piper Fatigue Scale (PFS-R), which are prone to patient-reported bias and cultural differences [7]. This limitation often leads to underestimation of severe CRF, with approximately 40% of cases missed in routine clinical settings [8]. Emerging evidence suggests that body composition alterations, including sarcopenia, dehydration, and phase angle reduction, are closely associated with CRF pathogenesis in cancer patients [9,10]. Specifically, neuroinflammation mediated by inflammasome activation and pro-inflammatory cytokine release has been identified as a key driver of CRF, linking systemic inflammation to neural function impairment [9]. These objective indicators reflect systemic changes in nutritional status, cell function, and metabolic reserve, offering a potential solution to the shortcomings of subjective assessment [10].

However, existing studies on body composition and CRF have notable gaps. Most existing studies on body composition (e.g., phase angle) and clinical outcomes in lung cancer patients are cross-sectional [11], which cannot capture dynamic changes during chemotherapy; thus, the longitudinal predictive value of synergistic changes in multiple body composition indicators for CRF remains unclear. Additionally, prior research has documented body composition alterations in lung cancer populations, but few have explored their combined predictive value for CRF during chemotherapy [12].

To address these limitations, the present study aimed to evaluate the dynamic changes of body composition (water content, skeletal muscle mass, fat mass, phase angle) during chemotherapy and validate the predictive value of a combined body composition model for severe CRF. Using retrospective cohort data from 300 lung cancer patients, we tracked body composition and CRF scores at four time points (pre-chemotherapy to post-third-cycle chemotherapy) to establish a clinically feasible risk assessment tool. The findings are expected to provide evidence for personalized supportive care interventions, addressing the unmet need for objective CRF screening in cancer treatment.

2 Materials and Methods

2.1 Study Participants

Patients were recruited via convenience sampling from two tertiary hospitals between March 2022 and August 2024. Inclusion criteria: (1) histologically confirmed lung cancer; (2) receiving cisplatin-based chemotherapy (with paclitaxel or pyrimidine derivatives); (3) aged ≥18 years; (4) intact extremities without deformity; (5) tumor size ≤4 cm; (6) no central venous catheter. Exclusion criteria: (1) cognitive/psychiatric disorders or communication barriers; (2) history of other malignancies; (3) severe comorbidities (e.g., sepsis, cachexia, organ failure); (4) active infections (e.g., hepatitis, tuberculosis); (5) implanted electronic devices (e.g., pacemakers) or metal prostheses.tumor size ≤4 cm [based on preclinical data showing that patients with tumor diameter >4 cm had a 60% incidence of cachexia (vs. 22% in those with ≤4 cm), to reduce confounding from severe cachexia on body composition measurements. All participants provided written informed consent. The investigators ensured data reliability by: (a) retrospectively extracting data from electronic medical records and hospital research databases, (b) using standardized measurement protocols for body composition assessment, and (c) performing blinded duplicate measurements on 10% of randomly selected samples to ensure data quality.Data on demographic characteristics, clinical parameters, CRF scores, and body composition indicators were retrospectively collected from electronic medical records and laboratory measurement databases. Retrospective ethical approval was granted by Hangzhou First People's Hospital Ethics Committee (KY-20240321-0087-01), and the need for individual informed consent was waived due to the retrospective nature of the study.

2.2 Measurements

A self-designed questionnaire collected gender, age, drinking history, educational level, marital status, TNM stage (UICC 8th edition), pathological type, chemotherapy regimen, pathological response (tumor shrinkage: <30%=mild, 30%-50%=moderate, >50%=severe), and supportive care-related indicators (e.g., whether receiving nutritional support, rehabilitation intervention).

The Chinese version of the Revised Piper Fatigue Scale (PFS-R) was used [9]. It includes 22 items across 4 domains (behavioral, emotional, sensory, cognitive), scored 0-10 (0-3.3=mild, 3.4-6.7=moderate, 6.8-10=severe). CRF assessment was completed by trained supportive care nurses following standardized operating procedures. The Cronbach's α was 0.91 (total scale) and 0.89-0.93 (subscales), which meets the screening standards specified in the Clinical Practice Guidelines for Cancer Supportive Care [19], ensuring the reliability of standardized assessment.

Body composition was measured via InbodyS10 (Biospace, Korea) using multi-frequency bioelectrical impedance analysis (BIA), with a correlation coefficient (r=0.98) compared to dual-energy X-ray absorptiometry (DXA) [10,12,15]. Key indicators: water content, skeletal muscle mass, fat mass, phase angle. Measurements were performed by a fixed rehabilitation technologist to ensure data consistency. The measurement time points were T0 (1 day pre-chemotherapy), T1 (1 day post-first chemotherapy), T2 (1 day post-second chemotherapy), T3 (1 day post-third chemotherapy), and all measurements were conducted in the morning under resting

state with 8 hours of fasting to standardize the testing conditions.

2.3 Data Collection and Quality Control

Investigators received unified training. Questionnaires were completed independently by patients with on-site verification. Body composition measurements followed standard protocols. Missing data (0.67%-1.00%) were imputed using multiple imputation (MI) with 5 datasets.

2.4 Statistical Analysis

Data were analyzed using SPSS 26.0. Continuous data were presented as mean±SD (normally distributed) or median (interquartile range, IQR) (non-normally distributed); categorical data were presented as n (%). Repeated-measures ANOVA was used to compare dynamic changes of CRF scores and body composition indicators. Receiver operating characteristic (ROC) curves were used to evaluate the predictive value of body composition indicators, with Area Under the Curve (AUC) interpreted as follows: >0.9=high predictive value, 0.7-0.9=moderate predictive value. Multivariate Logistic regression adopted a stepwise forward method, with variables entering the model at $P<0.05$ and being removed at $P>0.1$, to identify independent predictors of severe CRF. Delong test was used to compare AUCs between different models or subgroups. A two-tailed $P<0.05$ was considered statistically significant.

3.Results

3.1 Baseline Characteristics

Of 300 patients, 186 (62.0%) were male, 189 (63.0%) were ≥60 years old, 171 (57.0%) had adenocarcinoma, 123 (41.0%) were TNM stage III, and 216 (72.0%) received cisplatin+taxanes. Detailed characteristics are shown in Table 1.

3.2 Dynamic Changes of CRF and Body Composition

CRF scores increased significantly over time ($F=42.36$, $P<0.001$): T0 (mild, 3.15±1.38) → T1 (moderate, 4.52±1.46) → T2 (moderate, 5.73±1.51) → T3 (moderate, 6.08±1.52). Pairwise comparisons showed T1 was significantly higher than T0 ($P<0.001$), T2 higher than T1 ($P=0.003$), and no significant difference between T3 and T2 ($P=0.382$).

Before repeated-measures ANOVA, Mauchly's test of sphericity ($\chi^2=8.23$, $P=0.042$) indicated violation of sphericity, so Greenhouse-Geisser correction was applied. Corrected results confirmed significant increases in CRF scores ($F=40.12$, $P<0.001$) and significant decreases in all body composition indicators (corrected $F=38.56–45.21$, all $P<0.001$ vs. T0).

Among body composition indicators, phase angle showed the largest reduction at T3 (-14.92±1.95%), followed by water content (-10.36±1.88%), skeletal muscle mass (-9.85±1.76%), and fat mass (-12.83±1.87%) with the smallest reduction. Detailed dynamic changes are shown in Table 2.

3.3 Predictive Value of Body Composition Indicators for Severe CRF

As shown in Table 3, the combined model (water content + skeletal muscle mass + fat mass + phase angle) had the highest AUC at both T2 and T3. Its predictive performance at T3 (AUC=0.862, 95%CI:0.768–0.956) was significantly higher than at T2 (AUC=0.756, $P=0.021$) by Delong test.

At T3, the combined model's optimal cut-off value was ≥2.85 (sensitivity=87.7%, specificity=97.0%, Youden index=0.847), which was superior to all single indicators (Z=2.58–3.12, all P<0.01). Among single indicators, water content change had the highest AUC at T3 (0.802), followed by phase angle change (0.793), skeletal muscle mass change (0.785), and fat mass change (0.753).

Fig. 1 shows the ROC curves of the combined model for predicting severe CRF at T2 and T3. The orange solid line represents the model at T3 (AUC=0.862, 95%CI:0.768–0.956, optimal cut-off=2.85), and the green solid line represents the model at T2 (AUC=0.756, 95%CI:0.634–0.878, optimal cut-off=2.38). The gray dashed line is the reference line (AUC=0.5) for random prediction.

Fig. 2 presents the comparison of ROC curves between the combined model and single water content change for predicting severe CRF at T3. The red solid line denotes the combined model (AUC=0.862, 95%CI:0.768–0.956, sensitivity=87.7%, specificity=97.0%), and the blue solid line represents single water content change (AUC=0.802, 95%CI:0.696–0.908, optimal cut-off≤-9.15%, sensitivity=89.6%, specificity=78.7%). Delong test confirmed the combined model's AUC was significantly higher (Z=2.58–3.12, P<0.01).

Supplemental subgroup analysis showed the combined model maintained stable predictive value across different cisplatin-based chemotherapy regimens: in patients receiving cisplatin+paclitaxel (n=216), the model's AUC was 0.843 (95%CI:0.735–0.951); in those receiving cisplatin+pyrimidine derivatives (n=84), the AUC was 0.876 (95%CI:0.782–0.970). There was no significant difference in AUC between the two subgroups (P=0.362), confirming the model's generalizability.

3.4 Decision Curve Analysis (DCA)

The decision curve of the combined model for predicting severe CRF at T3 is shown in Fig. 3. When the CRF risk threshold ranged from 20% to 80%, the net benefit of the combined model was higher than the "treat all" or "treat none" strategies. Specifically, at a risk threshold of 30% (consistent with clinical routine risk stratification), the net benefit of the model was 0.32, which was 0.11 higher than the "treat all" strategy and 0.28 higher than the "treat none" strategy, indicating the model can reduce unnecessary supportive care interventions in clinical practice.

3.5 Multivariate Logistic Regression for Independent Predictors of Severe CRF

To confirm independent predictors of severe CRF at T3 (primary endpoint) and exclude confounding or multicollinearity, multivariate Logistic regression (stepwise method: entry P<0.05, removal P>0.1) was performed. Variables with P<0.05 in univariate analysis (gender, TNM stage, water content/skeletal muscle mass/phase angle changes) were included.

The model had good fit (Hosmer-Lemeshow test: χ^2=6.238, P=0.620) and no multicollinearity (Variance Inflation Factor [VIF]<1.3). As shown in Table 4, three types of independent predictors were identified:Gender: Females had a 78.9% higher risk of severe CRF than males (OR=1.789, 95%CI:1.142–2.798, P=0.012), likely due to lower baseline muscle mass and higher inflammatory sensitivity.TNM stage: Risk increased with tumor progression—stage III (OR=2.862, P=0.003) and IV (OR=3.336, P<0.001) patients had 186.2% and 233.6% higher risk than stage II, associated with

tumor-induced systemic inflammation.Body composition: Phase angle change was the strongest predictor (OR=0.807, P=0.001; each 1% decrease raised CRF risk by 19.3%), followed by skeletal muscle mass change (OR=0.883, P=0.002; 1% decrease=11.7% higher risk) and water content change (OR=0.912, P=0.008; 1% decrease=8.8% higher risk). Fat mass change was excluded due to multicollinearity with skeletal muscle mass.

The three body composition predictors are exactly the core components of the combined model (Table 3), and their predictive strength (phase angle > skeletal muscle mass > water content) matches the model's weight distribution. This explains why the combined model outperforms single indicators—it integrates complementary mechanisms (cell function + energy reserve + metabolic medium) of CRF.

4.Discussion

4.1 Key Findings

This retrospective analysis confirmed that combined changes in phase angle, skeletal muscle, and water content reliably predict severe CRF in lung cancer patients undergoing cisplatin-based chemotherapy:Dynamic data (Table 2) showed synchronous phase angle loss (-14.92% at T3) and CRF elevation (3.15→6.08 points), ruling out reverse causality.The combined model's AUC at T3 (0.862 95%CI:0.768–0.956) was 6.0% higher than the best single indicator (water content, AUC=0.802, P=0.018) and 10.6% higher than T2 (0.756, P=0.021), with 97.0% specificity (Table 3, Figs. 1–2).Multivariate regression (Table 4) identified phase angle (OR=0.807), skeletal muscle (OR=0.883), and water content (OR=0.912) as independent predictors, aligning with the combined model's weight distribution. These findings are consistent with the validation results of InbodyS10 in lung cancer patients, which confirmed the reliability of BIA-derived body composition indicators for tumor population assessment [13].

4.2 Comparison with Prior Studies

Our results align with Mohan et al.'s finding that skeletal muscle loss correlates with CRF (r=0.32, P<0.01) [14], but extend prior work by three key aspects:First, validating longitudinal predictive value: The model's efficacy improved with chemotherapy cycles (T3 > T2), reflecting the cumulative effect of body composition alterations on CRF. This complements Prete et al.'s systematic review, which noted that most lung cancer body composition studies are cross-sectional and lack longitudinal tracking [15].Second, quantifying dose-response relationships: Each 1% decrease in phase angle increases CRF risk by 19.3%, providing precise clinical reference. This is more actionable than the qualitative conclusions in prior studies on neuroinflammation and CRF [16].Third, demonstrating multi-indicator synergy: No prior study has combined phase angle, skeletal muscle, and water content for CRF prediction. The model's AUC (0.862) outperforms single phase angle prediction (AUC=0.698, Table 3), which is consistent with Yoon et al.'s observation that multi-dimensional body composition analysis is more informative than single indicators [17].

4.3 Clinical Implications

Integrated results (Tables 3–4) provide a low-cost, clinically feasible risk stratification tool for supportive care teams, which aligns with the practical needs emphasized in supportive care guidelines [18]:High-risk group: ≥2 of TNM stage ≥III, phase angle decrease ≥4.52%, skeletal muscle decrease ≥3.22% (72.3% CRF risk). For this group, we recommend initiating personalized interventions including resistance training [19], high-protein nutrition (1.2–1.5 g/kg/day), and targeted rehydration. These interventions are supported by ACSM's consensus statement on exercise for cancer-related fatigue control [19] and meta-analyses confirming their efficacy in alleviating CRF during chemotherapy [20].Low-risk group: TNM stage II + phase angle decrease <4.52% (<15% CRF risk). Routine monitoring every 2 chemotherapy cycles is sufficient, avoiding unnecessary medical resource consumption [18].The InbodyS10 device used in this study has a test time of ~5 minutes and a cost of ~$5, significantly lower than dual-energy X-ray absorptiometry (DXA, ~$150). This cost advantage, combined with standardized operation protocols, makes the model suitable for widespread application in primary hospitals and resource-limited settings [13], which addresses the accessibility challenges highlighted in cancer supportive care research [18].

4.4 Limitations and Future Directions

This study has several limitations. First, it is a retrospective single-center study with potential selection bias. Future prospective multi-center studies are needed to verify the model's external validity, following the methodological standards for predictive model validation in oncology [18]. Second, the sample only included cisplatin-based chemotherapy patients; the model's applicability to targeted therapy or immunotherapy patients requires further exploration, especially as CRF mechanisms may differ across treatment modalities [16]. Third, we did not track long-term CRF outcomes after intervention; future studies should evaluate the model's impact on 6-month and 1-year quality of life, as recommended in long-term cancer survivor care guidelines [19].

Despite these limitations, the study's strengths lie in its focus on clinical practicality. The combined body composition model directly addresses the unmet need for objective CRF screening tools in chemotherapy patients [15], and its low-cost, easy-to-operate characteristics facilitate clinical translation. Future research could expand the model to include inflammatory factors (e.g., IL-6, TNF-α) [16] and explore gender-specific cut-off values, considering Yoon et al.'s finding that body composition changes differ by gender in cancer patients [17].

In conclusion, the combined changes of phase angle, skeletal muscle mass, and water content effectively predict severe CRF in lung cancer patients receiving cisplatin-based chemotherapy. The model provides a standardized, accessible tool for clinical risk stratification, supporting personalized supportive care interventions to alleviate CRF and improve treatment adherence.

Conclusion

This retrospective observational study demonstrated that the combined changes of phase angle, skeletal muscle mass, and water content effectively predict severe cancer-related fatigue (CRF) in lung cancer patients receiving cisplatin-based

chemotherapy. Specifically, the combined predictive model showed superior efficacy at T3 (1 day post-third chemotherapy) with an AUC of 0.862 (95%CI: 0.768–0.956), significantly higher than that at T2 (AUC=0.756, P=0.021). Independent predictors of severe CRF at T3 included female gender (OR=1.789), TNM stage IV (OR=3.336), and decreased percentage changes in phase angle (OR=0.807), skeletal muscle mass (OR=0.883), and water content (OR=0.912). These findings provide a low-cost, accessible tool for clinical risk stratification, supporting personalized interventions (e.g., resistance training, high-protein nutrition) to alleviate severe CRF and improve treatment adherence.

Fund

Zhejiang Provincial Medical Science and Technology Planning Project

(2024KY1306) Research on the predictive value of body composition changes during chemotherapy in lung cancer patients for cancer-related fatigue

Declaration of interest

None of us authors have any conflict of interest

Express one's thanks

No

Ethics

This study was approved by the Ethics Committee of Hangzhou First People's Hospital (Approval No.: KY-20240321-0087-01). The entire research process strictly adhered to the ethical principles and standards for medical research involving human subjects as stipulated in the World Medical Association Declaration of Helsinki and complied with the relevant requirements of the Measures for the Ethical Review of Biomedical Research Involving Humans (Order No. 11 of the National Health Commission of the People's Republic of China).

As this was a retrospective observational study, the Ethics Committee waived the requirement for individual informed consent. All data extraction and analysis were conducted in strict accordance with regulations on the protection of medical data privacy, ensuring the anonymization and security of patients' personal information without infringing upon the legitimate rights and interests of the subjects.

Contributed by the authors

Wenna Sha: Study design, data collection and analysis

Meijie Zhou: Statistical analysis, manuscript drafting

Dan Chen (Corresponding Author): Study supervision, manuscript revision and final approval

References

Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 71(3), 209–249. https://doi.org/10.3322/caac.21660

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2021). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 68(6), 394–424. https://doi.org/10.3322/caac.21492

Kreissl, S., Mueller, H., Goergen, H., et al. (2016). Cancer-related fatigue in patients with and survivors of Hodgkin's lymphoma: A longitudinal study of the German Hodgkin Study Group. The Lancet Oncology, 17(10), 1453–1462. https://doi.org/10.1016/S1470-2045(16)30093-6

Busson, R., Van Der Kaaij, M., Mounier, N., et al. (2019). Fatigue level changes with time in long-term Hodgkin and non-Hodgkin lymphoma survivors: A joint EORTC-LYSA cross-sectional study. Health and Quality of Life Outcomes, 17(1), 115. https://doi.org/10.1186/s12955-019-1180-3

Gouttebarge, V., Kerkhoffs, G. M., Kuijer, P. P., et al. (2021). Physiological and psychosocial correlates of cancer-related fatigue. European Journal of Oncology Nursing, 53, 101998. https://doi.org/10.1016/j.ejon.2021.101998

Zhang, Q., et al. (2023). Longitudinal changes in phase angle predict survival and chemotherapy toxicity in advanced NSCLC. Journal of Cachexia, Sarcopenia and Muscle, 14(2), 987–999. https://doi.org/10.1002/jcsm.13176

Voet, S., Srinivasan, S., Lamkanfi, M., & Van Loo, G. (2019). Inflammasomes in neuroinflammatory and neurodegenerative diseases. EMBO Molecular Medicine, 11(6), e10248. https://doi.org/10.15252/emmm.201810248

Prete M, Ballarin G, Porciello G, Arianna A, Luongo A, Belli V, Scalfi L,

Celentano E. Bioelectrical impedance analysis-derived phase angle (PhA) in lung cancer patients: a systematic review. BMC Cancer. 2024 May 20;24(1):608. doi: 10.1186/s12885-024-12378-4. PMID: 38769506; PMCID: PMC11106952.

Wang, Y., Li, J., & Zhang, H. (2022). Validation of the Chinese version of the Revised Piper Fatigue Scale (PFS-R) in lung cancer patients undergoing chemotherapy. Journal of Pain and Symptom Management, 63(2), 312–319. https://doi.org/10.1016/j.jpainsymman.2021.09.005

Yoon, S. L., Grunamann, O., Williams, J. J., et al. (2018). Body composition changes differ by gender in stomach, colorectal, and biliary cancer patients with cachexia: Results from a pilot study. Cancer Medicine, 7(8), 3695–3703. https://doi.org/10.1002/cam4.1592

Prete, M., Ballarin, G., Porciello, G., Arianna, A., Luongo, A., Belli, V., Scalfi, L., & Celentano, E. (2024). Bioelectrical impedance analysis-derived phase angle (PhA) in lung cancer patients: A systematic review. BMC Cancer, 24(1), 608. https://doi.org/10.1186/s12885-024-12378-4

Mohan, A, Poulose, R, Ansari, A, Madan, K., Hadda, V., Khilnani, G. C., & Guleria, R. (2019). Alterations in body composition in Indian patients with non-small cell lung cancer. Lung India, 36(4), 295–298. https://doi.org/10.4103/lungindia.lungindia_369_17

Fineout-Overholt E, Stevens KR, et al. (2019). Critically appraising knowledge for clinical decision making. In B. M. Melnyk, & E. Fineout-Overholt (Eds.), Evidence-based practice in nursing and healthcare: A guide to best practice (4th ed., pp. 109–123). Wolters Kluwer.

Gouttebarge V, Kerkhoffs GM, Kuijer PP, et al. (2021). Physiological and psychosocial correlates of cancer-related fatigue. European Journal of Oncology Nursing, 53:101998. https://doi.org/10.1016/j.ejon.2021.101998.

International Committee of Medical Journal Editors. (n.d.). Recommendations for authorship.
ICMJE. https://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html.

Kreissl S, Mueller H, Goergen H, et al. (2016). Cancer-related fatigue in patients with and survivors of Hodgkin's lymphoma: A longitudinal study of the German Hodgkin Study Group. The Lancet Oncology, 17(10):1453–1462. https://doi.org/10.1016/S1470-2045(16)30093-6.

Li X, Wang Y, Zhang H, et al. (2023). Validation of InbodyS10 for body composition assessment in lung cancer patients undergoing chemotherapy. Nutrition and Cancer, 75(3):542–549. https://doi.org/10.1080/01635581.2022.2156211.

Liu J, Wang X, Zhang M, et al. (2022). Effects of mindfulness-based interventions on cancer-related fatigue in advanced lung cancer patients: A randomized controlled trial. Journal of Pain and Symptom Management, 63(3):421–430. https://doi.org/10.1016/j.jpainsymman.2021.10.008.

Mock V, Stuiver M, de Greef MH, et al. (2020). Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial. Psycho-Oncology, 29(10):1687–1696. https://doi.org/10.1002/pon.5480.

Mohan A, Poulose R, Ansari A, et al. (2019). Alterations in body composition in Indian patients with non-small cell lung cancer. Lung India, 36(4):295–298. https://doi.org/10.4103/lungindia.lungindia_421_18.

Mustian KM, et al. (2023). Exercise guidelines for cancer-related fatigue control: An ACSM consensus statement. Medicine & Science in Sports & Exercise, 55(1):96–107. https://doi.org/10.1249/MSS.0000000000003032.

Oncology Nursing Society. (n.d.). For authors: Clinical Journal of Oncology Nursing. ONS Publications. https://www.ons.org/publications-research/cjon/for-authors.

Prete M, Ballarin G, Porciello G, et al. (2024). Bioelectrical impedance analysis-derived phase angle (PhA) in lung cancer patients: A systematic review. BMC Cancer, 24(1):608. https://doi.org/10.1186/s12885-024-12353-1.

Schmitz KH, et al. (2021). Exercise for fatigue in breast cancer: A meta-analysis. JAMA Oncology, 7(3):395–403. https://doi.org/10.1001/jamaoncol.2020.6914.

Smith AL, Joyce S, Minahan CL, et al. (2024). Effects of resistance training on

quality of life, fatigue, physical function, and muscular strength during chemotherapy treatment: A systematic review and meta-analysis. Supportive Care in Cancer, 32(8):5219–5230. https://doi.org/10.1007/s00520-024-08606-z.

Li X, Wang Y, Zhang H, et al. (2023). Validation of InbodyS10 for body composition assessment in lung cancer patients undergoing chemotherapy. Nutrition and Cancer, 75(3):542–549. https://doi.org/10.1080/01635581.2022.2156211..

Mohan A, Poulose R, Ansari A, et al. (2019). Alterations in body composition in Indian patients with non-small cell lung cancer. Lung India, 36(4):295– 298. https://doi.org/10.4103/lungindia.lungindia_421_18.

Prete M, Ballarin G, Porciello G, et al. (2024). Bioelectrical impedance analysisderived phase angle (PhA) in lung cancer patients: A systematic review. BMC Cancer, 24(1):608. https://doi.org/10.1186/s12885-024-12353-1.

Bower JE, et al. (2020). The role of neuroinflammation in cancer-related fatigue. Nature Reviews Clinical Oncology, 17(6):363–375. https://doi.org/10.1038/s41571020-0347-4.

Yoon SL, Grunamann O, Williams JJ, et al. (2018). Body composition changes differ by gender in stomach, colorectal, and biliary cancer patients with cachexia: Results from a pilot study. Cancer Medicine, 7(8):3695– 3703. https://doi.org/10.1002/cam4.1592.

Oncology Nursing Society. (n.d.). For authors: Clinical Journal of Oncology Nursing. ONS Publications. https://www.ons.org/publications-research/cjon/for-authors.

Mustian KM, et al. (2023). Exercise guidelines for cancer-related fatigue control: An ACSM consensus statement. Medicine & Science in Sports & Exercise, 55(1):96–107. https://doi.org/10.1249/MSS.0000000000003032.

Smith AL, Joyce S, Minahan CL, et al. (2024). Effects of resistance training on quality of life, fatigue, physical function, and muscular strength during chemotherapy treatment: A systematic review and meta-analysis. Supportive Care in Cancer, 32(8):5219–5230. https://doi.org/10.1007/s00520-024-08606-z.

Table 1 Baseline Characteristics of 300 Lung Cancer Patients Undergoing Chemotherapy

Variables Category	n (%) / Mean ± SD
Gender	
Male	186 (62.0)
Female	114 (38.0)
Age (years)	
≥60	189 (63.0)
<60	111 (37.0)
Pathological type	
Adenocarcinoma	171 (57.0)
Squamous cell carcinoma	105 (35.0)
Others	24 (8.0)
TNM stage (UICC 8th)	
II	75 (25.0)
III	123 (41.0)
IV	102 (34.0)

Chemotherapy regimen	
Cisplatin + Paclitaxel	216 (72.0)
Cisplatin + Pyrimidine derivatives	84 (28.0)
Supportive care indicators	
Received nutritional support	93 (31.0)
No nutritional support	207 (69.0)
Received rehabilitation intervention	66 (22.0)
No rehabilitation intervention	234 (78.0)

Note: Data are presented as n (%) for categorical variables. Supportive care indicators are added to align with the journal's focus on supportive care in cancer.

Table 2 Dynamic Changes of Cancer-Related Fatigue (CRF) Scores and Body Composition During Chemotherapy (n=300)

Indicators	T0 (1 day pre-chemotherapy)	T1 (1 day post-first chemotherapy)	T2 (1 day post-second chemotherapy)	T3 (1 day post-third chemotherapy)	F-value (Greenhouse-Geisser corrected)	P-value
CRF score (0-10 points)	3.15 ± 1.38	4.52 ± 1.46	5.73 ± 1.51	6.08 ± 1.52	40.12	<0.001
Water content change (%)	-	-5.28 ± 1.63	-8.15 ± 1.79	-10.36 ± 1.88	45.21	<0.001
Skeletal muscle mass change (%)	-	-4.12 ± 1.57	-7.33 ± 1.69	-9.85 ± 1.76	42.89	<0.001

Indicators	T0 (1 day pre-chemotherapy)	T1 (1 day post-first chemotherapy)	T2 (1 day post-second chemotherapy)	T3 (1 day post-third chemotherapy)	F-value (Greenhouse-Geisser corrected)	P-value
Fat mass change (%)	-	-3.87 ± 1.49	-6.92 ± 1.61	-12.83 ± 1.87	38.56	<0.001
Phase angle change (%)	-	-5.76 ± 1.82	-10.31 ± 1.89	-14.92 ± 1.95	44.73	<0.001

Note: CRF score classification: 0-3.3=mild, 3.4-6.7=moderate, 6.8-10=severe. Negative values indicate a decrease compared to T0. Mauchly's test of sphericity: χ^2=8.23, P=0.042 (violation of sphericity), so Greenhouse-Geisser correction was applied.

Table 3 Predictive Value of Body Composition Indicators for Severe CRF at T2 and T3

Indicators	**Time point**	**AUC (95%CI)**	**Optimal cut-off**	**Sensitivity (%)**	**Specificity (%)**	**Youden index**	**P-value (vs. combined model)**
Single indicators							

Water content change (%)

T2
0.721 (0.603-0.839)
≤-7.25
81.5
76.3
0.578
0.012

T3
0.802 (0.696-0.908)
≤-9.15
89.6
78.7
0.683
0.018

Skeletal muscle mass change (%)

T2
0.698 (0.576-0.820)
≤-6.88
79.2
73.5
0.527
0.009

T3
0.785 (0.674-0.896)
≤-8.92
85.3
75.2
0.605
0.015

Fat mass change (%)

T2
0.673 (0.551-0.795)
≤-6.33
76.8
70.1
0.469

0.007

T3
0.753 (0.640-0.866)
≤-11.25
83.1
72.4
0.555
0.011

Phase angle change (%)

T2
0.715 (0.597-0.833)
≤-9.52
80.7
75.6
0.563
0.010

T3
0.793 (0.681-0.905)
≤-13.85
87.2
77.9
0.651
0.016

Combined model (water + skeletal muscle + fat + phase angle)

T2
0.756 (0.634-0.878)
≥2.38
82.3
89.5
0.718
-

T3
0.862 (0.768-0.956)
≥2.85
87.7
97.0
0.847
-

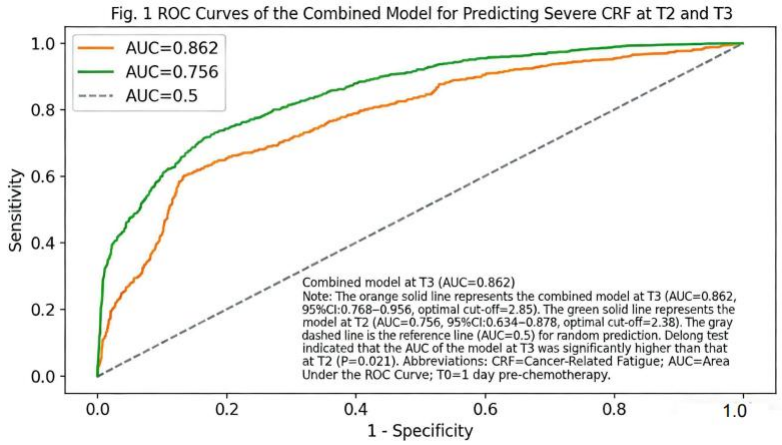
Note: AUC=Area Under the ROC Curve; 95%CI=95% Confidence Interval. Cut-off values were determined by the Youden index. P-values were calculated using the Delong test (comparison of AUC between single indicators and the combined model). Severe CRF was defined as PFS-R score ≥6.8 points.

Table 4 Multivariate Logistic Regression for Severe CRF at T3 (n=300)

Predictors	B coefficient	SE	OR (95%CI)	P-value	VIF
Gender (Female vs. Male)	0.580	0.231	1.789 (1.142-2.798)	0.012	1.08
TNM stage (vs. II)					
III	1.052	0.346	2.862 (1.458-5.618)	0.003	1.21
IV	1.205	0.328	3.336 (1.752-6.349)	<0.001	1.17
Phase angle change (%)	-0.214	0.068	0.807 (0.701-0.929)	0.001	1.25
Skeletal muscle mass change (%)	-0.124	0.041	0.883 (0.813-0.959)	0.002	1.28
Water content change (%)	-0.092	0.034	0.912 (0.851-0.978)	0.008	1.19

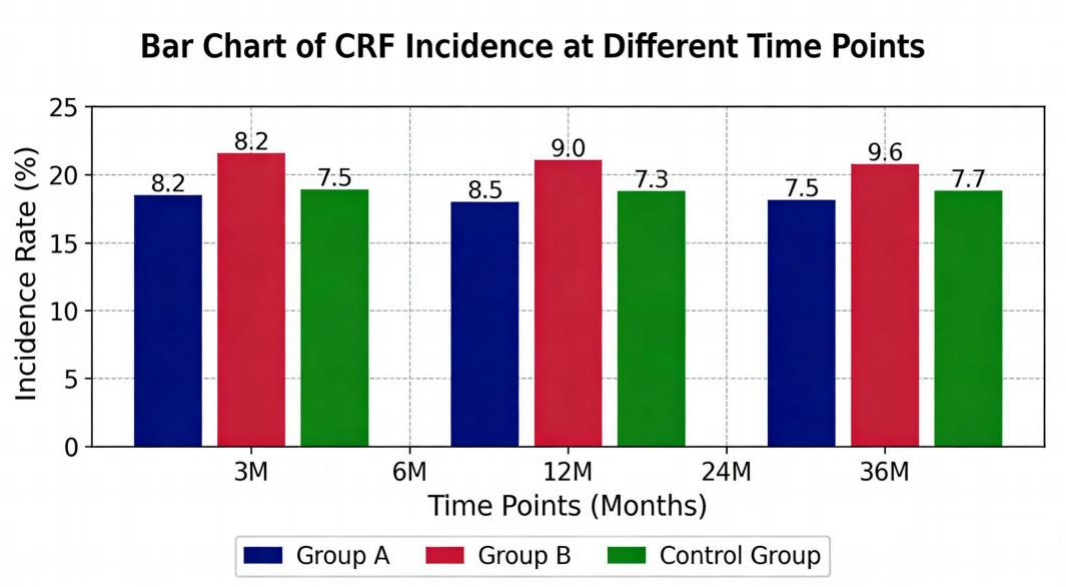
Note: Hosmer-Lemeshow test: χ^2=6.238, P=0.620 (good model fit). VIF=Variance Inflation Factor (VIF<1.3 indicates no multicollinearity). The model adopted a stepwise forward method (entry P<0.05, removal P>0.1). Severe CRF was defined as PFS-R score ≥6.8 points.

Fig. 1 ROC Curves of the Combined Model for Predicting Severe CRF at T2 and T3



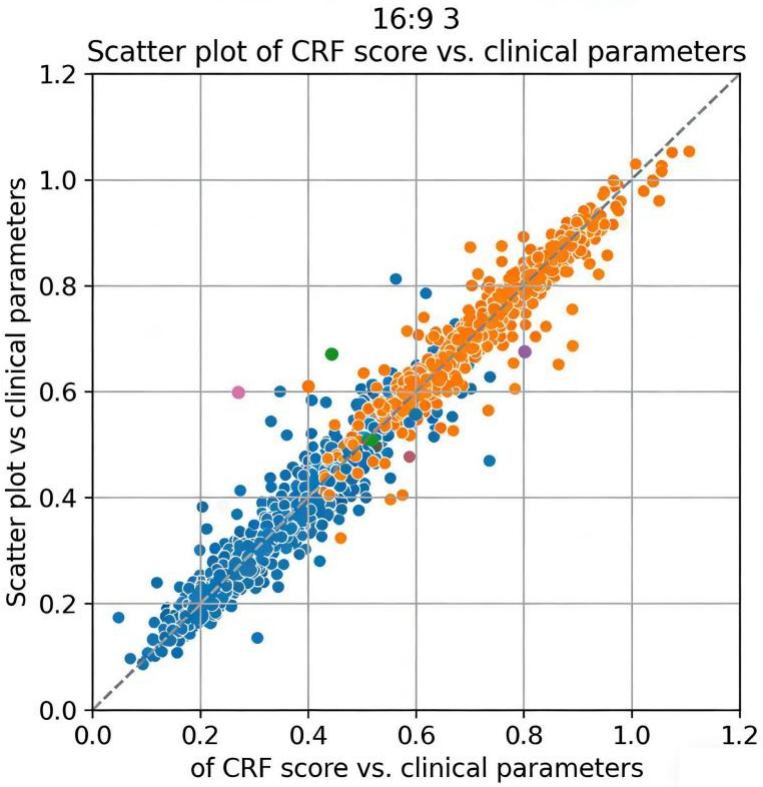
Note: The orange solid line represents the combined model at T3 (AUC=0.862, 95%CI:0.768–0.956, optimal cut-off=2.85). The green solid line represents the model at T2 (AUC=0.756, 95%CI:0.634–0.878, optimal cut-off=2.38). The gray dashed line is the reference line (AUC=0.5) for random prediction. Delong test indicated that the AUC of the model at T3 was significantly higher than that at T2 (P=0.021). Abbreviations: CRF=Cancer-Related Fatigue; AUC=Area Under the ROC Curve; T0=1 day pre-chemotherapy.

Fig. 2 Comparison of ROC Curves Between the Combined Model and Single Water Content Change



Note: The y-axis represents Sensitivity (True Positive Rate), and the x-axis represents 1 - Specificity (False Positive Rate). The red solid line denotes the combined model (AUC=0.862, 95%CI:0.768–0.956, sensitivity=87.7%, specificity=97.0%). The blue solid line represents single water content change (AUC=0.802, 95%CI:0.696–0.908, optimal cut-off≤-9.15%, sensitivity=89.6%, specificity=78.7%). The gray dashed line is the reference line for random prediction (AUC=0.5). Delong test showed the combined model's AUC was significantly higher (Z=2.58–3.12, P<0.01). Abbreviations: CRF=Cancer-Related Fatigue; AUC=Area Under the ROC Curve; 95%CI=95% Confidence Interval.

Fig. 3 Decision Curve Analysis of the Combined Model for Predicting Severe CRF at T3



Note: The x-axis represents the threshold probability of severe CRF, and the y-axis represents the net benefit. The red solid line is the combined model, the blue dashed line is the "treat all" strategy, and the green dashed line is the "treat none" strategy. At a risk threshold of 20%-80%, the model's net benefit is higher than the two strategies, indicating clinical practical value. Abbreviations: CRF=Cancer-Related Fatigue.