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Effect of nutritional screening in children with acute lymphoblastic leukemia undergoing the maintenance chemotherapy

Xuefen Zhao[1†], Juan Wang[1†], Li Chen[1], Xin Xu[1†] and Caihong Fu[1*†]

Abstract

Background To investigate the effectiveness of the routine nutritional screening for malnutrition risk in hospitalized children with acute lymphoblastic leukemia (ALL) on maintenance chemotherapy from the viewpoint of clinical outcomes.

Methods The reviews of 1038 pediatric patients were retrieved for the retrospective, propensity score-matched, superiority study. A 1:1 propensity score matching was utilized to match patients who received nutritional screening (screening cohort) to those who remained usual care without screening (control cohort). The primary endpoint was the long-term event-free-survival (EFS) after the last cycle of maintenance. Secondary outcomes included immune function, complications and long-term quality-adjusted life years (QALYs).

Results The proportion of cases with risk of malnutrition in screening was 25.8%. At the end of 4 weeks following the last cycle, the level of serum albumin was higher in screening cohort than control cohort ($p < 0.001$), while the cellular immune function significantly improved in screening cohort (all $p < 0.05$). During a mean of 11.09 ± 6.45 months follow-up, 28.6% of patients in screening cohort had an event including ALL-related emergency visits, readmitted hospitalizations and severe infections compared to 46.5% of cases in control cohort yielding a hazard ratio of 0.397 (95%CI: 0.306, 0.493 and a significant difference in long-term EFS (24.07 (95%CI: 23.09, 25.04) vs. 18.02 (95%CI: 16.62, 19.42), log-rank $p < 0.001$). The means of QALYs calculated by area under the curve up to 3, 6, 12 and 24 months after discharge were significantly lower in screening cohort as opposed to control cohort (all $p < 0.05$).

Conclusions Pediatric ALL receiving the specific-for-children nutritional screening during hospitalization exhibited a better EFS over the 24-month follow-up than cases without screening. The benefit accounted for a significant improvement in immune function and QALYs scores over long-term follow-up.

Clinical trial number Not applicable.

†Xuefen Zhao, Juan Wang and Li Chen contributed equally to the manuscript as co-first authors.

†Caihong Fu and Xin Xu contributed equally to the manuscript as co-corresponding authors.

*Correspondence:
Caihong Fu
Fucaihongvip@yeah.net

Full list of author information is available at the end of the article

Keywords Acute lymphoblastic leukemia, Nutritional screening, Event-free-survival, Readmission, Infection, Quality-adjusted life years

Introduction

Acute lymphoblastic leukemia (ALL) is the most common malignancy diagnosed in child, accounting for the world age-standardized incidence of 46.4 per million per year in children aged 0–14 years and 28.5 per million in adolescents aged 15–19 years [1]. The cancer registration data show the same trend in China [2]. Chemotherapy remains the standard treatment for pediatric ALL with a 5-year survival rate over 80% [3, 4]. However, the severity of post-treatment myelosuppression increases as the frequency and intensity of chemotherapy rise, leading to the vulnerability of malnutrition. Adverse reactions to aggressive chemotherapy drugs also result in a diminished appetite in patients [5]. Corticosteroids as an integral component of treatment are likely contributors to impact children's ability to take normal diet, and further lead to a further decrease in nutritional status [6]. In turn, patients with nutritional deficiencies have impaired haemopoietic and immune functions [7, 8]. Evidences suggest that under-nutrition has been emphasized to be closely correlated with clinical efficacy, chemotherapy tolerance and prognosis in cases of ALL [9]. Furthermore, malnutrition decreases quality of life and prolongs length of hospital stay [10].

It is well known that the European Society for Clinical Nutrition and Metabolism (ESPEN) expert group emphasized the screen cancer patients for nutritional risk early in course of their care [11]. Although malnutrition risk in patients at the induction or intensification chemotherapy was significantly higher as compared to cases during the maintenance therapy, a significant increase in the rate of malnutrition was reported as the therapy time prolonged due to the above-mentioned factors [9]. The proportion of nutritional status disorders with pediatric ALLs at diagnosis ranges from 6 to 21.2% from different parts of world, and increased to a median of 40% at the end of chemotherapy cycle [12, 13]. Therefore, screening was still required for patients undergoing the last maintenance cycle, which was the last but longest phase of chemotherapy for children with ALLs. Whereas, there is a lack of research addressing this aspect in Chinese children with ALL, which might due to the absence of a gold standard measure. Recently, the Subjective Global Nutritional Assessment (SGNA) has been proved to be a simple, comprehensive, organized and non-invasive tool with high sensitivity and good inter-observer reliability for assessing nutritional status in pediatric patients, who are hospitalized, with neurocognitive disabilities or chronic illness/disease [14].

Due to the limited evidences regarding its clinical use, the study aimed to evaluate the effectiveness of implementing the routine nutritional screen to identify "at risk" status in pediatric ALLs on the last cycle of maintenance therapy, that followed by a referral to the specialists in our nutrition department for early nutritional intervention, to influence the event-free survival (EFS) and quality-adjusted life years (QALYs) during long-term follow-up.

Methods

Study design and participant selection

The institutional Ethics Examining Committee of Human Research (TZRMH-2025KY-008) authorized ethical approval for a retrospective propensity score-matched cohort study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines based on the principles of the Declaration of Helsinki [15]. Informed consents were waived for adult patients, because all data were retrieved from the existing medical and administrative records to inform treatment. No patients were contacted for the study and no personal data were disclosed. Whereas, informed consents were obtained from the parents or legal guardians for participants younger than the age of 16 after enrollment.

Between January 1, 2020 and February 28, 2024, the reviews of pediatric patients who admitted to our hospital for the treatment of ALL according to the South China Children's Leukemia Group-ALL-2015 (CCCG-ALL-2015) protocol were extracted from the electronic medical records (EMRs) [16]. Inclusion criteria were as follows: (1) confirmed diagnosis of ALL by the criteria from the 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukmia [17]; (2) aged 0 to 18 years of age at diagnosis; (3) on maintenance chemotherapy after achieving complete remission according to the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (version 2.2021) [18] (4) undergoing 7 cycles of chemotherapy using 6-mercaptopurine 50mg/m^2 every day and methotrexate 25 mg/m^2 one day per week up to 8 weeks according to the CCCG-ALL-2015 protocol. Patients were excluded due to Philadelphia chromosome–positive ALL, relapsed/refractory disease, down syndrome, pulmonary/bone metastasis, neuromuscular disease, severe metabolic disease or gastrointestinal disease; hepatic or renal dysfunction and incomplete data.

The review of 515 consecutive patients who were identified as the screening cohort were retrospectively

retrieved from the EMRs. We performed a propensity-score matching analysis of patients, who did not receive nutritional screening over the same period, in a 1:1 ratio as control cohort. The score was estimated using the baseline variables by the nearest-neighbor method with a caliper of 0.20: (1) age; (2) gender; (3) ALL immunophenotype; (4) Karyotye analysis; (5) white blood cell (WBC) count at diagnosis; (6) ALL risk category based on the International Berlin-Frankfurt-Munster Group Study Group and IntReALL Consortium risk classification [19]; (7) end of induction-measurable residual disease (EOI-MRD); (8) post-induction condition; (9) extramedullary disease; (10) central nervous system leukemia (CNSL); (11) prednisone response; (12) serum albumin and body mass index (BMI) on the first day of admission.

Nutritional screening

Given that nutritional screening was not a routine procedure, the patients were engaged to selecting the management option most closely aligned with his/her values and preferences. Within 48 h upon admission at the last cycle of maintenance, screening for nutritional risk was performed by specially trained nurse staff using SGNA questionnaire for patients with agreement. Cases with a positive screening result were prescribed to a dietitian for detailed assessment to produce an early nutritional intervention or support.

Outcomes measurement

The SGNA nutrition-screening tool uses both subjective and objective nutrition-focused aspects to identify nutritional status, considering seven specific features of medical history (height-for-age, weight-for-height, changes in body weight, adequacy of dietary intake, gastrointestinal symptoms, functional capacity, and metabolic stress of disease) and three parameters of physical examination (loss of subcutaneous fat, muscle wasting, and edema) for signs of inadequate energy and/or protein intake. A child's nutritional status is categorized in accordance with the SGNA rating form as (1) normal/well nourished: The patient is growing and gaining weight normally, has a grossly adequate intake without gastrointestinal symptoms, shows no or few physical signs of wasting, and exhibits normal functional capacity. Normal ratings in most or all categories, or significant, sustained improvement from a questionable or moderately malnourished state. It is possible to rate a patient as well-nourished in spite of some reductions in muscle mass, fat stores, weight and intake. This is based on recent improvement in signs that are mild and inconsistent. (2) moderately malnourished: This patient has definite signs of a decrease in weight and/or growth, and intake and may or may not have signs of diminished fat stores, muscle mass and functional capacity. This patient is experiencing a downward trend, but started with normal nutritional status. Moderate ratings in most or all categories, with the potential to progress to a severely malnourished state. (3) severely malnourished: This patient has progressive malnutrition with a downward trend in most or all categories. There are significant physical signs of malnutrition—loss of fat stores, muscle wasting, weight loss >10%—as well as decreased intake, excessive gastrointestinal losses and/or acute metabolic stress, and definite loss of functional capacity. Severe ratings in most or all categories with little or no sign of improvement [20]. The levels of serum albumin (ALB), prealbumin (PA) and retinol binding protein (RBP) were measured from fasting blood specimens. The levels of T-cell subsets in peripheral blood were detected by immunofluorescence and flow cytometry to calculate the percentage of natural killer (NK) cells as immune indicators. Length of hospital stay (LOS) was predefined as days from admission to discharge from the ward, and prolonged LOS was considered as LOS>8 days. Early readmission was defined as readmission to hospital within 30 days post-discharge due to all-cause. The health-related quality of life (HR-QoL) was evaluated using the QALYs, which were calculated using the European quality of life five-dimensional (EQ-5D-5 L) utility values over time following the area under the curve (AUC) method. The EQ-5D-5 L questionnaire contained five domains: mobility, self-care, usual activity, pain or discomfort and anxiety or depression. Each dimension is scored using a 5-points likert scale, depending on whether the respondent has no, slight, moderate, severe or extreme problems. Utility scores were calculated by the Euro-QoL crosswalk set of utility index values to their EQ-5D-SL health states. The QALYs were generated via the AUC when the utility scores were plotted over time [21].

Data on demographic and clinical data were retrieved from EMRs. SGNA scores and QALYs scores were extracted from medical database, which were collected through telephone interview by specially trained nurses according to our clinical protocol. The primary endpoint was the long-term survival without ALL worsening that required acute care during long-term follow-up, defining as ALL-related emergency visits, readmitted hospitalizations and occurrence of severe infections.

Sample size calculation

PASS statistical software, version 22.0 (NCSS, LLC. Kaysville, Utah, USA) was used for sample size calculation. Based on a multidisciplinary experts' consensus from a series of cases discussion, an equal sample allocation superiority was designed to compare the hazard rates of ALL-pediatric patients receiving a routine nutritional screening to those without screening using a log-rank test. The hazard rate was supposed to be 2.0, we

wanted to show that it decreased by at least 25% when the nutritional screening was performed, which was considered to be clinically better for EFS of ALL [22]. We wanted to compare sample size when the power was 0.80 with two-side type I error of 5%, and the difference in hazard rates was between −0.8 and −0.3, specifying the value of the clinical superiority margin by 0.5. If the data-loss rate was estimated to be 20% in both two cohorts, the sample size was 587 cases in either screening or control cohort.

Statistical analysis

SPSS software version 22.0 (SPSS Inc, Chicago, IL) was used for statistics analysis. Significant level was reported as $p<0.05$. Data normality was performed using Kolmogorov-Smirnov Z test. Nominal distributed data, non-normally distributed data and categorical data were recorded as mean ± standard deviation (SD), median ± inter quartile range (IQR) and percentage. Differences between groups were compared using the student t test, Mann-Whitney U test and Chi-squared test. The probability of EFS was evaluated by the Kaplan-Meier method, and differences among cohorts were assessed by log-rank analysis with 95% confidence interval (CI). The censored point was defined as disease-free survival at the last follow-up assessment.

Results

Figure 1 showed the cohort flow diagram, a total of 1174 pediatric patients with ALL were identified for this study cohort. After propensity score matching, 515 cases were included in the screening cohort and 523 in the matched cohort. Table 1 showed the demographic and clinical characteristic of patients at baseline, which were well balanced between two study cohorts.

A total of 74.2%, 19.4% and 6.4% of cases in the screening cohort were respectively categorized as being at normal/well, moderately and severely malnourished based on the SGNA nutritional screening tool. Occurrence of hypoproteinemia with serum albumin level < 3.5 (g/dL) was reported in 11.1% and 31.5% cases in screening and control cohort at 4 weeks post-discharge following the last cycle of maintenance therapy, with significant between-group differences ($p<0.001$). In addition, 23.1% of patients in screening cohort had a prolonged LOS >8 days, compared with 40.1% of cases in control group

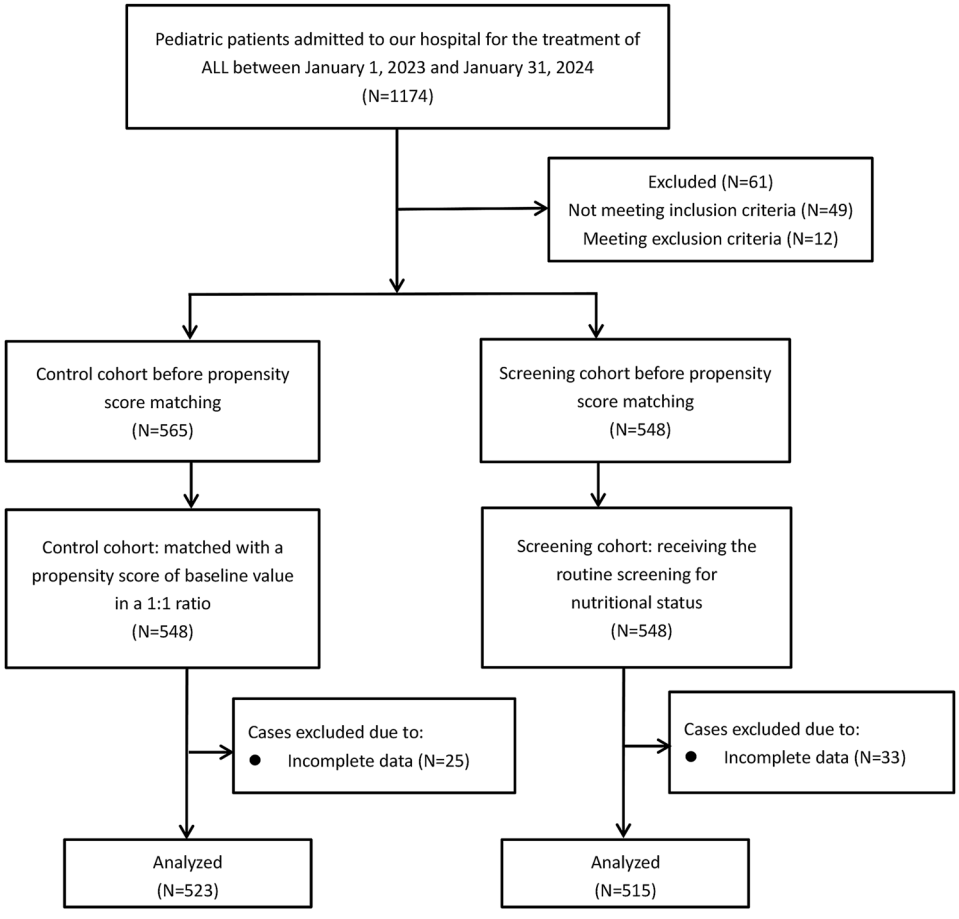

Fig. 1 The flow diagram of the study cohort. ALL: acute lymphoblastic leukemia

Table 1 Demographic data and clinical characteristics for pediatric patients with ALL at baseline

Variables	Control cohort (*N*=523)	Screening cohort (*N*=515)	t/x^2 value	*p* value
Age(years)(mean ± SD)	9.80±5.35	8.17±5.80	1.134	0.261
Gender, n (%)			2.364	0.135
Female	294 (56.2%)	265 (51.5%)		
Male	229 (43.8%)	250 (48.5%)		
Race, n (%)			0.019	0.934
Han Chinese	435 (83.2%)	430 (83.5%)		
Minority	88 (16.8%)	85 (16.5%)		
BMI (kg/m^2) (median (IQR))	22.2 (16.6, 32.6)	22.6 (16.9, 30.5)	0.348	0.530
Albumin (g/dl) (median (IQR))	3.9 (2.9, 4.4)	3.8 (2.9, 4.9)	0.639	0.791
Disease duration (months) (mean ± SD)	29.68±5.71	26.81±5.08	1.246	0.213
Disease risk of ALL, n (%)			1.274	0.269
Standard	447 (85.5%)	427 (82.9%)		
High	76 (14.5%)	88 (17.1%)		
Immunophenotype, n (%)			0.431	0.559
B-ALL	486 (92.9%)	473 (91.8%)		
T-ALL	37 (7.1%)	42 (8.2%)		
Karyotype, n (%)			0.662	0.718
Normal	407 (77.8%)	397 (77.1%)		
≥ 50	83 (15.9%)	79 (15.3%)		
Other abnormal type	33 (6.3%)	39 (7.6%)		
Initial WBC grades (×10^3/ul), n (%)			0.115	0.944
≥100	38 (7.3%)	35 (6.8%)		
≥50	40 (7.6%)	41 (8.0%)		
<50	445 (85.1%)	439 (85.2%)		
Central nervous system invasion, n (%)	4 (0.8%)	3 (0.6%)	0.129	0.720
Testicular aggression in male children, n (%)	2 (0.4%)	1 (0.2%)	0.319	0.572
Serum albumin level < 3.5 (g/dL), n (%)	51 (9.8%)	48 (9.3%)	0.056	0.833
Prednisone response, n (%)			0.169	0.737
Good responder	481 (92.0%)	470 (91.3%)		
Poor responder	42 (8.0%)	45 (8.7%)		
EOI-complete remission, n (%)	491 (93.9%)	478 (92.9%)	0.475	0.534
EOI-MRD, n (%)			0.038	0.867
<0.01%	438 (83.7%)	429 (83.3%)		
≥0.01%	85 (16.3%)	86 (16.7%)		
Cycles of maintenance (mean ± SD)	2.29±0.74	2.24±0.83	0.241	0.810

ALL=acute lymphoblastic leukemia; BMI=body mass index; WBC=white blood cell; EOI=end of induction; MRD= measurable residual disease; SD=standard deviation; IQR: interquartile range

($p<0.001$). As shown in Table 2, the levels of ALB, PA and RBP were significantly higher in screening cohort at 4 weeks after the last maintenance cycle (all $p<0.05$), while the lower in screening cohort as compared to the matched cohort at 4-week post-discharge following the last maintenance cycle (all $p<0.05$).

There were 26.8% of patients in screening cohort reporting ALL-related events requiring acute care as compared to 46.5% of cases in control cohort ($p<0.001$) according to the Kaplan-Meier curves showed in Fig. 2. Specifically, there were significantly lower proportion of patients from screening cohort in ALL-related emergency room visits (7.0% vs. 24.3%, $p<0.001$), re-hospitalization (13.2% vs. 28.5%, $p<0.001$) and severe infection (6.6% vs. 13.6%, $p<0.001$) as opposed to those in control cohort during the long-term follow-up. Superiority was met, as the hazard ratio of the primary outcome was 0.397, the 95% confidence interval of 0.306 to 0.493 which felt within the predefined superiority margin of 0.5. As a matter of fact, the mean of long-term EFS was significantly longer in patients receiving nutritional screening than those as controls (24.07 (95%CI: 23.09, 25.04) vs. 18.02 (95%CI: 16.62, 19.42), log-rank $p<0.001$).

Figure 3 illustrated the quality of life between two groups using the EQ-5D-5 L utility and the corresponding QALYs over the long-term follow-up. There was a trend to reduction in the mean of QALYs for patients in both two groups. However, the means of QALYs

Table 2 Comparisons of albumin levels and cellular immune function of pediatric alls on the last cycle of maintenance therapy

Variables		Control cohort (*N*=523)	Screening cohort (*N*=515)	t value	*P*
Baseline on first day of admission	ALB (g/L)	29.45±2.34	29.34±3.67	0.797	0.427
	PA (mg/L)	107.12±21.58	108.78±21.23	-0.565	0.574
	RBP (mg/L)	19.56±1.78	20.57±2.23	-0.645	0.521
4 weeks after last maintenance cycle	ALB (g/L)	32.81±8.16	44.52±11.74	-2.270	0.025
	PA (mg/L)	118.03±21.84	146.87±16.88	-7.199	<0.001
	RBP (mg/L)	19.56±2.49	25.84±3.99	-2.159	0.033
Baseline on first day of admission	CD3+	70.93±21.85	68.67±16.88	0.565	0.501
	CD4+	32.72±5.56	28.87±4.74	0.797	0.427
	CD8+	26.06±8.16	29.40±7.14	-0.645	0.521
	NK cell %	24.08±3.27	25.75±3.35	-0.565	0.574
4 weeks after last maintenance cycle	CD3+	54.50±20.91	53.68±16.88	2.364	0.020
	CD4+	26.06±8.16	17.59±7.14	2.233	<0.001
	CD8+	26.13±5.18	17.64±5.12	2.221	<0.001
	NK cell %	16.64±4.74	10.87±3.61	8.879	0.001

ALL=Acute Lymphoblastic Leukemia; ALB=serum albumin; PA= prealbumin; RBP= retinol binding protein

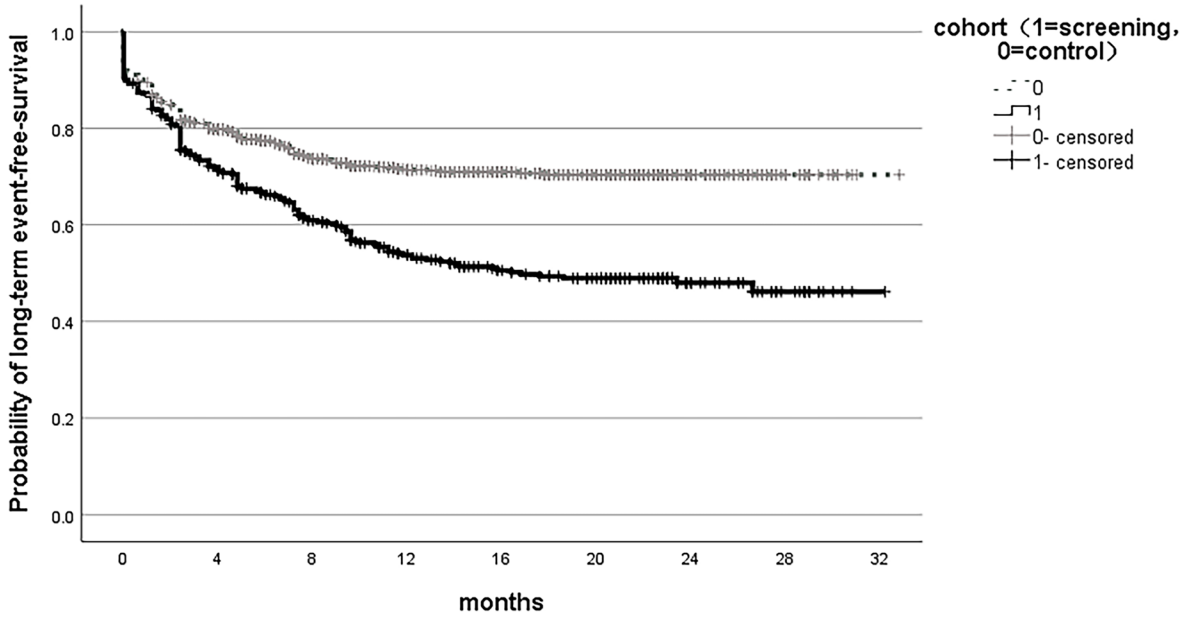

Fig. 2 Kaplan-Meier survival curves without ALL-related events that required acute care during long-term follow-up, defining as ALL-related emergency visits, readmitted hospitalizations and occurrence of severe infections for pediatric patients who received routine nutritional screening during hospitalization compared to the matched control cohort without screening during the long-term follow-up. The mean of EFS was significantly longer in screening cohort than control cohort (log-rank test: $p < 0.001$). EFS: event-free-survival

calculated by AUC up to 3 (20.94 ± 12.64 vs. 17.33 ± 3.18, $p = 0.039$), 6 (29.12 ± 13.64 vs. 17.91 ± 3.86, $p = 0.016$), 12 (34.95 ± 15.59 vs. 20.45 ± 4.05, $p = 0.009$) and 24 months (39.12 ± 16.17 vs. 21.03 ± 14.36, $p = 0.001$) after discharge were significantly lower in the screening group as opposed to the matched control group.

Discussion

The present study firstly examined the long-term consequence of post-discharge EFS in relation to an implementation of routine nutritional screening for pediatric patients with ALL undergoing the last cycle of maintenance chemotherapy. Our findings confirmed that the long-term EFS rate had been significantly improved in screening cohort, the average gain in immunocompetence and QALYs were higher for patients receiving nutritional screening as compared to control cohort, which might attribute to accurate assessment of nutritional status for early intervention.

Evidences revealed that the composition of pediatric body composition including bone density, fat- and fat-free mass and total body water, are changed primarily

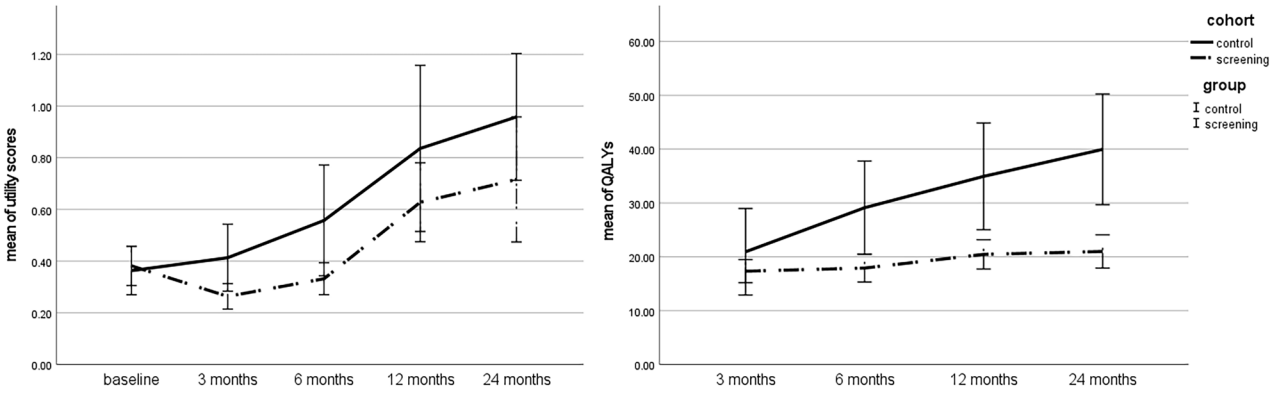

Fig. 3 Changes in health-related QoL from baseline to 24-month follow-up. (**a**) the mean of EQ–5D-5 L utility scores was significantly lower in the combined screening group as opposed to the control group using basic screening tool at 3-, 6-, 12-and 24- month follow-up; and (**b**) the mean of QALYs calculated by area under the curve in the combined screening group was significantly lower than that in control group across all time points during the 24 months follow-up. QoL: quality of life; QALYs: quality-adjusted life year. *$p < 0.05$

by caner itself, aggressive multimodal treatments, metabolism changes, unbalanced diet and physical activity reduction, influencing the patient's nutritional status [23]. In the present study, we employed a validated method for the overall pediatric population to identify the nutritional risk among the study population, which was not taken as a routinely reported practice up to now. Of the 515 cases in screening cohort, normal nutrition was reported in 74.2% of cases, moderate malnutrition in 19.4% and severe malnutrition in 6.4%, which was consistent with the range of 28–78% from previous systematic analysis [13].

In turn, nutritional status disorders can modify the metabolism, volume distribution and clearance of chemotherapy, then change the drug pharmacokinetics to impair the effectiveness of cancer treatment and alter the cytokine hormone function to decrease the ability of immune response against infection [24]. Although meeting the nutritional requirements in these pediatric cancer population is challenging, the enteral or parenteral nutritional support is frequently used to effectively reverse malnutrition associated with the anti-neoplastic treatment, promote treatment tolerance and improve immune function [25]. Yueqin Han et al. estimated the application of nutrition therapy in childhood ALL during chemotherapy, their results showed the concentrations of ALB were significantly increased, while the percentages of CD3+, CD4+, CD4+/CD8+, NK cell significantly decreased at 4 weeks post-treatment [26]. In this study, we also found a significantly better improvement of immune function in screening cohort than control cohort.

In contrast, malnutrition adversely affects several clinical outcomes in terms of disease progression, survival, treatment-related morbidity and risk of infection. Likewise, it has been proved to be associated with a poor health-related quality of life [30]. As result, patients with a malnourished status assessed by the SGNA were 1.95-time (95%CI: 1.12, 3.39) more likely to be readmitted as opposed to the well-nourished ($p = 0.017$) [27]. Moreover, malnourished ALL-children had 2 to 3 times prone to suffer from infection compared to well nourished ($p = 0.024$), and thus prolonged the duration of treatment, hospital stay, even could lead to death [28]. Consistent with previous evidences, our Kaplan-Meier survival analysis in screening cohort indicated a significantly greater outcome of the long-term probability of EFS than those did not receive screening for malnutrition risk in control cohort, which were in line with a meta-analysis concluding that malnutrition was associated with poorer overall survival (RR = 1.36 (95%CI: 1.16, 1.60) and EFS (RR = 1.56 (95%CI:1.32, 1.86)), respectively, supporting the essential to recognize and achieve optimal nutritional status by nutrition intervention to improve treatment results in pediatric ALL [29]. In addition, the implementation of a routine nutritional screening had a significantly markable impact on QoL over 24 months with a greater QALY score as opposed to control cohort without screening, which indicated that the routine nutritional screening was a useful process to distinguish the risk of malnutrition for pediatric patients with ALL, and minimized the delay in referral to a dietitian for early diagnosis and intervention to achieve a better nutritional status, therefore, further improved HR-QoL over time. Similarly, previous reviews showed nutritional assessment and early intervention in pediatric patients with caners could significantly improve their HR-QoL [30].

Limitations

There were several limitations. First, it was a single-center design, which limited its generalizability to all hospitalized pediatric ALLs. Second, investigators responsible for outcome assessment were not blinded due to the nature

of retrospective study, which might yield confounding bias. Third, although our hospital the largest tertiary center in the city, we did not capture all readmissions for cases in our cohort, because patients were likely to be readmitted in other medical centers. Four, we did not measure the micronutrients in both the cohorts. In the future, there is a need for a well-designed, randomized, controlled study to verify our results.

Conclusion

In conclusion, the implementation of routine nutritional screening in pediatric ALL patients could significantly improve the long-term ESF, when defining ALL-related events as ALL-related emergency visits, readmitted hospitalizations and occurrence of severe infections, and accounted for a significant improvement in scores of QALY over long-term follow-up.

Abbreviations

ALL	Acute Lymphoblastic Leukemia
EFS	Event-Free-Survival
QALYs	quality-adjusted life years
SGNA	Subjective Global Nutritional Assessment
EMRs	Electronic Medical Records
EOI-MRD	Induction-Measurable Residual Disease
BMI	Body Mass Index
HR-QoL	Health-Related Quality of Life
EQ-5D-5L	European Quality of life five-dimensional
LOS	Length of hospital Stay
AUC	Under the Curve
SD	Standard Deviation
IQR	Inter Quartile Range
CI	Confidence Interval

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None.

Author contributions

Caihong Fu was involved in the conception and design, analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content; and the final approval of the version to be published.Xin Xu was involved in the conception and design, analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content; and the final approval of the version to be published.Xuefen Zhao was involved in the conception and design, analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content. Juan Wang was involved in the conception and design; the drafting of the paper, revising it critically for intellectual content.Li Chen was involved in the conception and design; the drafting of the paper, revising it critically for intellectual content.And all authors agreed to be accountable for all aspects of the work.

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None.

Data availability

The data are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent

The ethic was approved by the institutional Ethics Examining Committee of Human Research (TZRMH-KY-2025015) based on the principles of the Declaration of Helsinki. Informed consents were waived for adult patients, because all data were retrieved from the existing medical and administrative records to inform treatment. No patients were contacted for the study and no personal data were disclosed. Whereas, informed consents were obtained from the parents or legal guardians for participants younger than the age of 16 after enrollment.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Hematology, Children's Hospital of Nanjing Medical University, No. 72 Guangzhou Road, Gulou District, Nanjing City, Jiangsu Province 210000, China

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References

1. Steliarova-Foucher E, Colombet M, Ries L, Moreno F, Dolya A, Bray F, et al. International incidence of childhood cancer, 2001-10: a population-based registry study. Lancet oncol. 2017;18:719–31.
2. Zheng R, Peng X, Zeng H, Zhang S, Chen T, Wang H, et al. Incidence, mortality and survival of childhood cancer in China during 2000–2010 period: A population-based study. Cancer Lett. 2015;363:176–80.
3. Cooper SL, Brown PA. Treatment of pediatric acute lymphoblastic leukemia. Pediatr Clin N Am. 2015;62:61–73.
4. Gaynon PS, Angiolillo AL, Carroll WL, Nachman JB, Trigg ME, Sather HN, et al. Long-term results of the children's cancer group studies for childhood acute lymphoblastic leukemia 1983–2002: a children's oncology group report. Leukemia. 2010;24:285–97.
5. Diamantaras AA, Dessypris N, Sergentanis TN, Ntouvelis E, Athanasiadou-Piperopoulou F, Baka M, et al. Nutrition in early life and risk of childhood leukemia: a case-control study in Greece. Cancer Cause Control. 2013;24:117–24.
6. Touyz LM, Cohen J, Neville KA, Wakefield CE, Garnett SP, Mallitt KA et al. Changes in body mass index in long-term survivors of childhood acute lymphoblastic leukemia treated without cranial radiation and with reduced glucocorticoid therapy. Pediatr blood cancer. 2017;64.
7. Chandra RK. Immunocompetence in undernutrition. J Pediatr-us. 1972;81:1194–200.
8. Lobato ME, Ruiz-Arguelles GJ. Leukemia and malnutrition. III. Effect of chemotherapeutic treatment on the nutritional state and its repercussion on the therapeutic response of patients with acute lymphoblastic leukemia with standard risk]. Sangre (Barc). 1990;35:189–95.
9. Brinksma A, Huizinga G, Sulkers E, Kamps W, Roodbol P, Tissing W. Malnutrition in childhood cancer patients: a review on its prevalence and possible causes. Crit Rev Oncol Hemat. 2012;83:249–75.
10. Espinoza M, Perelli J, Olmos R, Bertin P, Jara V, Ramirez P. Nutritional assessment as predictor of complications after hematopoietic stem cell transplantation. Rev Bras Hematol Hemoter. 2016;38:7–14.
11. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, Deutz N, et al. ESPEN expert group recommendations for action against cancer-related malnutrition. Clin Nutr. 2017;36:1187–96.
12. Viani K, Albuquerque L, Barr RD, Ladas EJ. Nutrition of children with Cancer in Brazil: A systematic review. Jco Glob Oncol. 2020;6:242–59.
13. Iniesta RR, Paciarotti I, Brougham MF, McKenzie JM, Wilson DC. Effects of pediatric cancer and its treatment on nutritional status: a systematic review. Nutr Rev. 2015;73:276–95.
14. Carter L, Hulst JM, Afzal N, Jeejeebhoy K, Brunet-Wood K. Update to the pediatric subjective global nutritional assessment (SGNA). Nutr Clin Pract. 2022;37:1448–57.
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg. 2014;12:1495–9.
16. Chu J, Cai H, Cai J, Bian X, Cheng Y, Guan X, et al. Prognostic significance of steroid response in pediatric acute lymphoblastic leukemia: the CCCG-ALL-2015 study. Front Oncol. 2022;12:1062065.
17. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. The 2008 revision of the world health organization (WHO) classification of

myeloid neoplasms and acute leukemia: rationale and important changes. Blood. 2009;114:937–51.
18. Brown PA, Shah B, Advani A, Aoun P, Boyer MW, Burke PW, et al. Acute lymphoblastic leukemia, version 2.2021, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Ne. 2021;19:1079–109.
19. Locatelli F, Schrappe M, Bernardo ME, Rutella S. How I treat relapsed childhood acute lymphoblastic leukemia. Blood. 2012;120:2807–16.
20. Secker DJ, Jeejeebhoy KN. How to perform subjective global nutritional assessment in children. J Acad Nutr Diet. 2012;112:424–31.
21. van Hout B, Janssen MF, Feng YS, Kohlmann T, Busschbach J, Golicki D, et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. Value Health. 2012;15:708–15.
22. Guzman-Leon AE, Gallegos-Castorena S, Romo-Rubio H, Casillas-Toral E, Lopez-Teros V, Stein K. Nutritional status at diagnosis and its relationship with survival and relapse in Mexican children with acute lymphoblastic leukemia: a retrospective study. BMC Cancer. 2025;25:325.
23. Schab M, Skoczen S. Nutritional status, body composition and diet quality in children with cancer. Front Oncol. 2024;14:1389657.
24. Schoon S, Makamo N, Uittenboogaard A, Bernhardt MB, Ozuah NW, Kaspers G et al. Impact of undernutrition on the pharmacokinetics of chemotherapy in children with cancer: A systematic review. Pediatr Blood Cancer. 2023:e30531.
25. Guzman-Leon AE, Avila-Prado J, Bracamontes-Picos LR, Haby MM, Stein K, Astiazaran-Garcia H, et al. Nutritional interventions in children with acute lymphoblastic leukemia undergoing antineoplastic treatment: a systematic review. Bmc Nutr. 2024;10:89.
26. Han Y, Zhang F, Wang J, Zhu Y, Dai J, Bu Y, et al. Application of Glutamine-enriched nutrition therapy in childhood acute lymphoblastic leukemia. Nutr J. 2016;15:65.
27. Letourneau J, Belanger V, Marchand V, Boctor DL, Rashid M, Avinashi V, et al. Post-discharge complications and hospital readmissions are associated with nutritional risk and malnutrition status in a cohort of Canadian pediatric patients. BMC Pediatr. 2024;24:469.
28. Hafiz MG, Mannan MA. Nutritional status at initial presentation in childhood acute lymphoblastic leukemia and its effect on induction of remission. Mymensingh Med J. 2008;17:S46–51.
29. Diakatou V, Vassilakou T. Nutritional status of pediatric Cancer patients at diagnosis and correlations with treatment, clinical outcome and the Long-Term growth and health of survivors. Children-Basel. 2020;7.
30. Pedretti L, Massa S, Leardini D, Muratore E, Rahman S, Pession A et al. Role of nutrition in pediatric patients with Cancer. Nutrients. 2023;15.

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